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Original Article

Flavor enhancement as a strategy to improve food liking in cancer patients with taste and smell alterations

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SUMMARY

Food liking is an essential component of the food intake experience. However, some conditions may alter the perception, thus the liking of food, leading to a reduced intake and increasing the risk of malnutrition. Particularly, in the context of cancer and related therapies, malnutrition is a major challenge with 25%–80% of cancer patients experiencing malnutrition at different degrees. The aim of the present exploratory study was to examine the effect of flavor enhancement on food liking in a group of cancer patients undergoing chemotherapy and with varying self-reported taste/smell abilities.

The liking of four eggplant creams enhanced with either salt, lemon, garlic or cumin was evaluated in comparison to a reference eggplant cream by a group of 154 cancer patients. Patients were stratified in two subgroups according to their self-reported taste and smell perception abilities. Results showed that adding salt and garlic significantly increased patients' liking of the eggplant cream ($P < 0.001$ in both cases) but not by controls ($P > 0.05$), while adding lemon reduced liking compared to the reference ($P < 0.001$).

Enhancing food flavor is likely to be a promising way to increase food liking in cancer patients undergoing chemotherapy. Future studies should include measurements of food intake during a full meal and over a defined period to examine whether increasing

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food liking helps to reduce risks of malnutrition by improving food intake in cancer patients.

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Introduction

Preventing malnutrition is a major challenge in oncology with 25%–80% of cancer patients experiencing malnutrition at different degrees [1]. Cancer treatments and especially those including cytotoxic chemotherapy may contribute to malnutrition through their resulting adverse effects [2]. Taste and smell alterations are frequent in cancer patients undergoing chemotherapy and negatively impact their food behavior [3–11] leading to a decreased energy intake [12,13], modifications in food preferences [14], and loss of food enjoyment [12,15]. Those alterations are expressed as either decreased sensitivity, an absence of sensation, a distortion of normal perception, or perception of taste and smell without the presence of stimuli (phantogeusia). However, in most cases, a decline in smell and taste abilities (hyposmia for olfaction and hypogeusia for gustation) is observed in cancer patients [7]. Considering the strong influence of sensory properties of food on its hedonic value [16], a decreased ability to perceive tastes and smells may result in modification of flavor perception and food liking, as reflected by patients' complaints on food being bland and tasteless during chemotherapy treatment [17]. Therefore, adapting food to the preference and sensory expectations of patients could improve food enjoyment, increase food intake and help to maintain an adequate nutritional status, especially for patients who experience alterations of taste and smell perceptions.

Oral nutritional supplements (ONS), enriched in calories and proteins to counter the energy deficit are the most common solution administered to cancer patients with risk of malnutrition [18]. ONS that come in various forms, flavors and compositions, are usually designed to respond to a caloric or protein deficiency. However, these products do not address the pleasure of eating, and taste is often cited as the most important consideration affecting compliance due to taste fatigue [19]. Therefore, innovative solution are still required to preserve patients' food enjoyment and food-related quality of life [20].

The effect of food flavor enhancement has been explored in elderly subjects with deficits in taste and smell acuity. This strategy was effective in increasing food enjoyment and improving dietary intake in elderly population [21–24]. However, adaptation of the sensory properties of food has never been tested as a coping strategy to improve food liking in cancer patients undergoing chemotherapy and experimenting taste and smell disorders.

The main aim of the present exploratory study was to examine the effect of flavor enhancement on food liking in a group of cancer patients undergoing chemotherapy. We hypothesize that eggplant creams enhanced with different ingredients will receive a higher liking rating by patients compared to the reference eggplant recipe. A group of healthy control participants was included and underwent the same protocol as the patients' group. The diversity in taste and smell perception abilities of patients was considered by stratifying patients in two groups based on their self-reported taste and smell abilities.

Material and methods

This pilot study was designed to test the impact of flavor enhancement on increasing the liking of food and encompasses two phases. Here, flavor enhancement corresponds to the modification of an eggplant cream flavor by adding ingredients that stimulate the chemo-sensory systems involved in flavor perception (i.e. gustation, olfaction and trigeminal sensory systems).

