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Complications of Treatment

The influence of chemotherapy on taste perception and food hedonics: A systematic review

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SUMMARY

Purpose: Altered food relationships in people receiving chemotherapy are prevalent and distressing. Whether, or to what extent, taste perception and food hedonics plays in altered food relationships is unknown among people receiving chemotherapy. This two-armed systematic review addressed the question "Does chemotherapy influence taste perception and hedonic experience of food?"

Methods: A systematic review was undertaken of (1) taste perception and (2) food hedonics. Search phrases used in the taste arm were: "chemotherapy AND taste", and in the food hedonics arm, "chemotherapy AND (liking OR food OR appetite OR hedonic*)". Databases searched were PsycINFO, PubMed, Medline, CINAHL, EMBASE and the Cochrane Library. English language, peer-reviewed publications investigating adults (>18 years) receiving chemotherapy as the only cancer treatment were eligible.

Results: One hundred and sixty three papers were screened in the taste arm, of which eight (5%) met inclusion criteria. Nine hundred and seventy two papers were screened in the food hedonics arm of which 25 (3%) met inclusion criteria. Chemotherapy had variable influence on both taste sensitivity and perceived intensity of the taste qualities sweet, salty, sour and bitter. Liking of food and drink decreased after chemotherapy treatment commenced. Caffeinated foods and drinks, red meat and citrus fruits or juices were most frequently reported as aversive during chemotherapy. A reduction in appetite was reported between baseline (pre-chemotherapy) and cycles 1–3 of chemotherapy with no further worsening in latter chemotherapy cycles and an improvement after completion of chemotherapy treatment.

Conclusions: There was a lack of consistency of results between studies due to differences in study design, chemotherapy regimen, tumor type and stage of treatment examined. These results provide insufficient evidence to suggest chemotherapy has a significant or consistent influence on taste. There is a consistent, albeit small, body of evidence indicating food liking and appetite are adversely affected by chemotherapy and some evidence that declines in liking and appetite are reversed over time. Overall, more longitudinal studies of specific classes of chemotherapy drugs are required to accurately define the nature, magnitude and time course of taste, food liking and appetite changes over the treatment trajectory.

Introduction

Taste is the fundamental foundation upon which flavor can be constructed.[1] Taste is one of several specialized but interacting sensory pathways which operates within the oral cavity[2] and refers specifically to the sensation derived when chemical molecules stimulate taste receptor cells[3]. Multiple peripheral and cognitive processes and interactions are responsible for the perceived flavor of foods and beverages but it is essential to note that taste is only one component of flavor.[1] Taste not only provides important sensory information about food, it also informs affects of pleasure and displeasure.[4] Chemotherapy related taste changes are linked to altered number or structure of taste cell receptors, interruption of neural coding,[5] neurotoxicity from systemic chemotherapy or detection of drug secretion in saliva.[6]

Altered flavor perception has profound effects on nutritional status, quality of life and morbidity and mortality due to an association with reduced appetite;[7] inadequate energy and nutrient intake;[8] weight loss;[8,9] malnutrition;[8,10] reduced compliance with treatment regimens;[11] reduced immunity;[12] impaired ability or desire to procure food; diminished food appreciation; altered food relationships;[13] changed patterns of food intake, rituals and social activities linked to eating and drinking;[14] and emotional distress and interference with daily life.[15–17] The extent to which taste (as a component of flavor) plays a role in these scenarios is unknown.

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Defining taste and hedonics

The taste system is responsible for detecting both nutritious and toxic value of food and to do this is subserved by five qualities: sweetness elicited by sugars reflecting carbohydrate; sourness elicited by free hydrogen ions (H^+) reflecting excessive acid; umami (or 'savory' taste) elicited by glutamic and other amino acids reflecting protein content; saltiness elicited by sodium and other ions (Na^+) reflecting mineral content, and bitterness reflecting potential toxins in foods. Taste is perceived when certain classes of chemicals, soluble in saliva,[18] contact taste receptor cells on taste buds located on the tongue, soft palette and oropharyngeal regions. Once taste receptors are chemically activated, afferent signals are sent via nerve fibers to the taste processing region of the brain and the appropriate taste quality is experienced.[1] A detailed account of the anatomy and physiology of taste in the oncology context has been reviewed elsewhere.[7] The present paper builds on the work of these authors to include an exploration of the five taste qualities and the independent process of food hedonics.

