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Smell and Taste Dysfunction Is Associated with Higher Serum Total Cholesterol Concentrations in Chinese Adults

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Abstract

Background: Several lipid-related hormones and peptides, such as glucagon-like peptide-1 and leptin, are involved in the regulation of taste and smell function. However, to our knowledge, it remains unknown whether these chemosensory functions are associated with lipid profiles.

Objective: We examined the cross-sectional association between taste and smell dysfunction and blood cholesterol concentrations.

Methods: With the use of a questionnaire, we assessed chronic smell and taste dysfunction in 12,627 Chinese participants (10,418 men and 2209 women; mean age: 54.4 y) who did not take hypolipidemic agents. Participants were categorized into 3 groups based on the number of smell and taste dysfunctions, ranging from 0 (best) to 2 (worst). A general linear model was used to test differences in serum concentrations of total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides (TGs) across groups with different smell and taste status after adjusting for age, sex, education, occupation, smoking, drinking, obesity, and history of cardiovascular disease, cancer, and head injury.

Results: The prevalence of smell and taste dysfunction was 2.4% and 1.2%, respectively. Worse smell and taste dysfunction was associated with higher total cholesterol concentrations (P-trend = 0.005). No significant differences were observed in LDL cholesterol, HDL cholesterol, and TG concentrations across groups with different numbers of chemosensory dysfunctions (P-trend > 0.1 for all). The associations between chemosensory dysfunction and total cholesterol concentrations were more pronounced in participants aged ≤60 y and in those who were nonsmokers relative to their counterparts (P-interaction < 0.05 for all).

Conclusions: In this large cross-sectional study, chemosensory dysfunction was associated with higher serum total cholesterol concentrations among Chinese adults. Prospective studies are needed to investigate the temporal relation between these chemosensory dysfunctions and hypercholesterolemia. *J Nutr* 2017;147:1546–51.

Keywords: general population, epidemiologic study, taste function, smell function, total cholesterol, lipids, lipoproteins

Introduction

Previous studies have suggested that chemosensory function (i.e., smell and taste function) and lipid metabolism might both be regulated by a group of hormones and neuropeptides such as glucagon-like peptide-1 (GLP-1), vasoactive intestinal peptide, cholecystokinin, neuropeptide Y, and leptin (1–4). These hormones and neuropeptides are also associated with metabolism, oxidation, and cholesterol activity (5–8). Furthermore, chemosensory dysfunction, including both olfactory and gustatory dysfunctions, has been associated with several lipid-related conditions such as hyperglycemia and obesity in the population (9–12). These observations suggest that individuals with poor chemosensory function could also have high lipid or lipoprotein concentrations. However, 3 epidemiologic studies (11, 13, 14) in which the associations between olfactory function (but not taste function) and lipid profiles were examined generated inconsistent results.

Therefore, we conducted a large-scale community-based study that included 12,990 Chinese adults to examine whether smell and

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ZH and SH contributed equally to this article.
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Abbreviations used: CVD, cardiovascular disease; GLP-1, glucagon-like peptide-1; MI, myocardial infarction; TC, total cholesterol.

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taste dysfunction was associated with high serum concentrations of total cholesterol (TC), independent of known risk factors for dyslipidemia. In secondary analyses, we also examined concentrations of LDL cholesterol, HDL cholesterol, and TGs.

Methods

Participants. Participants enrolled in this study were from the Kailuan study, an ongoing multicentered cohort that includes 101,510 Chinese adults (15, 16). As described previously (17, 18), we collected information on smell and taste function among 10,725 men and 2265 women aged 25–95 y in 2012 who underwent an examination at Kailuan General Hospital. In these analyses, we excluded participants with incomplete information on age (n = 20), smell or taste function (n = 12), or on serum concentrations of TC, LDL cholesterol, HDL cholesterol, or TGs (n = 238). We further excluded 93 individuals who reported using any cholesterol-lowering agents in 2012, leaving 12,627 participants for the analyses. The study was approved by the Kailuan General Hospital Ethics Committee.