Phase I: Recipes development, discrimination test and hedonic characterization

Recipes development

Recipes were developed with the help of professional research chefs from the Institut Paul Bocuse Research Centre. The eggplant cream recipes were designed to be easily reproducible by staff members of the hospital's kitchen. This eggplant-based food was selected particularly because of its low intensity taste so it could facilitate the flavor modification by the enhancement. Moreover, the creamy texture of the chosen recipe would not pose a constraint to patients with mouth dryness and mouth sores, which are common side effects of chemotherapy [25,26].

The base of eggplant cream was prepared by cooking 2250 g of raw eggplant in the oven (Electrolux Air-O-Steam Touchline 6) during 25 minutes at a temperature of 180° C in order to have 1000 g of cooked eggplant.

The non-enhanced recipe (REF) was prepared by blending oven-baked eggplant with 10% of its weight of oil, a mix of 70% of colza oil (Carrefour, France) and 30% of olive oil (18:1, Alexi Munoz, France) to keep the neutrality of taste. The eggplant and the oil mixture were blended (Vitamix 62827 Vita-Prep Commercial Blender) until the texture became smooth and homogeneous.

The four enhanced creams were prepared from the REF eggplant cream base (100 g) after adding 0.2 g of salt (Cérébos, France), 2 g of freshly squeezed lemon juice (Carrefour, France), 0.2 g of garlic (Bahadourian, France) and 0.2g of cumin (Bahadourian, France) for the enhancement of salty, sour taste and garlic and cumin aroma, respectively. The ingredients used in flavor enhancement were selected to stimulate different systems involved in flavor perception (i.e. salt and lemon juice for gustation, cumin and garlic for olfaction).

Discrimination test

A preliminary test was conducted on a group of 15 healthy individuals working at the Institut Paul Bocuse Research Centre to ensure that the enhanced eggplant creams were distinguishable from the reference (REF) and were dominated in flavor based on the added taste or aroma stimuli for each recipe.

Hedonic characterization by a control group of healthy volunteers

Moreover, the pleasantness of the 5 food samples was rated by a control group composed of 36 healthy women, with no history of cancer and/or chemotherapy and without diagnosed or self-reported taste and/or smell alterations. Women recruited for the control group signed a written consent to participate to the study. Their self-perceived taste and smell abilities were measured using a 10-cm visual analogue scale (VAS) labeled « extremely bad » at the left edge, and « extremely good » at the right edge. The four flavor-enhanced eggplant cream samples (salt, lemon, garlic and cumin, 50 g container) were presented to the healthy participants who were asked to rate the liking for each sample in comparison to REF (25 g container). The same procedure was applied for cancer patients (detailed below in the experimental phase).

Phase II. Hedonic characterization by cancer patients' group

Participants

Patients were recruited at the Institut de Cancérologie de l'Ouest Renée Gauducheau in Nantes (France) with the help of oncologists and dieticians that informed patients during their consultancy about the study and obtained their consent to participate. Patients enrolled in the study were men and women diagnosed with cancer and undergoing chemotherapy as the only treatment at the time of the study. Patients scheduled for radiotherapy sessions were included in the study only if oro-nasal/head and neck area was not concerned by radiations. Patients with head and neck cancer, and upper aerodigestive tract cancer, with other treatment than chemotherapy (immunotherapy, radiotherapy ...), or with bowel obstruction, and patients with a level of malnutrition requiring the use of Oral Nutritional Supplements, a specific diet, or a type of feeding other than oral feeding were excluded. All participants received oral and written information about the aim and stages of the study and signed a consent form as an approval for their participation. The study was approved by the ethical board of Anger University Hospital (n°2019/38).

Taste and smell abilities assessment

Prior to the tasting session, participants had to rate their self-perceived taste and smell abilities on a 10-cm visual analogue scale (VAS) labeled « extremely bad » at the left edge, and « extremely good » at the right edge. Patients were stratified into two sub-groups based on their self-rating taste and smell abilities. They also reported their subjective perception of hunger before and after the tasting session by answering the question “How hungry are you?” on a 10 cm VAS scale anchored at each end with opposing statement (0 represented “I am not hungry at all”, and 10 represented “I am extremely hungry”).

Eggplant creams liking assessment

Tasting sessions were scheduled from 10 am to noon, and from 3 to 5 p.m. in the afternoon, which is a usual time for snacking in the hospital setting. Participants were free to choose one of the two slots to perform the experiment. A tasting area was set up with shared tables to make the tasting session more convivial. However, the participants had the strict instruction not to discuss the products tasted.