Hedonics, was coined as a term by Beebe-Center in 1932[19] after conducting experiments to rate the pleasantness and unpleasantness of solutions representing the taste qualities of saltiness and sweetness. Based on a calculus of pleasures and pains, hedonics refers to psychological determination of the extent to which a life experience is pleasurable.[20] In relation to evaluating eating and drinking experiences, hedonics encompasses food liking, often referred to as simply 'liking'. Liking is defined as the immediate experience or anticipation of pleasure from the oro-sensory stimulation of eating a food.[21] Conversely to liking, food aversions are the result of unpleasant experiences with foods, generally at times of illness.[22] In the brain, liking and disliking reactions to taste are controlled by a network of systems determining hedonic impact and are influenced by many factors such as hunger, appetite and learned food aversions which can ultimately alter the level of pleasantness experienced.[23] 'Learned' or 'conditioned' food aversions were first linked to chemotherapy treatment through negative association or nausea experienced as a side effect of chemotherapy by Bernstein in 1978.[24] In human studies, conditioned food aversions may be observed when a person becomes ill after eating a specific food despite whether it was the food per se which caused the illness.[25] In studies investigating whether foods become aversive as a result of chemotherapy treatment, the introduction of a novel food item may be used to determine whether the novel food is subsequently targeted for food aversions.

Liking of food is also influenced by appetite. Appetite is a psychobiologically based sensation related to the maintenance of eating and a desire for specific foods.[26] This drive or wanting for specific foods may or may not correlate with subsequent food pleasure and may be altered by factors which are unrelated to food hedonics. For example, a person may have a good appetite and a drive to eat a certain food but on eating that food find they do not like it. It appears liking and wanting are dissociable processes, where wanting relates to a type of incentive motivation that promotes seeking and consumption of rewards.[23] In the context of food, this reward is not necessarily liking the taste of the food but perhaps some other reward such as the post-prandial effects experienced after consumption of caffeinated beverages.

Measuring taste

Taste sensitivity and perceived *taste intensity* are the measurable components of direct taste function.[27] *Taste sensitivity* encompasses the concentrations of prototypical chemical solutions (representing one of the five tastes) at which an individual can state the solution is different from water yet not identify a taste quality (detection threshold) and at which the specific taste can be recognized (recognition threshold). People with lower taste detection and recognition thresholds for a particular chemical tastant are therefore described as more sensitive to a particular taste or chemical. People with higher taste detection and recognition thresholds for a particular chemical tastant are described as less sensitive as they require a greater concentration of the chemical to elicit a perception. Individual variations in taste sensitivity between people are affected by several factors, including age,[28] gender, genetics,[29]clinical conditions,[30] and smoking behavior.[31] Additionally, within individuals, sensitivity to various compounds representing taste qualities may vary.[32–35]

Threshold measures, although important to determine absolute differences in taste sensitivity, do not reflect 'real-world' taste experience as they are not predictive of perceived intensity of food and drinks nor dietary behavior.[36] It is only above these threshold levels (suprathreshold range) that perceived taste intensity can be measured.[37] Suprathreshold taste is measured on intensity scales which require study participants to rate the perceived intensity of a chemical solution representing a taste quality. Appropriate measurement tools are dependent on study design. For longitudinal within-participant studies, visual analog scales or category scales labeled with intensity descriptors may be validly used.[38] However, because intensity descriptors are relative, scales using intensity descriptors assumed to have universal meanings are not valid for making comparisons across individuals or groups. Instead, magnitude matching tools allowing subjects to express perceived taste intensity relative to an unrelated standard should be used.[39]

Taste questionnaires are also used to assess subjective awareness of perceived taste change and its impacts on hedonic factors and levels of distress.[7] These measures often encompass aspects of flavor including smell and texture in their evaluation and therefore are not considered direct measures of taste function. These measures are relevant in so far as they provide information regarding the lived experience of flavor perception, however sensory perception is contextual[40] and it is not possible in such circumstances to separate the sense of taste from other influences which make up this experience of flavor such as aroma[41] or the halo effect of liking sweet foods, which can induce positive opinions on other characteristics of a food.[42] It is important to distinguish taste, which relates purely to perception of the five taste qualities, from flavor when evaluating the influence of chemotherapy as the definition used will determine the relevance and applicability of any future interventional strategies developed to ameliorate the symptoms of taste or hedonic changes in this patient population.

Measuring hedonics

Common methods of measuring food liking include the nine-point hedonic scale where, for example 1 = 'dislike very much' and 9 = 'like very much'.[43,44] Such measures are valid for within subject studies. Degree of appetite loss on a numeric scale at different time points is a valid way to measure appetite change over time and such scales are included in several validated cancer specific quality of life tools.[45–47]

The problem under investigation

Flavor related problems are an under-recognized toxicity of cancer treatment which lack standard definition, assessment and management[10] not least because flavor is a multimodal experience incorporating various sensory/physical inputs and influences.[1] Flavor perception is derived when the sensory systems of taste, olfaction and oronasal somatosensations (irritation, tactile and thermal) are activated.[1] Disorders identified as taste most likely also include elements of other inputs and influences which are not taste per se. For example, distinctions should be made between taste and