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A longitudinal study of altered taste and smell perception and change in blood pressure

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Abstract

Background and Aims: Previous studies suggest that olfactory receptors, which mediate smell chemosensation, are located in the kidney and involved in blood pressure regulation. Mammalian epithelial sodium channels located in taste receptor cells are also found to participate in blood pressure regulation. However, there is currently no human study that has examined the association between taste and smell function and blood pressure. We thus conducted a longitudinal study to examine whether participants with altered taste and smell perception had larger increases in blood pressure compared with those without altered perception in a community-based cohort.

Methods and Results: The study included 5,190 Chinese adults (4,058 men and 1,132 women) who were normotensive at baseline. Taste and smell perception were assessed via questionnaire in 2012 (baseline). Blood pressure was measured in 2012 and 2014 to determine relative change in blood pressure. Mean differences of 2-year blood pressure change and 95% confidence intervals (CIs) across four categories of taste and smell perception were calculated after adjusting for known risk factors for hypertension. After adjusting for potential confounders, individuals with altered taste and smell perception had larger increases in systolic blood pressure (adjusted mean difference=5.1 mmHg, 95% CI: 0.1–10.0, *p*-value: 0.04) and mean arterial pressure (adjusted mean difference=3.8 mmHg, 95% CI: 0.4–7.1, *p*-value: 0.03) after two years of follow-up

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Authors' Contributions

XG, SW, and YL designed research; ZH, JL, SW, and YL conducted research; JL and YL analyzed data and performed statistical analysis; YL wrote the manuscript; All authors provided study oversight and critical reading of manuscript; XG and SW had primary responsibility for final content. All authors read and approved the final manuscript.

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compared with those having neither altered taste nor altered smell perception. No significant association was observed in individuals with altered taste or smell perception only.

Conclusion: Our results suggest an association between chemosensory function and blood pressure.

Keywords

Blood pressure; Hypertension; Taste perception; Smell perception; Chemosensory function

Introduction

Hypertension is a known major risk factor for stroke, kidney dysfunction, and heart disease [1]. In the United States, there are over 70 million (~29%) American adults diagnosed with hypertension [2]. Known risk factors for hypertension include age, race, sex, overweight, smoking, dyslipidemia, diabetes, unhealthy diet, and sedentary lifestyle [3 4]. Identifying additional risk factors for hypertension may improve strategies to prevent its onset and target therapy.

Chemosensory functions, which are usually known as taste and smell functions, are the major pathways for mammals to sense and respond to chemical compounds in the environment, such as odor, flavor, and stimulant [5]. The chemosensory process involves several signaling mechanisms, which may be associated with the development of some diseases; however, this process is relatively under-examined in general populations [6]. Previous studies have found that olfactory receptors are located in various tissues other than the nose, especially the kidneys [7 8]. The renal olfactory receptors have been observed to be involved in renin secretion and could have a role in regulating blood pressure [8]. Mammalian epithelial sodium channels located in taste receptor cells have also been found to participate in sodium sensing by the tongue and blood pressure regulation [9 10]. Furthermore, people with a decreased ability to taste sodium may have higher risk of developing hypertension due to higher sodium intake [11]. In this context, we hypothesized that altered chemosensory perception is associated with higher blood pressure. To test this hypothesis, we conducted a longitudinal study in a community-based cohort including 5,190 Chinese adults who were free of hypertension to examine whether individuals with altered taste and smell perception had larger increases in blood pressure in a two-year period compared with those without altered taste and smell perception after adjustment for known risk factors for hypertension.

Methods

Study population

The Kailuan study is a prospective study including 101,510 Chinese adults who were 18 to 98 years old in 2006–2007 (baseline of the cohort) living in the Kailuan community which is located in Tangshan city in northern China. Detailed information regarding the Kailuan cohort has been previously described [12]. In 2012 (the baseline for the current study), 12,990 participants from a subset of the Kailuan cohort were recruited and screened for sleep disorders as well as prodromal symptoms of Parkinson's diseases, including questions

about taste and smell [13–14]. In 2014, we followed these participants to update their health status. In the current study, we excluded 634 participants without information regarding chemosensory function and/or blood pressure-related measurement in 2012. Because taste and smell function could be affected by hypertension-related clinical conditions and use of relevant medications, we excluded 5,877 participants with hypertension and/or usage of any antihypertensive medications. We further excluded 1,289 participants who did not participate in the 2014 survey, leaving a total of 5,190 participants included in the primary analysis (Figure 1). Study approval was obtained from the Ethics Committee of the Kailuan General Hospital.