For each participant, the tasting was carried in two consecutive steps: the first step was the liking assessment of the REF eggplant cream. A container with 50 g of the REF was presented to the participant who was asked to assess the liking on a 10 cm-VAS scale labeled from « I do not like it at all » on the left edge, to « I like it a lot » on the right edge. The second step was a comparative liking task, whereby participants were asked to assess the relative liking for each flavor enhanced cream in comparison to the reference. For this second step, the four containers with 50 g of salt, lemon, garlic and cumin eggplant creams were anonymized with three digit random codes as per sensory protocols and presented to each participant in a randomized order, with the instruction to rate the overall liking compared to the reference recipe tasted just before. The participant tasted the four recipes in sequential monadic, using a plastic spoon and were asked to drink some water to rinse their palate after each tasted cream. Participants were allowed to go back to the reference recipe if needed. The liking of the four enhanced creams was assessed in comparison to the reference on a continuous scale going from (-5) « I don't like it at all » to (+5) « I like it a lot » where the REF cream was set at zero (0) and labelled « I like it as much as the reference ». The distance between the location of the line representing the liking attributed to a sample and the line representing the reference in the center of the scale was measured in centimeters and constituted the difference in liking between the sample and the reference.

Data analysis

Given the exploratory nature of the study design, a power analysis was not performed, thus the obtained results must be interpreted accordingly. Patients were classified as a function of their self-reported taste and smell abilities using a hierarchical clustering. Given the direct comparison of each flavor enhanced cream with the reference, the liking of the enhanced recipes was compared to the liking of the reference recipe using one-sample t-test. To examine whether the experimental session (morning vs. afternoon) was influenced by the level of hunger, a statistical analysis (t-test) was conducted to compare mean liking of the reference between participants tested in the morning and those tested in the afternoon. One-sample t-test was also performed for each recipe to compare liking differences of the enhanced recipes in comparison to the reference. These statistical analyses were conducted on the entire group of patients ($n = 154$), with heterogeneous cancer localizations, and on a homogeneous sub-group composed of breast cancer patients only ($n = 84$). For all statistical analyses, a P -value < 0.05 was considered as significant. Data are presented as means and standard errors of the mean unless otherwise indicated. All analyses were performed using the statistical software JASP 0.9.0.1 (<https://jasp-stats.org/2022>, Amsterdam, The Netherlands).

Results

Phase 1. Hedonic characterization by the control group

The control group was composed of 36 women with a mean age of 57.7 ± 7.7 , mainly non-smokers (80%). Results showed that the cumin cream was significantly more appreciated than the REF cream ($+1.67 \pm 0.46$, $t(35) = 3.63$, $P < 0.001$), but not the salt ($+0.63 \pm 0.37$, $t(35) = 1.71$, $P = 0.09$), lemon (-0.26 ± 0.41 , $t(35) = -0.63$, $P = 0.52$) and garlic creams ($+0.72 \pm 0.45$, $t(35) = 1.6$, $p = 0.11$) (Figure 1c).

Phase 2. Hedonic characterization by all type of cancer patients' group The demographic and clinical characteristics of participants are summarized in Table 1.

Given that 55% of patients had a breast cancer diagnosis, a subset analysis including those patients is presented separately.

Cancer patients' subgroups according to taste and smell self-ratings

A hierarchical clustering method based on the self-reported rating of taste and smell abilities resulted in a classification of patients in two groups (Figure 1a). The first group was composed of 102 patients (66.2%) and attributed a high rating to their taste and smell abilities (7.92 ± 1.6 and 7.83 ± 1.75 respectively). This group was labelled "unaltered". The second group included 52 patients (33.8%) who poorly rated their taste perception ability (3.33 ± 1.64) and attributed an average rating to their sense of smell (5.87 ± 2.66). This second group was labelled "altered". The taste and smell ratings of patients with "unaltered" abilities were similar to healthy controls' ratings ($P > 0.05$), whereas the altered group ratings were lower (taste: $t(86) = 13.03$, $P < 0.001$; Smell: $t(86) = 3.17$, $P = 0.002$) (Figure 1b).

