Relationship between olfactory and gustatory functions: The Iwaki Health Promotion Project 2019
（嗅覚と味覚の関係性についての検討 ～岩木健康増進プロジェクト 2019 の結果から～）

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ABSTRACT

Objective: Olfactory and gustatory functions are important sensory aspects in humans. Although they are believed to influence each other, their interrelationship is not well understood. In this study, we aimed to investigate the relationship between the olfactory and gustatory functions based on the results of a large-scale epidemiological study (Iwaki Health Promotion Project) of the general local population.

Methods: We analyzed 565 participants who underwent taste and olfactory tests in the 2019 Iwaki Project. Gustatory function was tested for four taste qualities (sweet, sour, salty, and bitter) using whole-mouth taste tests. Olfactory function was tested using the University of Pennsylvania Smell Identification Test modified for Japanese (UPSIT-J). We evaluated sex-related differences between olfactory and gustatory functions and the effects of various factors on olfactory identification using multivariate analysis. Furthermore, we compared the percentage of accurate UPSIT-J responses between the normal and hypogeusia groups. We also analyzed the effects of taste and olfactory functions on eating.

Results: Olfactory and gustatory functions were lower in men than in women. Among the four taste qualities, salty taste was the most closely associated with olfactory identification ability, with lower olfactory scores of salty taste in the hypogeusia group than in the normal group. Moreover, the hyposmia group had higher daily salt intake than the normal olfaction group in women.

Conclusion: These results suggest that olfactory identification tests may be useful in predicting elevated salt cognitive thresholds, leading to a reduction in salt intake, which may contribute to hypertension prevention.

Keywords: olfactory dysfunction, hypogeusia to salty taste, olfactory identification test, salt reduction, hypertension

1. Introduction

Olfaction and gustation are important sensory functions in humans. Olfactory function is associated with various factors, such as dementia, smoking, and exercise habits [1-3], and olfactory evaluation is useful for the early detection of dementia [4-6]. Gustatory function is involved in diverse diseases, such as diabetes and dementia [7-9].

Olfactory and gustatory functions are believed to influence each other. One indication of the relationship between olfaction and taste is flavor disorder. Some patients complain of both olfactory and taste disorders; some, of course, have impaired olfactory and taste function, while others are diagnosed with flavor disorders in which taste function is normal and olfactory function is impaired [8]. Despite the importance of olfactory and gustatory functions for a healthy life, few epidemiological studies have comprehensively investigated the relationship between these two functions.

The present study aimed to investigate the relationship between olfactory identification ability and the detection and cognition thresholds of four taste qualities (sweet, sour, salty, and bitter), as well as blood data and dietary content in the participants of the Iwaki Health Promotion Project 2019. This community-based program that aims to promote healthy life expectancy has been conducted since 2005 in the Iwaki area of Aomori Prefecture [10].

2. Materials and Methods

2.1. Participants

In total, 1,073 individuals participated in the 2019 Iwaki Project. Gustatory testing was conducted for all ages, whereas olfactory testing was conducted only for 593 participants aged ≥50 years. A total of 565 (220 men and 345 women) participants with no missing data from either test were enrolled in the present analysis. Written informed consent was obtained from all the participants. This study was approved by the Ethics Committee of Hirosaki University Graduate School of Medicine, Hirosaki, Japan (No. 2019-009).

2.2. Assessment of health-related information

Blood tests, including serum zinc, copper, and iron levels, were performed on all participants. Smoking status, alcohol consumption, medical history, and perceived olfactory and gustatory disorders were assessed using a self-administered questionnaire. Respondents who indicated that they were currently in the habit of smoking and drinking alcohol were defined as having a history of smoking and drinking, respectively. Nutrient and food intake over the past month were also investigated using the Brief-type Self-administered Diet History Questionnaire (BDHQ).

2.3.Assessment of gustatory function

Gustatory function was tested for four taste qualities (sweet, sour, salty, and bitter) using whole-mouth taste tests with D-saccharose, citric acid, sodium chloride, and quinine hydrochloride, respectively. The concentrations and volumes of the test solutions were based on previous reports [11,12]. Preliminary tests were conducted on 30 men and women aged 65–79 years in Chiba City and 63 men and women aged 54–86 years in Hirosaki City. The final concentration interval was set at 2.83× dilutions to derive five concentrations (Sweet: 0.078, 0.22, 0.63, 1.8, and 5.0%; Sour: 0.0013, 0.0038, 0.011, 0.03, and 0.086%; Salty: 0.02, 0.055, 0.16, 0.44, and 1.3%; Bitter: 0.0005, 0.0014, 0.004, 0.011, and 0.032%), and the volume of the test solution was set at 6.6 mL. The test solutions for each taste quality were scored from 1 to 5 in order of the lower concentration. If a correct answer could not be obtained even at the highest concentration, the score was set as 6. The participants were instructed to answer with the following six options: (1) sweet, (2) sour, (3) salty, (4) bitter, (5) unknown, and (6) no taste. When they answered correctly, they rinsed their mouth with water and proceeded to the next taste. The test was conducted using an ascending method, with the score for answering one of the tastes as the detection threshold and the score for the correct answer as the recognition threshold. Based on preliminary tests and previous reports [11-13], we classified four or more scores as hypogeusia.

