Relationship between sensory liking for fat, sweet or salt and cardiometabolic diseases: mediating effects of diet and weight status

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Title page

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Conflicts of interests

The authors declare that they have no conflicts of interest.

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Abstract

Purpose: It has been suggested that individual sensory liking is an important predictor of dietary intake and weight status, and may consequently influence development of cardiometabolic diseases (CMDs). We investigated the association between sensory liking for fat-and-salt, fat-and-sweet, sweet or salt and the onset of hypertension, diabetes and cardiovascular diseases (CVDs) over 6 years in adults, and the mediating effects of dietary intake and BMI.

Methods: We examined the CMDs risk among 41,332 (for CVD and diabetes) and 37,936 (for hypertension) French adults (NutriNet-Santé cohort). Liking scores, individual characteristics, diet and anthropometry were assessed at baseline using questionnaires. Health events were collected during 6 years. Associations between sensory liking and CMDs risk, and the mediating effect of diet and BMI, were assessed using Cox proportional hazards models.

Results: Sensory liking for fat-and-salt was associated with an increased risk of diabetes, hypertension and CVD (hazard ratios (HR) for 1-point increment of the sensory score: HR=1.30 [95%CI 1.18,1.43], HR=1.08 [1.04,1.13] and HR=1.10 [1.02,1.19], respectively). BMI and dietary intake both explained 93%, 98% and 70%, of the overall variation of liking for fat-and-salt liking in diabetes, hypertension and CVD, respectively. Liking for fat-and-sweet and liking for salt were also associated with an increased risk of diabetes (HR=1.09 [1.01,1.17] and HR=1.09 [1.01,1.18], respectively) whereas liking for sweet was associated with a decreased risk (HR=0.76 [0.69,0.84]).

Conclusions: Higher liking for fat-and-salt is significantly associated with CMDs risk, largely explained by dietary intake and BMI. Our findings may help to guide effective targeted measures in prevention.

Keywords

Cardiovascular disease, diabetes, hypertension, sensory liking, dietary intake, mediating factor

Background

Cardiovascular disease (CVD) is the cause of death of 18 million people around the world, with diabetes and hypertension as the major risk factors [1]. The role of excessive consumption of saturated and trans fats, simple sugar and sodium in the etiology of major chronic diseases and increased mortality has been well documented in literature [2-4]. Most public health programs worldwide target nutritional recommendations, which include limitations in fat, salt and sugar intake [2,5]. However, these components contribute to eating pleasure due to the sensory properties they drive, and the important effect of sensory function on food intake has been highlighted [6]. Individual sensory liking for fat appears to be a potential determinant of dietary intake [7-9] and weight status [10-12], and may consequently influence development of CMDs (defining as hypertension, diabetes and CVD in our study). In addition, the specific role of sweet and salt liking in food intake need further research, especially in a large cohort.

To our knowledge, very few studies have investigated relationships between sensory liking and CMDs. A cross-sectional study with a convenience sample of 88 women has shown that women reporting higher liking for high-fat foods had greater adiposity and blood pressure [13]. Another cross-sectional study has highlighted that fat preference was associated with higher BMI and waist circumference in men, and no association was found with sweet preference [14]. Furthermore, a case-control study has shown that heart failure patients had higher salt liking than healthy volunteers. In addition, salt preference was associated with increased mortality from stroke in men and women in a Japanese cohort study [15]. In previous studies, sensory liking components considered were limited, evidence is still lacking on this topic and hypotheses need to be further investigated.

No study has investigated the contribution of dietary intake and body mass index (BMI) to explain the influence of sensory liking on CMDs. Nevertheless, sensory fat liking has already been highlighted as strongly associated with higher fat intake but also with lower intake of nutrient-dense foods such as fruits and vegetables, dairy products, whole grains products and fish [7-9], which increased the risk of weight gain and obesity [10-12]. This emphasizes the need to consider the overall dietary intake and body mass index as potential mediators in the relationship between high liking for fat, sweet or salt and the CMDs risk.

The aim of our study was therefore to assess the prospective association between individual liking for fat-and-salt, fat-and-sweet, sweet or salt and the risk of developing CVDs, type 2 diabetes and hypertension over 6 years, in a large population of French adults. In addition, we investigated the mediating effect of dietary intake and weight status on the relationship between sensory liking and CMDs.

Methods

Study population

We used data from the NutriNet-Santé study, a large web-based observational cohort launched in France in 2009 with a scheduled follow-up of 10 years. It was implemented in a general population and targeted Internet-using adult volunteers. Briefly, eligible participants were recruited by a variety of means. Initially a vast multimedia campaign called for volunteers, then campaigns were repeated every six months. Further information is maintained on a large number of websites (national institutions, city councils, private firms) and a billboard advertising campaign is regularly updated via professional channels (e.g., doctors, pharmacists, dentists, business partners, municipalities). The study was designed to investigate the relationship between nutrition and health, as well as determinants of dietary behavior and nutritional status [16]. Briefly, in order to be included in the cohort, participants had to fill out an initial set of questionnaires assessing dietary intake, physical activity, anthropometry, lifestyle, socio-economic conditions and health status. As part of their follow-up, participants complete the same set of questionnaires every year. Moreover, each month, they are invited to fill out complementary questionnaires related to determinants of dietary behavior, nutritional and health status. All questionnaires are completed online via the NutriNet-Santé website. Compared to the general population, included individuals were more often women, relatively more educated and those who are married were notably larger than the general French population [17].