Assessment of smell and taste dysfunction. Smell and taste dysfunction was assessed with the use of a questionnaire derived from the National Health Interview Survey (19). All participants were asked the following question: "Do you have any problems with your sense of smell, such as not being able to smell things or things not smelling the way they are supposed to for ≥3 mo?" Those who answered yes were considered to have smell dysfunction. The following question regarding taste status was also asked: "Do you have any problems with your sense of taste, such as not being able to taste things or things not tasting the way they are supposed to for ≥3 mo?" Those who answered yes were considered as having taste dysfunction. In this study, we categorized participants into 3 groups based on the number of smell or taste dysfunctions [ranging from 0 (best) to 2 (worst)]: normal chemosensory function, smell or taste dysfunction, and both dysfunctions.

Assessment of lipid and lipoprotein profiles. During the survey, 12-h overnight fasting blood samples were obtained and transfused into vacuum tubes containing EDTA. All blood samples were processed and analyzed with the use of a Hitachi 747 auto-analyzer. As a primary outcome, serum TC concentrations were measured with the use of the endpoint test method, with an upper limit of detection of 20.68 mmol/L, as detailed elsewhere (20). The serum concentrations of LDL and HDL cholesterol were measured with the direct test method, with LDL and HDL cholesterol upper-limit detections of 12.9 and 3.88 mmol/L, respectively. TG serum concentration was measured with the use of the enzymatic colorimetric method (interassay CV: <10%) (Mind Bioengineering Co. Ltd.), with an upper limit of detection of 11.30 mmol/L.

Assessment of covariates. We collected participant information on education, monthly income, occupation, physical activity, salt consumption, smoking status, and alcohol consumption with the use of a questionnaire in 2012. Perceived salt consumption was assessed from the question regarding the perceived dietary salt consumption preference and was classified as light (<6 g/d), moderate (6–11 g/d), and salty (>11 g/d) (21). Physical activity was evaluated by asking participants their frequency of physical activity (≥20 min at a time). According to their response, participants were classified as inactive, moderately active, and active (21). Weight, height, and waist circumference were measured by trained fieldworkers during the 2012 interview, and BMI (in kg/m^2) was calculated. Normal, overweight, and obesity were respectively defined as BMI <24, 24–27, and ≥28 based on the specific standards for the Chinese population (22). Blood pressure was measured twice with participants in a seated position after ≥5 min of rest with the use of a mercury sphygmomanometer. The mean of the 2 readings was used for the analyses. Hypertension was diagnosed as systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg, a history of physician-diagnosed hypertension, or the use of antihypertensive medicines. Prehypertension was defined as systolic blood pressure between 120 and 139 mm Hg or diastolic blood pressure between 80 and 90 mm Hg. Blood concentrations of glucose were measured by an enzymatic method with the use of the previously mentioned auto-analyzer. Diabetes was diagnosed as fasting blood glucose ≥7 mmol/L (126 g/L), history of physician-diagnosed diabetes, or the use of glucose-lowering medication. Impaired fasting glucose was diagnosed as fasting blood glucose between 5.6 and 7.0 mmol/L (100–125 mg/dL). The presence of myocardial infarction (MI), stroke, head injury, or cancer was ascertained with the use of medical records (16, 17).

Statistical analysis. Statistical analyses were completed with SAS version 9.2 (SAS Institute). All CIs were estimated at the 95% level, and significance was set at $P \leq 0.05$. Categorical data are presented as percentages; continuous data are presented as means ± SEMs. The general linear model was used to test differences in mean TC concentrations and other lipids across groups with different smell and taste status. We fit 2 multivariate models to the data. In model 1, we adjusted for age and sex. In model 2 (fully adjusted model), we further adjusted for all covariates. To minimize the potential effects of major chronic diseases, we further conducted several sensitivity analyses by separately excluding participants with diabetes or obesity or a medical history of MI, stroke, or cancer. We explored interactions between these potential confounders and chemosensory dysfunction in relation to concentrations of lipids, adjusting for other covariates. For significant interaction variables, we assessed the association in subgroups stratified by age and smoking status.

Results

The prevalence of smell and taste dysfunction was 2.4% (n = 302) and 1.2% (n = 156), respectively, and 0.6% (n = 76) of the participants had both chemosensory dysfunctions at the same time. Individuals with greater chemosensory dysfunction than normal individuals were more likely to be older coal miners and had a higher proportion of head injury (all $P < 0.05$) (**Table 1**).