Assessment of blood pressure

The primary outcome for this analysis was change in systolic blood pressure at the two-year follow-up visit. Changes in other blood pressure indexes including diastolic blood pressure, pulse blood pressure, and mean arterial pressure were also examined. Systolic and diastolic blood pressure were measured in duplicate by mercury sphygmomanometer in 2012 after participants were seated for at least 5 minutes according to guidelines provided by “The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure” [15]. In 2014, an electronic blood pressure monitor (model: HEM-8102A; Omron Corporation, Kyoto, Japan) was used to measure systolic and diastolic blood pressure in duplicate. The average of two blood pressure measurements was calculated. Hypertension at baseline was defined as systolic blood pressure greater than or equal to 140 mmHg, diastolic blood pressure greater than or equal to 90 mmHg, or the use of an antihypertensive agent. Pulse blood pressure was calculated as: systolic blood pressure – diastolic blood pressure. Mean arterial pressure was calculated as: $[(1/3 * \text{systolic blood pressure}) + (2/3 * \text{diastolic blood pressure})]$.

Assessment of exposures and potential confounders

Altered taste and smell perception was collected via a questionnaire from the National Health Interview Survey regarding self-reported senses of taste and smell problems [16]. Participants were asked to answer two questions related to taste and smell functions including “Do you have any problems with sense of taste/smell, such as not being able to taste/smell things or things not tasting/smelling the way they are supposed to?” and “Have you had problems with sense of taste/smell for at least three months?”. In the current study, we categorized participants into four chemosensory groups: no altered perception, altered taste perception only, altered smell perception only, and altered taste and smell perception.

Characteristic information including age, sex, education level, history of diseases, physical activity, smoking status, salt intake, alcohol consumption, and usage of medication was collected through questionnaire assessments at baseline. Information regarding head injury was obtained by medical record review. Weight and height information was collected by trained clinical staff at baseline. Body mass index (BMI) was calculated as weight (kg)/height (m²). Blood samples were collected at baseline and analyzed by auto-analyzer (Hitachi 747; Hitachi, Tokyo, Japan) in the central laboratory in Kailuan General Hospital. Dyslipidemia was defined as triglycerides concentration ≥ 6.22 mmol/L, low-density lipoprotein (LDL) cholesterol concentration ≥ 4.14 mmol/L, or high-density lipoprotein

(HDL) cholesterol concentration < 1.04 mmol/L. Estimated glomerular filtration rate (eGFR) was calculated by adapting the Chronic Kidney Disease Epidemiology (CKD-EPI) collaboration equation. Diabetes mellitus was defined as fasting glucose level ≥ 7 mmol/L or being treated with insulin or oral hypoglycemic medications. Assessment of plasma high-sensitivity C-reactive protein (hs-CRP) concentration was conducted by using high sensitivity particle-enhanced immunonephelometry assay (Cias Latex CRP-H, Kanto Chemical Co. Inc.).

Statistical analyses

Statistical analyses were performed by using SAS version 9.4 (SAS Institute, Cary, NC). We used multivariate regression models to estimate adjusted mean differences and 95% confidence intervals (CI) in blood pressure change across four chemosensory categories with the no altered perception group as reference, after adjusting for potential confounders, including age, sex, education level, physical activity level, salt intake, smoking status, alcohol consumption, BMI, diabetes, dyslipidemia, hs-CRP, eGFR, and blood pressure index at baseline.

To minimize the possibility that medical conditions may influence chemosensory status, we conducted a sensitivity analysis by restricting the analysis to 4,944 participants without a history of myocardial infarction, head injury, cancer, or stroke. We also performed a sensitivity analysis excluding participants with hs-CRP ≥ 3 mg/L to explore whether the association between chemosensory status and blood pressure would be affected by potential allergic reaction or other chronic inflammation. In order to address potential bias caused by missing blood pressure data at study end point, we conducted an additional sensitivity analysis using multiple imputation based on the Markov chain Monte Carlo (MCMC) method to replace missing blood pressure with plausible values for those who did not participate in the 2014 survey [17].