This study was conducted according to guidelines laid down in the Declaration of Helsinki, and all procedures were approved by the Institutional Review Board of the

French Institute for Health and Medical Research (IRB Inserm n°0000388FWA00005831) and the “Commission Nationale Informatique et Libertés” (CNIL n°908450 and n°909216). Electronic informed consent was obtained from all subjects. This study is registered in EudraCT (n°2013-000929-31).

Data collection

Assessment of liking for fat-and salt, fat-and-sweet, sweet and salt

Liking for fat-and-salt, fat-and-sweet, sweet and salt was assessed using PrefQuest, an original web-based questionnaire [18]. In May 2010, included participants in the Nutrinet-Santé cohort (n=65,683) were invited to complete this questionnaire available online for six months. This questionnaire assesses liking for fat, saltiness and sweetness via several items, enabling an assessment of overall liking, i.e. liking primarily derived from sensation independently of the food product. The development and validation of the questionnaire have been described elsewhere [18]. Briefly, PrefQuest is composed by 83 items divided into liking for salt (11 items) and sweet (21 items) tastes, fat-and-salt (31 items) and fat-and-sweet (20 items) sensations. The questionnaire included four types of items: (i) liking for sweets, fatty-sweet and fatty-salty foods; (ii) preferred level of salt, sweet, fat-and-salt or fat-and-sweet seasoning; (iii) preferred drinks (sweet/sweetened or unsweetened) on a restaurant menu; and (iv) dietary behavior in terms of sweet, salty and fatty foods. PrefQuest was internally validated by studying the underlying structure of each taste using exploratory factor analysis and confirmatory factor analysis, and also compared with sensory tests that included 32 food models conducted in a diversified sample (n=557) [19] (Deglaire et al. 2011, personal communication). The salty taste was unidimensional, unlike the sweet taste and the fat sensation. The sweet taste was formed by the factors ‘sweet foods’, ‘added sugar’ and ‘natural sweetness’ and the fat sensation was composed of the fat-and-salt sensation based on ‘added fat-and-salt’ and ‘fatty-salty foods’ and the fat-and-sweet sensation based on ‘added fat-and-sweet’ and ‘fatty-sweet foods’.

Events’ ascertainment

Participants self-declared health events through the yearly health status questionnaire (in which they can also declare family medical history), using a specific check-up questionnaire for health events (every three months) or at any time through a specific interface on the study website. Following this declaration, participants were invited to send their medical records (diagnosis, hospitalization, radiological reports, electrocardiograms, etc.). If necessary, the study’s physicians contacted the participants' treating physician or the medical structures to collect additional information. Then, data were reviewed by an independent physician expert committee, which validated all major health events. The present study focused on cases of hypertension, type 2 diabetes, and cardiovascular events (strokes, transient ischemic attacks, myocardial infarctions, acute coronary syndromes and angioplasties) diagnosed between May 2010 and November 2016.

Assessment of dietary intake

At enrollment and each year thereafter, participants were invited to provide three non-consecutive validated web-based 24h dietary records randomly assigned over a 2-week period (1 weekend day and 2 weekdays). The accuracy of web-based 24h dietary records has been assessed by comparing to interviews by trained dietitians [20] and against 24h urinary and blood biomarkers [21,22]. The dietary record was completed via an interactive interface designed for self-administration on the Internet.

The web-based dietary assessment method relied on a meal-based approach, recording all foods and beverages (type and quantity) consumed at breakfast, lunch, dinner and all other eating occasions. Portion sizes were assessed via a validated picture booklet [23] or according to standard measurements. Foods were classified according to the information provided in the French National Nutrition and Health Program guides [24]. Food groups (in grams/day) considered in the present study were vegetables, fruits, meat, processed meat, fish, starchy foods, whole grain products, milk and yogurt, cheese, butter and other added fats, oil, sugar and sweetened products, sweetened cream desserts, fatty-sweet products, savory sauces, salted snacks and appetizers, sweetened soft drinks and alcoholic beverages. Values for energy were estimated using published nutrient databases [25]. We used the three closest dietary records to the PrefQuest questionnaire (or two if one was missing).

Anthropometric data

Height and weight data were collected at enrollment and each year thereafter by a validated self-administered anthropometric questionnaire [26]. BMI (kg/m^2) was calculated as the ratio of weight to the square of height. The closest available anthropometric data to the PrefQuest questionnaire were used in this analysis.

Sociodemographic and lifestyle data

Potential confounding factors of the relationship between sensory liking for fat-and-salt, fat-and-sweet, sweet or salt and the CMDs risk previously identified [27-29] were collected using web-based questionnaires at the same time as sensory liking data: age (years), sex, education (elementary school, secondary school, college graduate or advanced degree), smoking status (never, former or current smoker), and physical activity level using the short French version of the International Physical Activity Questionnaire (low, moderate or high) [30].