Greater chemosensory dysfunction was significantly associated with higher concentrations of TC. After adjusting for potential confounders, the association remained significant (P-trend = 0.005). Sensitivity analyses in which we separately excluded participants who were obese, hypertensive, diabetic, or had a history of MI, stroke, and cancer generated similar significant associations between chemosensory dysfunction and TC (P-trend <0.05 for all) (**Table 2**). In contrast, there were no significant associations between chemosensory dysfunction and LDL cholesterol, HDL cholesterol, and TGs (P-trend >0.1 for all) (**Table 3**). Individuals with both smell and taste dysfunction had significantly higher concentrations of non-HDL cholesterol than those without any dysfunction (adjusted means were 4.15 and 3.76, respectively) (P-difference = 0.03), although the trend test was not significant (P-trend = 0.07).

We found significant interactions between age, smoking status, and chemosensory status in relation to TC (P-interaction <0.05 for all). In subsequent subgroup analyses stratified by age and smoking status, we found the associations between chemosensory dysfunction and TC concentrations were more pronounced in participants aged <60 y and in those who were nonsmokers relative to their counterparts (**Supplemental Table 1**). Smell dysfunction alone was associated with a higher concentration of TC (P = 0.005) (**Supplemental Table 2**).

Discussion

In this study, we found a significant association between chemosensory dysfunction and a higher concentration of TC, particularly among younger adults and nonsmokers. The association was independent of potential relevant risk factors such as smoking, drinking, salt consumption, or the presence of major chronic diseases.

TABLE 1 Basic characteristics of Chinese adults by smell and taste status in 2012[1]

	No smell or taste dysfunction (n = 12,245)	Smell or taste dysfunction (n = 306)	Smell and taste dysfunction (n = 76)	P value
Age, y	53.5 ± 0.13[2]	56.8 ± 0.64	57.0 ± 1.3	<0.0001
Men	10,106 (82.5)	247 (80.7)	65 (85.5)	0.56
Education				0.06
Primary	611 (5.0)	21 (6.9)	6 (7.9)	
Secondary	8689 (71.0)	218 (71.2)	57 (73.7)	
College	2566 (21.0)	54 (17.7)	9 (11.8)	
Income, RMB/mo				0.69
<500	237 (1.9)	8 (2.6)	0 (0.0)	
500–1000	2206 (18.0)	54 (17.7)	13 (17.11)	
>1000	8353 (68.2)	201 (65.7)	53 (69.7)	
Occupation				<0.0001
White collar	1240 (10.1)	33 (10.8)	3 (4.0)	
Blue collar	6713 (54.8)	141 (46.1)	33 (43.4)	
Coal miner	2450 (20.0)	66 (21.6)	28 (36.8)	
Physical activity				0.005
Inactive	5738 (46.9)	159 (52.0)	24 (31.6)	
Moderate	4530 (37.0)	98 (32.0)	41 (54.0)	
Active	1808 (14.8)	43 (14.1)	8 (10.5)	
Perceived salt consumption				0.008
Light	1543 (12.6)	24 (7.8)	3 (4.0)	
Moderate	9184 (75.0)	244 (79.7)	65 (85.5)	
Salty	1348 (11.0)	32 (10.5)	5 (6.6)	
Smoking status				0.22
Never	6859 (56.0)	168 (54.9)	50 (65.8)	
Past	697 (5.7)	16 (5.2)	3 (4.0)	
Current	4517 (36.9)	116 (37.9)	20 (26.3)	
Drinking status				0.08
Never	7289 (59.5)	201 (65.7)	52 (68.4)	
Past	68 (0.6)	1 (0.3)	1 (1.3)	
Current	4888 (39.9)	104 (34.0)	23 (30.3)	
Previous history of MI	131 (1.1)	4 (1.3)	0 (0)	0.61
Previous history of stroke	264 (2.2)	12 (3.9)	3 (4.0)	0.07
Previous history of cancer	24 (0.2)	2 (0.7)	0 (0)	0.20
Hypertension				0.13
No	1613 (13.2)	46 (15.0)	6 (7.9)	
Prehypertension	4514 (37.0)	93 (30.4)	34 (44.7)	
Yes	5641 (46.1)	150 (49.0)	33 (43.4)	
Diabetes				0.02
No	9689 (79.1)	232 (75.8)	70 (92.1)	
Prediabetes	1203 (9.8)	29 (9.5)	3 (4.0)	
Yes	1353 (11.1)	45 (14.7)	3 (4.0)	
Previous head injury	308 (2.5)	12 (3.9)	5 (6.6)	0.03
BMI[3]				0.21
Normal	5162 (42.2)	127 (41.5)	25 (32.9)	
Overweight	5101 (41.7)	130 (42.5)	42 (55.3)	
Obese	1982 (16.2)	49 (16.0)	9 (11.8)	
Waist circumference[4]				0.22
Normal	5579 (45.6)	134 (43.8)	36 (47.4)	
Central obesity	5412 (44.2)	129 (42.2)	30 (39.5)	