Results

We observed that 2.1% of participants (n=109) self-reported an abnormality in taste or smell perception and 0.6% of participants (n=30) self-reported abnormalities in both taste and smell perception. As expected, individuals with both altered taste and smell perception had older age, significantly higher baseline systolic blood pressure, and lower renal function, as assessed by eGFR, relative to those without altered perception (Table 1).

Presence of both altered taste and smell perception was associated with larger increases in systolic blood pressure after two years of follow up (adjusted mean difference=5.1 mmHg, 95% CI: 0.1–10.0, *p*-value: 0.04) compared with those without altered perception (Table 2). The observed results did not materially change after we excluded those with major chronic diseases or hs-CRP ≥ 3 mg/L (Table 2). By utilizing multiple imputation to replace missing data for blood pressure at study end point, we observed similar and significant associations (Supplementary Table 1). Similarly, we observed significant associations between altered taste and smell perception and larger increases in mean arterial pressure, and similar trends for diastolic blood pressure and pulse blood pressure (Table 3).

There was no significant interaction between altered taste and smell perception and covariates, including age, sex, BMI, salt intake, and systolic blood pressure at baseline (p -interaction>0.1 for each).

Discussion

In this longitudinal cohort study, we found that individuals with both self-reported altered taste and smell perception had larger increases in systolic blood pressure and mean arterial pressure compared with individuals without altered taste and smell perception. When analyzing altered taste or smell perception alone, no significant association was observed. Excluding participants with common chronic conditions generated similar results, suggesting the association between altered taste and smell perception and change in blood pressure to be independent of known medical conditions.

Systolic blood pressure has been shown to be one of the most important predictive factors for determining the risk of stroke, coronary heart disease, heart failure, and mortality [18 19]. Longitudinal changes in systolic blood pressure are associated with risk of mortality and developing cardiovascular disease [20 21]. A recent meta-analysis showed that a 10 mmHg reduction in systolic blood pressure was associated with a 20% reduction in major cardiovascular disease risk and a 13% reduction in all-cause mortality risk [21]. In our analysis, we found that individuals with altered taste and smell perception had an adjusted mean of 5.1 mmHg larger increases in systolic blood pressure over two years, which may be associated with approximately 12.1% higher risk of cardiovascular diseases and 7.4% higher risk of all-cause mortality, compared with those without altered perception.

There are several potential metabolic mechanisms which may support our findings that individuals with altered taste and smell perception had larger increases in the blood pressure indexes. Because only the presence of both altered taste and smell perception at the same time, rather than altered taste or smell perception alone, was associated with larger increases in blood pressure, we speculate that the associations could be due to some common pathways shared by both taste and smell perception. Taste and smell function can affect individuals' food intake behavior and thus diminished taste or smell perception may result in increasing consumption of condiments-rich food [22]. Although we did not observe any interaction between altered taste and smell perception and self-reported salt intake in this study, several studies have found that dietary sodium intake is positively correlated with blood pressure level [23 24]. In this study, questionnaire for dietary salt intake was not validated, which may explain the lack of interaction. However, in previous studies based on the Kailuan cohort, self-reported salt intake was significantly associated with future risk of developing cardiovascular disease and stroke [25]. Sodium may be involved in epithelial sodium channel-mediated volume homeostasis and blood pressure regulation in taste receptor cells as well as other tissues including baroreceptors, brain, blood vessels, kidney, and central nervous system in mammals [10 26]. In addition to increased dietary salt consumption and changes in epithelial sodium channel compensating for the loss of taste, smell function may be associated with blood pressure regulation through being involved in the renin-angiotensin system [7]. Recent studies revealed a novel mechanism that olfactory receptors, especially olfactory receptor 78 (Olfr78), is induced by short-chain fatty acid

produced by gut microbiota and plays an important role in up-regulating renin which can in turn stimulate the conversion of angiotensinogen to angiotensin I and further result in an increase in blood pressure [8 27]. Though participants' gut microbiota compositions were not determined in our study, our results support the experimental findings that senses of taste and smell are associated with blood pressure regulation. These findings indicate the potential importance of sensory receptors in mammalian metabolic pathways besides their traditional roles in sensory tissues.