Statistical analyses

The present analysis focused on participants of the NutriNet-Santé cohort, living in metropolitan France, who had completed the PrefQuest and the set of complementary questionnaires, and who had self-reported health information, even no event to declare, over 6 years of follow-up.

Liking scores for fat-and-salt, fat-and-sweet, salt and sweet were computed as detailed previously, ranging from 0 to 10 and considered as continuous variables [18,27]. Regarding dietary intake, for each participant, daily mean quantities of the food group (in grams) and energy intake were calculated from two or three 24h records, weighted according to the day (week or weekend). Diet-underreporting participants were identified by the method proposed by Black [31]. Briefly, basal metabolic rate (BMR) was estimated by Schofield equations [32] according to sex, age, weight and height collected at enrollment in the study. Energy intake and BMR were compared to a physical activity level of 1.55 or below, the WHO value for 'light' activity, to identify energy-underreporting subjects [31]. They were consequently excluded for analysis.

Comparisons between included and excluded participants were performed using Student’s t-test and chi-square test, as appropriate. Individual characteristics and dietary intake were compared between individuals who have developed a CMD during the follow-up and those who had not, using Student’s t-test and chi-square test, as appropriate. Dietary intake and BMI were compared between quartiles of liking for fat-and-salt, fat-and-sweet, salt and sweet using analysis of covariance. Sex interaction has been tested but was not significant. Cox proportional hazard models with age as the primary time variable were used to calculate hazard ratios (HR) and 95% confidence intervals (95% CI) for 1-point increment of the sensory score, for the association between scores of sensory liking for fat-and-salt, fat-and-sweet, sweet and salt and the risk of cardiometabolic diseases. First, Cox base models were performed to study the effect of liking for fat-and-salt, fat-and-sweet, sweet and salt on the risk of developing cardiovascular diseases (CVD), type 2 diabetes or hypertension, adjusted for sex. Secondly, education, smoking status, alcohol consumption, physical activity and family medical history (CVD, diabetes and hypertension) were added in the h model as confounding factors. Thirdly, to assess the mediating effect of dietary intake, we selected food groups which were associated with CVD, type 2 diabetes or hypertension risk, as well as with liking for fat-and-salt, fat-and-sweet, sweet or salt using Cox and linear regression models, as appropriate ($P \leq 0.10$). Then, Cox models assessing the mediating effect of dietary intake on the relationship between sensory liking and the risk of cardiometabolic diseases were performed adjusted for daily energy intake and month of inclusion. Finally, BMI was added to the previous model to assess its mediating effect on the relationship between sensory liking and risk of cardiometabolic diseases.

The magnitude of the mediating effect was assessed by the percentage change in the HRs between models computed as [(HR base model – HR base model + mediator) / (HR base model − 1)] × 100 [33]. Dietary intake and BMI were considered as a mediating factor when the percentage change of the HR was higher than 10% and there was no increase of other HRs [33]. In addition, we calculated the part of the reduction in deviance attributable to sensory liking, which was accounted for by inclusion of the potential mediator and confounders. The reduction in deviance related to sensory liking quantifies the percentage of the sensory liking impact on the outcome explained by the mediator/confounder [34]. The deviance of sensory liking in the base model was compared to the deviance of sensory liking in the extended model. The percentage of reduction of deviance (RD) due to sensory liking explained by inclusion of the mediating factor or confounders was calculated as follows [(RD due to sensory liking in base model) − (RD due to sensory liking in base model + mediator/confounders) / RD due to sensory liking in base model] × 100 [33].

The actuarial method was used and assumptions of proportionality were satisfied through examination of the log-log (survival) compared with log-time plots. Data management and statistical analyses were performed using SAS software (version 9.3, SAS Institute Inc, Cary, NC, USA). Criterions for statistical significance was $p<0.05$ and for practical significance was >10% change of HRs.

Results

Among the 65,683 participants in the NutriNet-Santé study in May 2010, 49,066 responded to the PrefQuest (75% participation rate). Among responders, 48,336 had available health information in 2010. Then, we excluded 1902 subjects with a history of CVD or with diabetes at baseline, 3785 who were identified as diet-underreporting participants or who did not answer to 24h dietary records in 2010 and 1327 women who were pregnant at baseline, which left 41,322 participants available for analysis of cardiovascular diseases and diabetes (32,055 women and 9267 men). Regarding hypertension analysis, starting from the 48,336 participants, 5609 subjects with a history of CVD or hypertension at baseline were excluded, as well as 3469 who did not have dietary intake data and 1322 pregnant women, which left 37,936 participants for analysis of hypertension (29,828 women and 8108 men). Compared with excluded subjects, individuals included in our analysis were slightly younger, had a lower BMI, the percentage of those with high education was higher and the proportions of men and smokers were lower ($P<0.05$; data not shown).