Level of hunger and liking of the reference eggplant cream

Patients in the "unaltered" group had a significantly higher level of hunger before the tasting session (5.71 ± 2.72) compared to the "altered" (3.75 ± 2.62 ; $t(151) = -4.285$, $P < 0.001$) group. Regardless of their chemosensory abilities, patients that were tested in the morning session ($n=91$) reported a higher level of hunger in comparison to patients tested in the afternoon ($n=62$) (morning: 5.44 ± 2.85 , afternoon: 4.47 ± 2.74 ; $t(151) = -2.1$, $P = 0.03$). There was no significant difference in the liking of the reference recipe neither between the two groups nor between the two sessions (morning vs. afternoon) ($P > 0.05$).

Liking ratings of the enhanced recipes compared to the reference by all cancer patients

The salt and garlic creams were appreciated significantly more than the reference by altered and unaltered patients ($P < 0.001$ in both cases) but not by controls ($P > 0.05$). The liking of the eggplant cream enhanced in lemon was significantly lower compared to the reference only in the unaltered

Table 1
Demographic and clinical characteristics of patients

Participants n (%)	Total	154	(100%)
	Female	128	(83%)
	Male	28	(17%)
Mean age years \pm SD	60.63 \pm 12		
Smoking status n (%)	Smokers	13	(8.4%)
	Non-smokers	137	(89%)
Cancer types n (%)	NA	4	(2.6%)
	Breast	84	(54.5%)
	Gynecologic	20	(13%)
	Digestive	17	(11%)
	Bronchial	9	(5.8%)
	Prostate	6	(3.9%)
	Liver	5	(3.3%)
	Bladder	4	(2.6%)
	Pancreas	4	(2.6%)
Chemotherapy regimen n (%)	Others	5	(3.3%)
	Taxol – based	76	(49.3%)
	Platinum	16	(10.3%)
	Folfox	13	(8.4%)
	EC/AC/FEC	18	(11.7%)
	Gemcitabine	9	(5.8%)
Others	22	(14.5%)	

EC: Epirubicine and cyclophosphamide/AC: Adriamycin and cyclophosphamide/FEC: 5-fluorouracil, epirubicine and cyclophosphamide.