Taste and smell disturbances have been frequently reported in the elderly with compromised taste and smell functions and people using certain medications, including antihypertensive drugs, antihyperlipidemic drugs, antibiotics, neurologic drugs, and endocrine drugs [28]. Several medical conditions can also lead to the impairment of taste and smell functions due to alteration of metabolic as well as cellular pathways, such as cancer, diabetes, and thyroid disease [29]. However, the relationship between taste and smell functions and disease outcome is relatively understudied. Understanding the potential impact of taste and smell function on the risk of disease development would be valuable in determining disease prevention strategies. To our knowledge, this current study is the first study to examine the association between taste and smell perception and changes in blood pressure indexes in human.

The major limitation of this study is that different methods of blood pressure measurement were utilized at baseline and study end point, which would introduce systematic errors in the assessment of blood pressure. To address this limitation, we examined the differences in blood pressure changes over two-year follow-up among four taste and smell perception groups, which is unlikely affected by the change of blood pressure measurement approaches. Another limitation of this study is the lack of participants' dietary intake information other than self-reported sodium intake. However, dietary intake could be an intermediate step in the association between chemosensory function and change in blood pressure and thus may not be considered a confounder. It is also important to note that participants' taste and smell functionality was determined by using questionnaire containing self-reported senses of taste and smell problems. While self-reported taste and smell perception can reflect participants' perceived physical condition of taste and smell, clinical diagnosis using standard assessments including tongue tip taste test, whole-mouth taste test, and scratch and sniff test are regarded as more sensitive and specific [30]. In addition, participants' allergic conditions (e.g. allergic rhinitis) which might affect taste and smell perception were not assessed in this study. However, our findings were not changed after excluding participants with hs-CRP ≥ 3 mg/L. Furthermore, only participants who had both altered taste and smell perception were associated with larger blood pressure increases and the sample size in this group is rather small (n=30). Our findings should thus be interpreted with caution.

In summary, our results demonstrate that individuals with self-reported altered taste and smell perception had larger increases in blood pressure independent of known risk factors. Because of several potential limitations mentioned above, our findings should be considered preliminary. These findings indicate that senses of taste and smell may be associated with the risk of incident hypertension and blood pressure trajectories and may provide insights for future studies regarding risk factors for hypertension.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Abbreviations used:

BMI	body mass index
hs-CRP	high-sensitivity C-reactive protein
eGFR	estimated glomerular filtration rate

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Highlights

- This study is the first study to examine the association between taste and smell perception and changes in blood pressure indexes in human.
- This observation may provide preliminary insights for identifying novel risk factors for hypertension and improving our understanding regarding pathogenesis of hypertension.

Figure 1.

Flow chart of study participant recruitment and analysis process. There were 12,990 participants from a subset of the Kailuan cohort recruited in 2012. After excluding 634 participants without chemosensory and blood pressure measurement in 2012, 5,877 participants with hypertension and usage of any antihypertensive medications at baseline, and 1,289 participants without blood pressure measurement in 2014, 5,190 participants were included for primary analysis. In sensitivity analysis I, 246 participants with certain chronic diseases were excluded. In sensitivity analysis II, 707 participants with high-sensitivity C-reactive protein (hs-CRP) ≥ 3 mg/L were excluded. In sensitivity analysis III, multiple imputation was conducted to replace the missing blood pressure at study end point with plausible values for 1,289 participants who were free of hypertension and antihypertensive medications at baseline.

Table 1.

Baseline characteristics of cohort in 2012 by taste and smell perception

	# of individuals	No altered perception	Altered taste perception only	Altered taste and smell perception only	Altered taste and smell perception	<i>p</i> -value ⁵
Age (years) ^{1,2}		49.0 ± 0.2	51.5 ± 2.1	54.3 ± 1.2	52.5 ± 2.0	<0.001
Sex (%)						0.33
Men		78.2	74.1	74.4	90.0	
Women		21.8	25.9	25.6	10.0	
BMI (kg/m ²) ^{1,3}		24.2 ± 0.1	25.1 ± 0.6	24.7 ± 0.4	25.0 ± 0.6	0.12
Education level (%)						<0.001
Primary		5.3	7.4	17.1	10.0	
Middle		81.9	66.7	75.6	90.0	
College		12.9	25.9	7.3	0.0	
Physical activity (%)						0.003
Never		47.1	55.6	59.8	20.0	
Less than 4 times/week		40.5	44.4	26.8	66.7	
More than 4 times/week		12.5	0.0	13.4	13.3	
Salt intake (%) ⁴						0.03
Low		14.6	11.1	6.1	6.7	
Medium		75.2	88.9	81.7	93.3	
High		10.2	0.0	12.2	0.0	
Smoking status (%)						0.94
Never		56.7	63.0	51.2	53.3	
Past smoker		5.1	3.7	4.9	6.7	
Current smoker		38.3	33.3	43.9	40.0	
Alcohol consumption (%)						0.21
Never		60.0	74.1	67.1	60.0	
Past drinker		29.4	14.8	18.3	26.7	
Current drinker		10.6	11.1	14.6	13.3	