During a median follow-up of 5.5 y, 655 individuals developed CVD (342 women and 313 men), 342 developed type 2 diabetes (205 women and 137 men), and 1907 developed hypertension (1264 women and 643 men).

Sociodemographic characteristics, lifestyle and dietary intake according to cardiometabolic status are presented in **Table 1**. Individuals with cardiometabolic diseases were older, less often women, and had higher BMI than individuals who did not developed a CMD during the follow-up. A smaller proportion had a university degree, a higher proportion were former smokers, they were less physically active (except for diabetes subjects), and had higher percentages of family medical history than healthy individuals. Finally, subjects with CMD had higher intake of energy, alcohol, fish and starchy foods, whereas they had lower intake of fatty-sweet products compared with healthy individuals at baseline.

Food group consumption and BMI according to liking levels were presented in supplementary tables S1 and S2. Individuals with higher liking for fat-and-salt, fat-and-sweet, salt and sweet (quartile 4) had lower intake of fruits, vegetables and whole grain products, but higher intake of meat, processed meat, cheese, butter and other added fats, salted snacks and appetizers, savory sauces, starchy foods, sweetened soft drinks and higher energy intake compared to individuals with lower liking for fat-and-salt, fat-and-sweet, salt and sweet (quartile 1). In addition, higher BMI was found in individuals with higher liking for fat (fat-and-salt and fat-and sweet) and salt.

Hazard ratios for 1-point increment of the sensory score of associations between sensory liking for fat-and-salt, fat-and-sweet, sweet and salt, and the risk of CMDs are presented in **Tables 2, 3 and 4**. Liking for fat-and-sweet, sweet and salt were not associated with CVD risk (HR=0.96 [0.91;1.02] p=0.15, HR=0.97 [0.90;1.04] p=0.37 and HR=0.98 [0.93;1.04] p=0.44, respectively) and with risk of hypertension (HR=0.98 [0.95;1.02] p=0.34, HR=0.99 [0.95;1.04] p=0.79 and HR=0.99 [0.96;1.03] p=0.63, respectively), results were therefore not tabulated.

In base model (table 2), liking for fat-and-salt was associated with increased risk of cardiovascular diseases (increased risk of 10%), and when dietary intake was adding to the model, the association became non-significant. Dietary factors explained 30% of the decreased HRs in CVD (RHR), and the addition of BMI explained 40%. In addition, dietary factors furthermore explained 61% (RD) of the overall variation of fat-and-salt liking, i.e. sensory liking reduction in deviance in CVD, and dietary factors and BMI explained together 70% of the overall variation of fat-and-salt liking in CVD.

Liking for fat-and-salt was associated with increased risk of developing type 2 diabetes (increased risk of 30%) whereas sweet liking was associated with lower risk (24%) (table 3). Dietary intake and BMI largely explained together the decreased HR for fat-and-salt liking (73%) and the increased HR for sweet liking (54%), and they explained 93% and 84% of the overall variation of fat-and-salt and sweet liking in diabetes, respectively. Furthermore, fat-and-sweet and salt liking were associated with a higher risk of type 2 diabetes, but the practical criterion was not met (9%).

Finally, liking for fat-and-salt was associated with increased risk of developing hypertension but the criteria for practical significance was not met (8%) (table 4). In addition, with diet and BMI, the association became not statistically significant, and they explained together 88% of the decreased HRs in hypertension. The overall variation of fat-and-salt liking in hypertension was largely explained by dietary intake and BMI (98%).

Discussion

This prospective study highlights original findings on the influence of sensory liking on cardiometabolic disease risk. We have shown that liking for fat-and-salt was prospectively associated with an increased risk of CVD, type 2 diabetes and hypertension, and diet and BMI substantially explained this relationship. Results have also raised that liking for fat-and-sweet and salt liking were statistically associated with an increased risk of diabetes, mainly explained by dietary intake and weight status. Sweet liking was associated with a decreased risk of diabetes, partially explained by diet and BMI. Finally, no relationship was found between fat-and-sweet, sweet and salt liking, and incidence of CVD and hypertension.

Findings regarding the positive association between fat-and-salt liking and the risk of CMDs are concordant with previous cross-sectional studies that highlighted liking for fat as a predictor of adiposity and blood pressure in women [13], and a positive association with BMI and waist circumferences in men [14]. In these studies, only liking for fat was assessed, but due to the higher numbers of fatty-salty foods items compared to fatty-sweet items, fatty-salty foods had potentially more weight than fatty-sweet foods in liking assessment. We have highlighted that dietary intake and BMI substantially explained the relationship between fat-and-salt liking and the risk of CVD, diabetes and hypertension. A previous study conducted in the NutriNet-Santé cohort has shown that individuals with higher fat-and-salt liking were more likely to have high intake of energy and fatty foods, compared to individuals with lower fat-and-salt liking [7]. Excessive consumption of red meat, processed meat and especially processed food rich in trans fat, is associated with higher risk of cardiometabolic diseases [35-37]. Participants with high fat liking may be less interested in healthy foods because they find them less tasty; consequently, they may tend to replace healthy foods by their energy-dense variants [7]. In addition, the large variation in fruit and vegetable intake according to levels of liking for fat-and-salt may contribute to this increased risk, highlighted in a previous study [7] in concordance with our data (supplementary table S1). Indeed, this difference [110 g/d in women and 139 g/d in men] represents more than one serving per day, i.e. 80 g, as defined by international recommendations [38]. Much research has shown beneficial effects upon cardiometabolic morbidity of additional servings of fruits and vegetables [39,40] that may greatly explained the effect of fat-and-salt liking on CMDs.