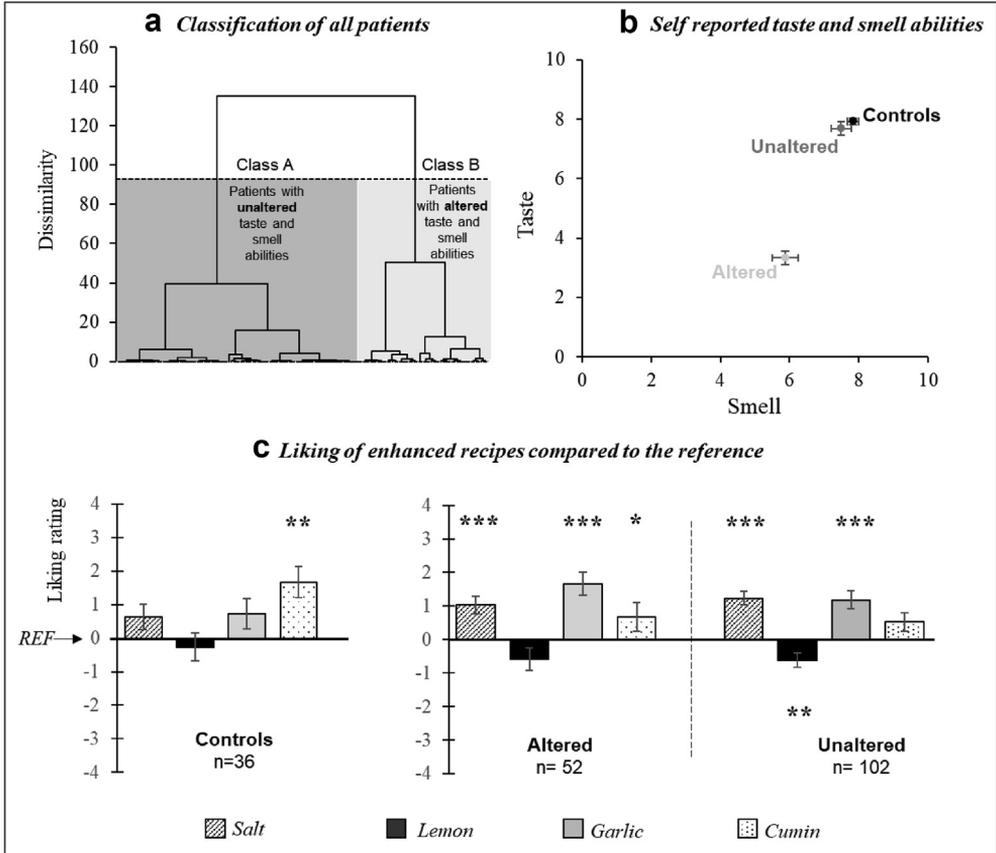


Figure 1. (a) Classification of all patients based on self-reported taste and smell abilities. The hierarchical clustering resulted in two groups: unaltered (class A in dark grey), altered (class B in light grey). (b) Chemosensory profiles of “altered”, “unaltered” and “control” groups. No difference was observed in taste and smell ratings between controls and patients with “unaltered” abilities. Patients with altered abilities ratings were significantly lower compared to controls (taste: $t(84) = 13.03, P < .001$; smell: $t(84) = 3.17, P = 0.002$), and compared to “unaltered” patients group (taste: $t(152) = -19.87, P < .001$; smell: $t(152) = -5.58, P < .001$). (c) Liking of the four enhanced recipes compared to the reference (REF) fixed at zero (0). Error bars correspond to Standard Errors. * $P < .05$ ** $P < .01$ *** $P < .001$.

group ($t(51) = -1.71; P < 0.001$). The eggplant cream enhanced with cumin was appreciated more than the reference by patients in both altered and unaltered groups, but the observed effect was not statistically significant ($P > 0.05$) (Figure 1c).

Results for breast cancer patients

Breast cancer patients' subgroups according to taste and smell self-ratings

A hierarchical clustering method based on the self-reported rating of taste and smell abilities resulted in a classification of patients with breast cancer in two groups (Figure 2a). The first group was composed of 49 breast cancer patients (58.3%), who attributed a high rating to their taste and smell abilities (8.31 ± 1.05 and 8.69 ± 0.93 respectively). This group is referred to as “unaltered”. The second group of patients ($n = 35, 41.7\%$) poorly rated their taste perception abilities (4.38 ± 2.36) and attributed an average rating to their sense of smell (5.35 ± 2.22). We referred to this group as “altered”. Similar to the above presented results on the whole sample, the taste and smell self-ratings of patients with