[1] Values are n (%) unless otherwise indicated. MI, myocardial infarction; RMB, renminbi.
[2] Mean ± SEM adjusted for age and sex (all such values).
[3] BMI (in kg/m^2) was categorized as follows: normal, <24; overweight, 24–27; and obese, ≥28.
[4] Normal was defined as a waist circumference of <90 cm for men and <85 cm for women; central obesity was defined as a waist circumference of ≥90 cm for men and ≥85 cm for women.

The assessment of TC concentration via the presence of chemosensory dysfunction has clinical significance. Previous studies have reported that having a history of cardiovascular disease (CVD) was associated with a higher prevalence of taste or smell disorders (23, 24). Hyperlipidemia is a major risk factor for CVD. Although individual lipid components, including HDL, LDL, and VLDL cholesterol, play an important role in the development and progression of atherosclerosis, TC concentrations are still important

TABLE 2 Serum total cholesterol concentrations (expressed as mmol/L) in Chinese adults by smell and taste status in 2012[1]

	No smell or taste dysfunction (n = 12,245)	Smell or taste dysfunction (n = 306)	Smell and taste dysfunction (n = 76)	P-trend
Adjusted for age and sex	5.20 ± 0.02	5.36 ± 0.09	5.49 ± 0.18	0.05
Fully adjusted	4.84 ± 0.49	5.01 ± 0.50	5.22 ± 0.52*	0.005
Excluding participants with MI, stroke, and cancer	5.24 ± 0.45	5.43 ± 0.46*	5.66 ± 0.49*	0.002
Excluding participants with hypertension	4.66 ± 0.53	4.94 ± 0.54*	5.49 ± 0.58**	0.0001
Excluding participants with diabetes	4.81 ± 0.47	4.89 ± 0.48	5.21 ± 0.50*	0.04
Excluding participants with a BMI (in kg/m^2) >28	4.76 ± 0.49	5.01 ± 0.50**	5.25 ± 0.52**	0.001

[1] All values are means ± SEMs unless otherwise indicated. The full model was adjusted for age, sex, education, income, occupation, physical activity, perceived salt consumption, smoking status, drinking status, BMI, waist circumference, and history of diabetes, hypertension, MI, stroke, cancer, and head injury. *$P < 0.05$ and **$P < 0.01$ relative to individuals without smell and olfactory dysfunction. MI, myocardial infarction.

for a global risk assessment for an unfavorable lipid profile. This is supported by a recent meta-analysis (25), in which a 1-mmol/L increase in TC was significantly associated with a 20–24% increased risk of coronary heart diseases in men and women. The association between chemosensory dysfunction and a higher TC concentration found in this study might partially explain the relation between CVD and impaired chemosensory dysfunction. Interestingly, after excluding individuals with a history of CVD in this study, we still observed a significant association between chemosensory dysfunction and TC. This suggests that the assessment of chemosensory function may contribute to the identification of populations with a higher-than-average CVD risk.

The relation between chemosensory function and cholesterol concentrations has been examined in several previous studies (11, 13, 14). In a Korean population, Lee et al. (13) reported a significant difference in HDL cholesterol between normal olfactory function and dysfunction but not in TC, TGs, and LDL cholesterol among 10, 533 Korean adults. However, after adjusting for potential confounders such as smoking, drinking, and BMI, the association between olfactory dysfunction and low HDL cholesterol was no longer significant. A case-control study that included 41 elderly women aged 61–81 y and an equal number of young women aged 21–27 y from a Korean population (11) reported no correlation between smell and taste threshold and TC, HDL cholesterol, LDL cholesterol, and TGs. Unlike our study, these studies did not consider the use of hypolipidemic agents. Hypolipidemic agents have been reported in perturbations of taste and smell (26) and could confound the real association between chemosensory function and lipid profiles. In another smell study that included 119 patients with type 2 diabetes and 35 controls (14), general hyperlipidemia [use of hypolipidemic medication; TC: ≥5.17 mmol/L (200 mg/dL); LDL cholesterol: ≥3.36 mmol/L (130 mg/dL); or TGs: ≥1.7 mmol/L (150 mg/dL)] was associated with worse olfactory scores. Inconsistent results from these studies could be partially attributed to the different confounders across studies and relatively small sample sizes.