2.4.Assessment of olfactory identification function

The olfactory identification function was evaluated using the University of Pennsylvania Smell Identification Test series modified for the Japanese market (UPSIT-J) (Eisai, Tokyo, Japan) [14]. When the participant scratched the card with a cotton swab, the encapsulated microcapsules broke, generating an odorant. Eight odorants (strawberry, chocolate, mint, smoke, rose, onion, grape, and soap) were used in the test, and 1 point was scored for each correct answer, for a total score of 8 points. We classified the UPSIT-J scores as follows: ≥6, normal, and ≤5, hyposmia, based on the report [1].

2.5.Analysis of the relationship between gustatory and olfactory functions

Sex differences in olfaction and gustation were also examined. Multivariate analysis was used to investigate the effects of various factors on olfactory identification ability, accounting for potential confounding factors, including four taste qualities (detective or cognitive thresholds), age, sex, life history (smoking and alcohol consumption), blood tests (serum iron, copper, and zinc levels), and medical history (hypertension, diabetes, cancer history, depression, allergic rhinitis, and chronic sinusitis).

To determine the influence of gustation on olfaction, the percentages of correct responses to each odorant we compared between the normal and dysgeusia groups. Additionally, the effects of gustatory and olfactory functions on eating were analyzed.

2.6.Statistical analyses

Comparisons between the two groups were performed using multivariate analyses, the Mann–Whitney U-test, and χ^2 test. A p-value of ≤ 0.05 was considered statistically significant. SPSS version 22.0 J software (IBM, Armonk, NY, USA) was used for statistical analyses.

3. Results

3.1.Demographics, medical history, and blood test values of the participants

After excluding those with missing data, 565 (220 men and 345 women) participants were enrolled in the present analysis. The mean age of the participants was 64.4 ± 7.8 years for men and 64.2 ± 8.1 years for women, with no significant differences between them ($p = 0.567$, χ^2 test). Regarding lifestyle habits, the smoking rates were 19.0% for men and 5.9% for women, and the drinking rates were 72.3% for men and 29.3% for women, both of which were significantly higher in men than in women ($p < 0.001$, respectively, χ^2 test).

Regarding medical history, hypertension was more prevalent in men than in women, and depression was more prevalent in women than in men; however, no significant differences were detected in other diseases, including nasal complications (Table 1). Blood tests showed that serum zinc levels were significantly lower ($p = 0.044$), whereas serum copper levels were significantly higher in women than in men ($p < 0.001$).

3.2.Sex differences between gustatory and olfactory identification tests

Detection thresholds for sour and salty tastes were significantly higher in men than in women. Similarly, the cognitive thresholds for sour and salty tastes were significantly higher in men than in women, and significant differences were also observed for bitter taste (Figure 1). In the olfactory test, the overall UPSIT-J total scores were 6.4 ± 1.8 for men and 7.0 ± 1.4 for women, which was significantly lower for men than for women ($p < 0.001$, U-test). The frequencies of hyposmia (UPSIT-J score of ≤5) and hypogeusia (cognitive function test score >3) in the sour and salty tastes were significantly higher in men than in women (hyposmia: 24.1% vs. 11.0%, $p < 0.001$; hypogeusia to sweet taste: 50.0% vs. 42.3%, $p = 0.074$; hypogeusia to sour taste: 15.9% vs. 7.2%, $p = 0.001$; hypogeusia to salty taste: 35.0% vs. 24.1%, $p = 0.005$; hypogeusia to bitter taste: 45.5% vs. 32.8%, $p = 0.051$, χ^2 test).

3.3.Effects on olfactory identification ability and cognition thresholds of salty taste

Multiple logistic regression analysis of the factors associated with olfactory impairment was performed (Table 2). The results showed that age and sex were significantly associated with the olfactory identification ability. Among the four taste qualities, only an increase in the salt cognitive threshold was significantly associated with olfactory function. Hypertension was also associated with olfactory impairment. In addition, the effect on salt cognitive thresholds was examined using multiple logistic regression analysis (Table 2B). The results showed that sex, alcohol consumption, history of chronic rhinosinusitis, and olfactory identification ability were significantly associated with the salt cognitive thresholds. Although the cognition thresholds of sweet, sour, and bitter tastes were similarly examined, no significant relationship with the olfactory identification ability was observed.