Furthermore, in the same cohort, obese individuals had higher fat-and-salt liking scores compared to normal-weight participants in a cross-sectional design [41] and men with high fat-and-salt liking were more at risk to become obese over 5 years [10]. High liking for fat-and-salt therefore appears to predict higher risk of developing CMDs, mediated by unhealthy dietary intake and higher BMI. In addition, education, lifestyle and family medical history also contribute to explain the association between fat-and-sat liking and CVD. It has already been shown in NutriNet santé cohort study that high liking for fat-and-salt was associated with low socioeconomic position and smoking [27] which are risk factors of CVD. Indeed, the harmful effects of smoking [42], low educational level [43] and physical inactivity [44] on CVD risk are well-known, regardless of dietary intake and BMI effects.

Liking for fat-and-sweet sensation and liking for salty taste were statistically significantly associated with an increased risk of type 2 diabetes and both associations were mainly but partially explained by dietary intake and weight status. Indeed, individuals with high liking for salt and fat-and-sweet had unhealthy dietary intake which can contribute to explain the increased risk of diabetes [45]. Individuals with high liking for fat-and-sweet, compared to those with low liking, had higher intake of energy, sweetened soft drinks, fatty-sweet products, cream desserts and processed meat, and lower intake of fruits, vegetables and whole grain products (supplementary table S1). In addition, individuals with higher liking for salt had also unhealthy food intake, compared with those who have a lower liking, with higher intake of energy and alcoholic beverages and lower intake of whole grain products, fruits and vegetables (supplementary table S2).

Regarding salt preference, we did not replicate results of the study of Ikehara et al. [15] which have highlighted that high salt preference was associated with a 20% increased risk of mortality from stroke. When we considered only stroke as events in our study, the relationship was not significant [data not shown] and the fact that we did not study the mortality. However, as in our study, they failed to show a relationship between total CVD mortality and high salt preference [15]. Although salt liking is predictive to sodium use, and sodium intake is associated with CVD incidence [46], expected association was not found in our study, probably due to salt liking assessment. Indeed, salt liking was mainly assessed by questions about preferred level of salt seasoning, since salty foods without fats are not consumed in the French food culture [18]. But as more than 75% of the daily sodium intake comes from industrially processed foods which are also rich in fats [47], this may explain the absence of association between liking for salt and CMDs.

Our results surprisingly showed that liking for sweet taste was associated with a decreased risk of diabetes, and was not associated with CVD or hypertension risks. In a previous work, we have shown that liking for sweet was also associated with a decreased risk of obesity, driven by liking for natural sweetness, and mediated by healthy dietary intake [10]. When analysing the association of sub-factors of sweet liking with diabetes risk, i.e. sweet foods, natural sweetness and added sugar, the inverse association was driven by liking for natural sweetness (i.e. honey, added jam, sweet dried fruits) and liking for added sugar (i.e. sugar in coffee, yogurt, crepe). Considering dietary intake of individuals with higher liking for natural sweetness, they had a diet rich in fruits, vegetables and whole grain products, compared to those with lower liking. Surprisingly, those with high liking for added sugar had food intake similar to those with high liking for fat-and-sweet, but had slightly lower BMI (supplementary tables S1 and S2), which can contribute to explain the difference of results. In addition, as liking for fat-and-sweet is statistically associated with higher risk of diabetes, this may suggest that the fatty component of fat-and-sweet liking is driving the increased risk of diabetes.

Interpretation of the present results must take into account several limitations. Subjects were volunteers in the NutriNet-Santé cohort so probably more concerned about healthy lifestyle and nutrition than the general population. Moreover, incidences of CVD, type 2 diabetes and hypertension in participants were lower than in the general French population [48] which might underestimate our association. Caution is therefore needed when interpreting and generalizing the results. In addition, dietary data were collected using 24h dietary records, which can underestimate energy intake [49]. Individual characteristics, sensory liking and dietary intake were assessed at baseline only, so cumulative effect of these behaviors on the development of CMDs could not be assessed. Furthermore, residual confounding cannot be excluded because other confounders of sensory liking in CMDs risk such as genetics or psychological factors could not be taken into account in the analysis. Finally, some association did not succeed to attain the cut-off of 10% for practical significance, thus low effect sizes of some HRs suggest caution when interpreting. However, the strength of our study is its prospective design with the 6 years of follow-up that allows us to explore the inference of causality between sensory liking and the CMDs risk. Another limitation was that self-reported data could be not accurate as measured data. Compared with liking as assessed by sensory tests, self-reported liking by questionnaire may lead to misreporting. Recalled liking can be influenced by the recalled pleasure arising from the sensory cues, but also by other external cues such dietary habit, dietary restraint, social desirability, health considerations and other variables [9,50]. However, this questionnaire was carefully developed through a series of pretests and pilots that demonstrated its repeatability, feasibility and internal validity [18], and positive correlations with sensory test measurements have been shown (Deglaire et al. 2011 personal communication). Although CMDs were validated, misclassification bias has to be considered as they were also self-reported.