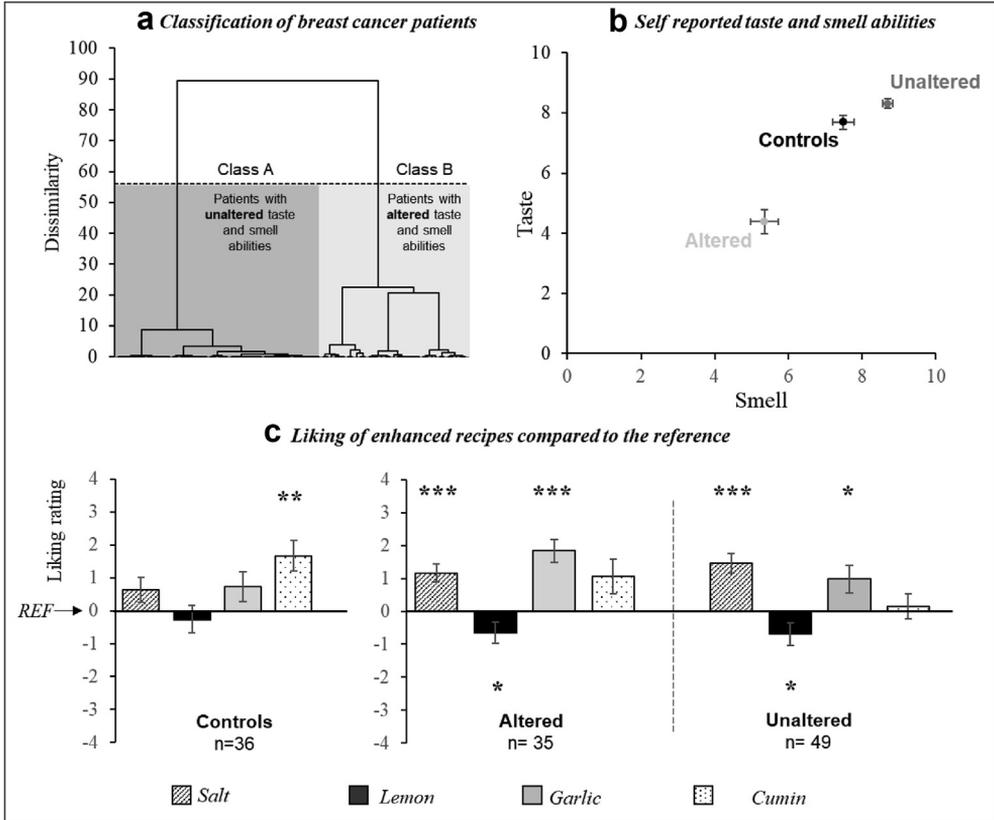


Figure 2. (a) Classification of breast cancer patients based on self-reported taste and smell abilities. The hierarchical clustering resulted in two groups: unaltered (class A in dark grey), altered (class B in fair grey). (b) Chemosensory profiles of “altered”, “unaltered” and “control” groups. No difference was observed in taste and smell ratings between controls and patients with “unaltered” abilities. Patients with altered abilities ratings were significantly lower compared to controls (taste: $t(69) = -8.55, P < .001$; smell: $t(69) = -5.45, P < .001$), and compared to “unaltered” patients group (taste: $t(82) = 10.89, P < .001$; smell: $t(82) = -9.13, P < .001$). (c) Liking of the four enhanced recipes compared to the reference (REF) fixed at zero (0). Error bars corresponds to Standard Errors. * $P < .05$ ** $P < .01$ *** $P < .001$.

“unaltered” abilities were close to healthy controls ratings ($P > 0.05$), while the altered group was lower (taste: $t(69) = -8.55, P < 0.001$; smell: $t(69) = -5.45, P < 0.001$) (Figure 2b).

Level of hunger and liking of the reference by breast cancer patients

Breast cancer patients in “unaltered” group had a significantly higher level of hunger before the tasting (6.28 ± 2.3) compared to the “altered” (4.14 ± 2.19 ; $t(82) = -3.82, P < 0.002$) group. Regardless of their chemosensory abilities, no difference in hunger rating was found between patients that were tested in the morning session ($n=48$) in comparison to patients tested in the afternoon ($n=36$) ($P > 0.05$). There was no significant difference in the liking of the reference eggplant cream between the two groups (altered vs. unaltered) and between the two sessions (morning vs. afternoon) ($P > .05$).

Liking ratings of the enhanced recipes compared to the reference by breast cancer patients

Liking comparison between the sensory enhanced creams and the REF showed that the cumin enhanced cream was more appreciated than the reference by patients in the altered group ($t(34) = 2.02, p = 0.05$) but not by patients in the unaltered group ($p > 0.05$). The salt and garlic enhanced creams were appreciated significantly more than the reference by patients in the altered

($t(34) = 4.36, p(0.001)$ and $t(34) = 5.28, p(0.001)$ respectively) and the unaltered groups (salt : $t(48) = 4.97, p(0.001)$; $t(48) = 2.36; p = 0.02$). The liking of the lemon recipe was significantly lower compared to the reference in altered ($p = 0.04$) and unaltered group ($p = 0.04$) (Figure 2c).

Discussion

To our knowledge, this is the first exploratory study that examined the effect of flavor enhancement on food liking in cancer patients undergoing chemotherapy considering their self-reported taste and smell alterations. Two major findings emerged from the results: (i) Flavor enhancement resulted in a modification in liking ratings, but the four types of enhancement had differential effects on food liking; (ii) There was a contrasted pattern of liking between patients and control group.

Adding salt significantly improved the liking in both altered and unaltered patients' groups. Adding salt might have compensated the deficit in salt taste perception, and fulfilled patients' sensory expectations, as a reduced ability to perceive salty taste has already been highlighted in previous studies on cancer patients undergoing chemotherapy [27,28]. Moreover, beyond imparting salty taste to the overall flavor, adding salt increases liking by improving the perception of food [29]. The mechanisms that underlie this complex effect are not fully understood. However, salt was shown to enhance sweetness, mask metallic or chemical off-notes and suppress bitterness in different foods [30]. This may counter the bitter taste dysgeusia and metallic taste perception frequently reported by cancer patients. Similarly, adding garlic to the eggplant cream increased its liking, but the hedonic dimension of garlic as a condiment is much less documented than salt in the literature. Aromatic molecules diffused by garlic are detected by olfactory receptors through retro nasal way [31], but the same molecules can also stimulate the trigeminal nerve endings and temperature-activated ion channels [32]. Although trigeminal perception has a prominent role in flavor development, this sensory modality and its possible alteration by cancer and its treatment are yet to be explored.