To our knowledge, the underlying mechanism for the association between chemosensory dysfunction and higher blood concentrations of TC remains unclear. This association could be partially explained by hormones and neuropeptides that regulate both chemosensory function and lipid or lipoprotein status. For example, leptin, a hormone produced in adipose tissue, modulates sweet taste perception (4) and is positively associated with higher olfactory capacities (27). Another lipid metabolism–related hormone, GLP-1, also presents within the taste and smell systems. Studies in humans and rodents have demonstrated that GLP-1 influenced smell and taste function (2, 28, 29). Mice lacking the GLP-1 receptor displayed a substantial reduction in sensitivity to sweet taste and hypersensitivity to umami (2, 28). However, we did not assess leptin concentrations in this population. Future studies are warranted to investigate the potential role of these hormones in the relation between chemosensory dysfunction and cholesterol.

In our study, we did not observe significant associations between chemosensory dysfunctions and TGs, LDL cholesterol, and HDL cholesterol individually, which was similar to a previous study (11). However, we observed a trend between lower chemosensory function and higher LDL cholesterol and TG concentrations. The nonsignificant results could have been caused by the low prevalence of chemosensory dysfunction in this community-based population, resulting in inadequate power to detect significance. It is also possible that among individuals with chemosensory dysfunction, the impact of hyperleptinemia might be offset by high neuropeptide Y concentrations, which has been reported to be able to inhibit TG secretion by altering liver lipase activity via the sympathetic nervous system (30–36).

Interestingly, we observed significantly higher TC concentrations in the group with reported smell dysfunction than normal smell function but not in those groups with reported taste dysfunction.

TABLE 3 Serum LDL cholesterol, HDL cholesterol, and TG concentrations (expressed as mmol/L) in Chinese adults by smell and taste status in 2012[1]

	No smell or taste dysfunction (n = 12,245)	Smell or taste dysfunction (n = 306)	Smell and taste dysfunction (n = 76)	P-trend
LDL cholesterol	2.18 ± 0.33	2.25 ± 0.34	2.29 ± 0.35	0.28
HDL cholesterol	1.16 ± 0.21	1.23 ± 0.21*	1.16 ± 0.22	0.14
TGs	3.05 ± 0.63	3.01 ± 0.64	3.27 ± 0.67	0.60

[1] All values are means ± SEMs unless otherwise indicated. The full model was adjusted for age, sex, education, income, occupation, physical activity, perceived salt consumption, smoking status, drinking status, BMI, waist circumference, and history of diabetes, hypertension, myocardial infarction, stroke, cancer, and head injury. *$P < 0.05$ relative to individuals without smell or taste dysfunction.

The smaller sample size of individuals with taste dysfunction might be a possible explanation for this finding. Similarly, a previous study reported a lower prevalence of taste dysfunction compared with an olfactory dysfunction in an American population (19). It is also possible that such a difference could have resulted from the different pathophysiologic pathways in smell compared with taste dysfunction. Future studies are warranted to confirm our findings.

This cross-sectional study has some limitations. First, it was designed to examine whether chemosensory function could be used as a marker for blood lipid profiles. Thus, it was impossible to infer a causal relation between key study variables. Further longitudinal studies should be conducted to investigate the temporal relation between chemosensory dysfunction and lipid profiles. Second, chemosensory function was evaluated with the use of a questionnaire instead of psychophysical test. However, this questionnaire was validated in an earlier study (19), and despite possibly lower specificity than laboratory tests, a questionnaire is more convenient and cost-effective for a large-scale population study. Third, we did not collect information on some chemosensory-related diseases such as colds and rhinitis, although these conditions may not affect the blood cholesterol concentrations. Finally, apart from salt consumption, we did not collect comprehensive dietary intake data. However, we adjusted factors related to dietary intake such as BMI and waist circumference that could indirectly reflect the diet and nutritional status. We found a similar association between chemosensory dysfunction and TC even after excluding those with a BMI >28.

In conclusion, in this large-scale community-based study, we found that smell and taste dysfunction was associated with higher blood concentrations of TC. Further prospective studies should be conducted to investigate the temporal relation between these chemosensory dysfunctions, hyperlipidemia, and CVDs.

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