Conclusions

In conclusion, fat-and-salt liking was associated with an increased risk of hypertension, diabetes and CVDs, mainly explained by unhealthy dietary intake and BMI. Our findings have clinical implications for management of persons at risk of chronic diseases. Taking into account an individual’s liking may help dietitians and practitioners provide effective dietary counseling while supporting individual preference. In addition, our results may help to guide effective targeted measures in prevention. For instance, sensory education measures tailored to individual liking could provoke a shift in liking toward more complex foods in persons who strongly favor fatty foods, thereby leading to reduced acceptance of fatty-salted or fatty-sweetened foods and greater dietary variety [51]. Indeed, previous works demonstrated that the preferred amounts of fat, salt and sugar in foods have an innate basis that can be changed by modifying the frequency of sensory exposure to the fatty, salty and sweet tastes [52-54]. Another potential alternative would be to reduce content of fats, sugar and salt of industrialized products while maintaining the same consumer appreciation and pleasantness by encouraging more technical and commercial innovation.

List of abbreviations

BMI: body mass index

HR: hazard ratio

M: men

RD: reduction of deviance

RHR: reduction in hazard ratio

W: women

Ethics approval and consent to participate

This study was conducted according to guidelines laid down in the Declaration of Helsinki, and all procedures were approved by the Institutional Review Board of the French Institute for Health and Medical Research (IRB Inserm n°0000388FWA00005831) and the "Commission Nationale Informatique et Libertés" (CNIL n°908450 and n°909216). Electronic informed consent was obtained from all subjects. This study is registered in EudraCT (n°2013-000929-31).

Competing interests

The authors declare that they have no competing interest.

Authors' contributions

AL: conducted the literature review and drafted the manuscript; AL: performed analyses; SA, KC, AD, PS, SP, LF, SH and CM: were involved in the interpretation of results and critically reviewed the manuscript; and SH and CM: were responsible for the development of the design and the protocol of the study. All authors read and approved the final manuscript.

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Table 1: Baseline characteristics of subjects who developed a CMD or not during the follow-up, NutriNet-Santé cohort, 2010-2016, France

	Cardiovascular diseases			**Diabetes**			**Hypertension**		
	Healthy participants n=40667	**Cases n=655**	***P***	**Healthy participants n=40980**	**Cases n=342**	***P***	**Healthy participants n=36029**	**Cases n=1907**	***P***
General characteristics									
Age, y	44.4 ± 14.2	59.4 ± 11.1	<0.0001	44.6 ± 14.3	56.2 ± 10.2	<0.0001	42.7 ± 13.7	55.8 ± 11.7	<0.0001
Sex, % women	78.0	52.2	<0.0001	77.7	59.9	<0.0001	79.3	66.3	<0.0001
BMI, kg/m²	23.7 ± 4.4	25.1 ± 1.3	<0.0001	23.7 ± 4.3	30.2 ± 6.3	<0.0001	23.3 ± 4.1	25.8 ± 4.8	<0.0001
Educational level, %			<0.0001			<0.0001			<0.0001
Elementary school	2.8	5.0		2.8	4.1		2.4	5.1	
Secondary school	33.5	43.4		33.5	48.5		31.9	42.0	
College graduate	30.6	24.4		30.5	23.4		31.2	26.5	
Advanced degree	32.5	26.0		32.5	22.5		33.9	25.3	
Other	0.6	1.2		0.7	1.5		0.6	1.1	
Smoking status, %			<0.0001			<0.0001			<0.0001
Never-smoker	48.5	35.4		48.3	35.4		49.0	43.1	
Former smoker	35.3	51.2		35.5	50.3		34.0	44.9	
Current smoker	16.2	13.4		16.2	14.3		17.0	12.0	
Physical activity, %			0.0003			0.01			<0.0001
Low	29.7	37.4		29.8	28.1		29.0	35.4	
Moderate	38.8	36.0		38.8	35.1		39.2	35.8	
High	23.3	19.4		23.2	30.4		23.5	21.7	
Missing data	8.2	7.2		8.2	6.4		8.3	7.1	
Family history of myocardial infarction, %	11.2	22.0	<0.0001	11.3	18.1	<0.0001	10.1	17.3	<0.0001
Family history of stroke, %	11.7	20.9	<0.0001	11.8	19.9	<0.0001	10.5	18.2	<0.0001
Family history of diabetes, %	13.5	14.1	0.68	13.3	33.0	<0.0001	13.3	17.7	<0.0001
Family history of hypertension, %	32.0	40.3	<0.0001	32.1	40.6	0.0007	28.7	41.6	<0.0001
Sensory liking scores									
Liking for fat-and-salt	4.00 ± 1.4	3.80 ± 1.4	0.0003	4.00 ± 1.4	4.17 ± 1.3	0.02	4.02 ± 1.4	3.83 ± 1.4	<0.0001
Liking for fat-sweet	3.85 ± 1.8	3.25 ± 1.6	<0.0001	3.84 ± 1.8	3.75 ± 1.7	0.33	3.91 ± 1.8	3.46 ± 1.7	<0.0001
Liking for sweet	3.80 ± 1.3	3.65 ± 1.3	0.006	3.80 ± 1.3	3.57 ± 1.3	0.002	3.81 ± 1.3	3.67 ± 1.3	<0.0001
Liking for salt	3.73 ± 1.6	3.88 ± 1.6	0.19	3.79 ± 1.6	4.14 ± 1.6	<0.0001	3.80 ± 1.6	3.67 ± 1.5	0.004
Food group consumption, g/d									
Fruits	262 ± 183	304 ± 189	<0.0001	262 ± 184	255 ± 171	0.45	259 ± 183	290 ± 193	0.45
Vegetables	222 ± 128	239 ± 136	0.001	223 ± 128	228 ± 128	0.44	220 ± 128	239 ± 129	<0.0001
Meat	46 ± 46	48 ± 45	0.27	46 ± 46	64 ± 52	<0.0001	45 ± 45	52 ± 46	<0.0001