Patients appreciated less the lemon enhanced eggplant cream. It is common to cancer patients to experience various modifications in the oral cavity including the increased acidity of oral microflora [33], mouth ulcerations, and mucositis [34]. Those symptoms cause mouth pain and discomfort in mouth, which may be accentuated when exposed to sourness. Furthermore, in some cases, sourness accentuates the unpleasant perceived metallic taste frequently reported by patients [35,36]. Finally, the cumin eggplant cream was significantly more appreciated than the reference in the control but not in both patients' groups. Overall, spices and spicy foods such as Mexican or Indian dishes are considered too spicy and are consequently avoided by patients [35].

Contrary to what we were expecting, there was no difference in liking ratings between patients with and without taste and smell alterations. It is therefore possible that factors other than the deficit in perception of tastes and odors contributed to the increased liking rating. For instance, the trigeminal component brought by garlic, or the subjective perception of texture modification possibly due to added salt [29] could have contributed to the modification in liking rating, independently of patients' taste and smell abilities.

Another interesting result concerns the significant difference found in hunger level between patients of altered and unaltered groups. Hunger is a major driver of food intake, and plays an essential role in appetite regulation [37]. Previous study reported decreased appetite in patients with taste and smell alterations during a chemotherapy for lung cancer [12] and breast cancer [38]. Furthermore, Boltong *et al.*, found that a lower ability to identify tastes at different cycles of chemotherapy was correlated to a lower appetite in breast cancer patients [5]. In accordance, our results showed that the feeling of hunger is lower in patients that have lower taste and smell abilities, highlighting the need to further explore the consequences of taste and smell alterations on patients' food intake.

The analysis conducted on the sub-group of women diagnosed with breast cancer patients led to the same conclusions found in the whole cancer patients' group concerning the effect of flavor enhancement on food liking. Those results, however, do not allow drawing conclusions on the role of cancer type influencing the flavor enhancement strategy on food liking since breast cancer patients represented 54% of the initial cancer patients' group.

In conclusion, enhancing food flavor is likely to be a promising strategy to increase food liking in cancer patients undergoing chemotherapy. Both salt and garlic enhancement increased liking in patients but not in the control group suggesting that flavor enhancement is recommended to adapt food to sensory expectations of patients. However, the ingredients used for flavor enhancement should be selected carefully and take into account the specificities of this population, mainly because of the numerous oral problems patients have in addition to taste and smell alterations such as mouth dryness and mouth sores.

This research has some limitations. First, it is difficult to accurately identify the causes of the difference observed between patients and control group. Further studies should also collect data about the nutritional (e.g. BMI, loss of body weight, sarcopenia) and metabolic status (e.g. systemic inflammation) of the patients. Also, it might be of interest to study whether patients not undergoing chemotherapy would have similar hedonic ratings as those seen in the present study group. Furthermore, other possible oro-nasal cavity symptoms that may interfere with food liking were not assessed. Subjective taste and smell abilities assessment should be completed with an objective assessment. Additionally, frequent symptoms observed during chemotherapy such as mouth dryness, metallic taste perception, and mucositis should be considered in future research. Furthermore, those results were obtained by testing the enhancement of one type of food (eggplant creams). The flavor enhancement should be tested with other food to allow the generalization of the observed results. Finally, our data do not allow saying whether improving food liking leads to an improvement in food intake. In addition to hunger, there is evidence that food liking is a driver of food intake during lifespan and in some particular populations such as in elderly in nursing home [22]. Future studies in cancer population should include measurements of food intake in addition to food appreciation during a full meal and over a defined period to examine whether increasing food liking can be a promising strategy to improve food intake in cancer patients and help in preventing malnutrition.

Authors contribution

KD, AG, AD, and MB designed the study, KD, DV and HL collected the data, KD and MB analyzed the data, KD drafted the publication, all authors proofread the publication.

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Conflicts of interest

Authors declare that there is no conflict of interest.

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