	Altered taste and smell perception			Altered taste and smell perception only		Altered taste and smell perception	<i>p</i> -value ⁵
	No altered perception	Altered taste perception only	Altered smell perception only	27	82	30	
# of individuals	5,051						
Diabetes (%)	7.0	7.4	8.5			6.7	0.76
Dyslipidemia (%)	25.4	22.2	30.5			13.3	0.70
History of myocardial infarction (%)	0.6	0.0	1.3			0.0	0.84
History of stroke (%)	1.7	3.7	4.9			3.3	0.13
History of cancer (%)	0.2	0.0	0.0			0.0	0.97
Head injury (%)	2.1	7.4	3.7			6.7	0.07
Blood pressure ^{1,3}							
Systolic (mmHg)	116 ±0.2	114 ±2.0	115 ± 1.1			121 ± 1.9	0.02
Diastolic (mmHg)	77.1 ±0.1	74.4 ± 1.2	76.6 ±0.7			77.3 ± 1.1	0.13
Estimated glomerular filtration rate (eGFR) (ml/min/1.73m ²) ^{1,3}	104 ±0.3	98.1 ±3.4	104 ±2.0			96.1 ±3.3	0.03

¹ Shown as mean ± standard error (SE)² Adjusted for sex³ Adjusted for age and sex⁴ Categorized based on participants' self-reported dietary salt intake⁵ Differences across four categories

Table 2.

Mean differences of systolic blood pressure (95% confidence interval) after two-year follow-up according to taste and smell perception

Systolic blood pressure (mmHg)	No altered perception	Altered taste perception only	Altered taste and smell perception	
			Altered smell perception only	Altered taste and smell perception
Model 1 ¹	# of individuals	5,051	27	82
		0 (ref.)	1.1 (-4.1, 6.4)	-1.7 (-4.8, 1.3)
Model 2 ²	# of individuals	4,818	24	75
		0 (ref.)	1.0 (-4.2, 6.2)	-1.7 (-4.7, 1.3)
Excluding participants with myocardial infarction, head injury, cancer, and stroke at baseline ²		0 (ref.)	-0.3 (-5.7, 5.2)	-1.6 (-4.7, 1.5)
Excluding participants with hs-CRP ≥ 3mg/L ²		4,367	22	67
		0 (ref.)	1.7 (-4.0, 7.4)	-1.9 (-5.2, 1.4)

¹ Adjusted for age, sex, and systolic blood pressure at baseline

² Adjusted for covariates in model 1 plus education level, physical activity, salt intake, smoking status, alcohol consumption, body mass index (BMI), diabetes, dyslipidemia, high-sensitivity C-reactive protein (hs-CRP), and estimated glomerular filtration rate (eGFR)

Table 3.

Mean differences of additional blood pressure index (95% confidence interval) after two-year follow-up according to taste and smell perception

	No altered perception	Altered taste and smell perception	
	Altered taste perception only	Altered smell perception only	Altered taste and smell perception
# of individuals	5,051	27	82
			30
Diastolic blood pressure (mmHg)[/]	0 (ref.)	1.7 (-1.7, 5.1)	-1.2 (-3.2, 0.7)
			3.1 (-0.1, 6.3)
Pulse blood pressure (mmHg)[/]	0 (ref.)	-1.0 (-5.2, 3.3)	-0.7 (-3.2, 1.7)
			2.7 (-1.3, 6.8)
Mean arterial pressure (mmHg)[/]	0 (ref.)	1.7 (-1.8, 5.2)	-1.4 (-3.4, 0.7)
			3.8 (0.4, 7.1)

[/] Adjusted for age, sex, blood pressure index at baseline, education level, physical activity, salt intake, smoking status, alcohol consumption, body mass index (BMI), diabetes, dyslipidemia, high-sensitivity C-reactive protein (hs-CRP), and estimated glomerular filtration rate (eGFR)