Processed meat	33 ± 34	34 ± 36	0.16	33 ± 34	41 ± 36	<0.0001	32 ± 34	33 ± 34	0.30
Fish	43 ± 48	53 ± 51	<0.0001	43 ± 48	54 ± 55	0.0002	42 ± 48	49 ± 49	<0.0001
Milk and yogurts	169 ± 158	164 ± 150	0.48	168 ± 158	174 ± 164	0.50	168 ± 159	178 ± 157	0.006
Cheese	37 ± 31	37 ± 30	0.96	37 ± 31	43 ± 33	0.002	37 ± 31	38 ± 37	0.18
Butter and other added fats	14 ± 14	15 ± 16	0.0005	14 ± 14	16 ± 16	0.0009	14 ± 14	14 ± 14	0.02
Oil	9 ± 9	9 ± 10	0.60	9 ± 9	9 ± 9	0.91	9 ± 9	9 ± 9	0.79
Salted snacks and appetizers	6 ± 12	5 ± 11	0.63	6 ± 12	6 ± 13	0.78	6 ± 12	5 ± 11	0.0007
Savory sauces	18 ± 18	17 ± 17	0.17	18 ± 18	20 ± 20	0.01	18 ± 18	17 ± 18	0.38
Starchy foods	188 ± 105	202 ± 118	0.0006	188 ± 105	218 ± 117	<0.0001	187 ± 104	196 ± 115	0.0003
Whole grain products	33 ± 50	34 ± 46	0.77	33 ± 50	30 ± 44	0.30	33 ± 50	34 ± 51	0.56
Sugar and sugary products	22 ± 25	25 ± 26	0.002	22 ± 25	17 ± 23	<0.0001	22 ± 25	23 ± 25	0.04
Fatty-sweet products	71 ± 64	58 ± 58	<0.0001	71 ± 64	61 ± 62	0.003	73 ± 65	59 ± 59	<0.0001
Sweetened cream desserts	36 ± 55	32 ± 55	0.10	36 ± 55	32 ± 50	0.18	36 ± 56	32 ± 53	0.001
Sweetened soft drinks	45 ± 107	27 ± 73	<0.0001	44 ± 107	38 ± 110	0.28	47 ± 110	30 ± 82	<0.0001
Alcoholic beverages	102 ± 162	154 ± 197	<0.0001	102 ± 162	146 ± 204	<0.0001	98 ± 159	131 ± 187	<0.0001
Energy, kcal/d	1901 ± 511	1970 ± 508	0.0005	1901 ± 511	2015 ± 526	<0.0001	1901 ± 511	1930 ± 523	0.02

[1] P values are for the comparison between subjects with illness and those who not and were determined by using Student's t-test or chi-square test as appropriate.

[2] Mean ± SD (all such values)

Table 2: Associations between liking for fat-and-salt and risk of cardiovascular disease from multivariable Cox proportional hazards model

	Cardiovascular disease n=41,322			
	HR[1] (95% CI)	P	RHR%[2]	RD%[3]
Liking for fat-and-salt				
Base model (sex and age adjusted)	1.10 (1.02;1.19)	0.01		
M2 Adjusted model[4]	1.08 (1.00;1.16)	0.04		35
M3 Model assessing the mediating effect of dietary intake[5]	1.07 (0.99;1.15)	0.11	30	61
M4 Model assessing the mediating effect of body mass index[6]	1.06 (0.98;1.14)	0.16	40	70

[1] Hazard ratio and 95% confidence interval

[2] % RHR: percentage reduction in HR by inclusion of mediator ((HR base model – HR base model + mediator) / (HR base model − 1))*100

[3] % RD: percentage of sensory liking reduction in deviance explained by inclusion of mediator and confounders ((reduction in deviance due to sensory liking of base model) − (reduction in deviance due to sensory liking of base model + mediator and confounders) /RD due to sensory liking of base model)*100

[4] M2: adjusted model: M1 + educational level, alcohol consumption, smoking status, physical activity and family medical history (family history of stroke and myocardial infarction)

[5] M3: model assessing the mediating effect of dietary intake: M2 + energy intake, month of inclusion and food groups intake (fruits, meat, processed meat, fish, salted snacks and appetizers, cheese, oil, butter and other added fats, starchy foods, whole grain products, sugar and sugary products)

[6] M4: model assessing the mediating effect of body mass index: M3 + body mass index

Table 3: Associations between liking for fat-and-salt, fat-and-sweet, sweet and salt, and risk of type 2 diabetes from multivariable Cox proportional hazards model

	Diabetes n=41,322			
	HR[1] (95% CI)	P	RHR%[2]	RD%[3]
Liking for fat-and-salt				
Base model (sex and age adjusted)	1.30 (1.18;1.43)	<0.0001		
M2 Adjusted model[4]	1.27 (1.15;1.41)	<0.0001		18
M3 Model assessing the mediating effect of dietary intake[5]	1.15 (1.04;1.28)	0.009	50	75
M4 Model assessing the mediating effect of body mass index[6]	1.08 (0.97;1.20)	0.16	73	93
Liking for fat-and-sweet				
Base model (sex and age adjusted)	1.09 (1.01;1.17)	0.02		
M2 Adjusted model	1.07 (0.99;1.15)	0.08		43
M3 Model assessing the mediating effect of dietary intake	1.06 (0.99;1.14)	0.10	33	50
M4 Model assessing the mediating effect of body mass index	1.04 (0.97;1.12)	0.30	56	80
Liking for sweet				
Base model (sex and age adjusted)	0.76 (0.69;0.84)	<0.0001		
M2 Adjusted model	0.78 (0.70;0.86)	<0.0001		23
M3 Model assessing the mediating effect of dietary intake	0.86 (0.77;0.95)	0.004	42	70
M4 Model assessing the mediating effect of body mass index	0.89 (0.80;0.99)	0.04	54	84
Liking for salt				
Base model (sex and age adjusted)	1.09 (1.01;1.18)	0.02		
M2 Adjusted model	1.08 (1.00;1.17)	0.04		16
M3 Model assessing the mediating effect of dietary intake	1.06 (0.98;1.14)	0.16	33	62
M4 Model assessing the mediating effect of body mass index	1.07 (0.99;1.16)	0.08	22	42

[1] Hazard ratio and 95% confidence interval

[2] % RHR: percentage reduction in HR by inclusion of mediator ((HR base model – HR base model + mediator) / (HR base model − 1))*100

[3] % RD: percentage of sensory liking reduction in deviance explained by inclusion of mediator and confounders ((reduction in deviance due to sensory liking of base model) − (reduction in deviance due to sensory liking of base model + mediator and confounders) /RD due to sensory liking of base model)*100

[4] M2: adjusted model: M1 + educational level, alcohol consumption, smoking status, physical activity and family medical history of diabetes

[5] M3: model assessing the mediating effect of dietary intake: M2 + energy intake, month of inclusion and food groups intake (fruits, vegetables, meat, processed meat, savory sauces, cheese, butter and other added fats, starchy foods, whole grain products, sugar and sugary products, sweetened soft drinks)

[6] M4: model assessing the mediating effect of body mass index= M3 + body mass index

Table 4: Associations between liking for fat-and-salt and risk of hypertension from multivariable Cox proportional hazards model

	Hypertension n=37,936			
	HR[1] (95% CI)	P	RHR%[2]	RD%[3]
Liking for fat-and-salt				
Base model (sex and age adjusted)	1.08 (1.04;1.13)	0.0002		
M2 Adjusted model[4]	1.07 (1.03;1.12)	0.001		24
M3 Model assessing the mediating effect of dietary intake[5]	1.05 (1.00;1.10)	0.04	38	68
M4 Model assessing the mediating effect of body mass index[6]	1.01 (0.97;1.06)	0.57	88	98

[1] Hazard ratio and 95% confidence interval

[2] % RHR: percentage reduction in HR by inclusion of mediator ((HR base model – HR base model + mediator) / (HR base model − 1))*100

[3] % RD: percentage of sensory liking reduction in deviance explained by inclusion of mediator and confounders ((reduction in deviance due to sensory liking of base model) − (reduction in deviance due to sensory liking of base model + mediator and confounders) /RD due to sensory liking of base model)*100

[4] M2: adjusted model: M1 + educational level, alcohol consumption, smoking status, physical activity and family medical history of hypertension

[5] M3: model assessing the mediating effect of dietary intake: M2 + energy intake, month of inclusion and food groups intake (fruits, vegetables, meat, processed meat, savory sauces, milk and yogurts, oil, starchy foods, whole grain products, sugar and sugary products)

[6] M4: model assessing the mediating effect of body mass index: M3 + body mass index