3.4.Relationship between olfactory identification and gustatory functions

In the comparison of the percentage of correct responses for each odorant and hypogeusia to salty taste, men in the hypogeusia group had significantly lower percentages of correct answers than those in the control group for strawberry, mint, smoke, rose, and onion (Figure 2A). Significant differences were also observed in women for chocolate, grapes, and soap (Figure 2B). No differences were observed between the two groups in terms of hypogeusia to sweet and bitter tastes, and the percentage of correct responses in hypogeusia to sour taste was significantly lower for strawberry and onion in men (hypogeusia to sour tastes vs. normal; strawberry: 69% vs. 83%, p = 0.043, onion: 63% vs. 86%, p = 0.001, χ^2 test) and onion in women (80% vs. 93%, p = 0.014, χ^2 test).

In addition, the average daily salt intake calculated from the BDHQ was assessed in the hyposmia and normal groups. No difference was observed in men between the two groups (normal vs hyposmia: 12.41g vs. 12.27g, p = 0.669, Mann–Whitney U-test). However, women in the hyposmia group consumed significantly more salt per day than those in the normal group (normal vs. hyposmia: 10.36g vs. 11.49g, p = 0.024, Mann–Whitney U-test).

4. Discussion

Women have better olfactory function than men [14], and various factors are thought to contribute to the sex-related differences. Because the frequency of exposure to smells is important for olfactory function [15], women have more exposure to smells in their daily lives, such as cooking, than men [16], which may have a positive effect on olfactory function. The discrepancy is also attributed to smoking, which induces inflammation of the olfactory mucosa and is more common in men than in women [17]. It is also due to the complex relationship between sex hormones and olfactory function [14,18]. In addition, recent studies have reported that differences in adiponectin between men and women are associated with sex differences in olfactory function [19]. The present results, showing higher UPSIT-J scores in women than in men, are also consistent with those of previous reports [14-18].

In terms of gustatory function, women are superior to men, and sex differences become more pronounced with age. Tomita et al. attributed this effect to the fact that women are more involved in cooking and have more opportunities to discriminate tastes than men, as with olfaction [20]. Moreover, men have greater thickening and keratinization of the tongue papillae than women due to smoking and alcohol consumption, among other factors [21]. Sex differences may also vary according to taste quality. Functional magnetic resonance imaging has shown that women have higher neural responses to citric acid stimulation in the thalamus and insula during fasting than men [22]. In the present study, significant sex-related differences were also identified in the recognition thresholds for bitter, sour, and salty tastes. Smoking affects bitter taste thresholds [23, 24], and a higher smoking rate in men may have influenced a decrease in bitter taste sensation.

In the present study, biochemical tests also showed significant sex-related differences in blood zinc and copper levels. Zinc levels are higher in men than in women because zinc is found in muscles and bones. Zinc and copper exhibit a competitive relationship in the body, and a zinc/copper ratio of less than 0.7 indicates a potential zinc deficiency [25]. Although zinc deficiency is a well-known cause of taste disorders, there is no significant difference in the taste threshold between the normal and zinc deficiency groups [26]. Moreover, in the previous reports of this project, no difference in the proportion of normal and taste-impaired participants with serum zinc/copper <0.7 [27]. Overall these findings suggest that the sex-related differences in zinc and copper concentrations observed in this study did not significantly affect gustatory function.

In addition, the results of multiple logistic regression analysis in our study suggested an interaction between olfactory identification and the recognition threshold of salty taste. The five basic tastes, including umami, are perceived by three taste cells: types I, II, and III. Sweet, bitter, and umami tastes are sensed by G protein-coupled receptors expressed on type II cells, whereas acidity is perceived by type III cells via the H^+-selective ion channel otopetrin1 [28]. Salty taste reception can be divided into amiloride-sensitive and amiloride-insensitive pathways. As with other taste qualities, it is transmitted from the stimulated gustatory nerve to the lower brainstem and projected through the thalamus and amygdala to the cortical gustatory cortex. The amiloride-sensitive pathway mediates salty preference and involves epithelial Na channels (ENaC), whereas the amiloride-insensitive pathway mediates saltiness aversion. Salt concentrations of approximately 100–200 mM are considered the preferred concentration [29], and all five concentrations of salty taste used in the taste test in the present study were in the amiloride-sensitive range. Moreover, there are four subtypes of ENaC: α, β, γ, and δ. Each subtype is expressed in the human nasal epithelium [30], and approximately 50% of amiloride-sensitive Na+ transport is associated with δ-ENaC [31], which may interact with the degenerin (DEG)/ENaC family of sodium channel subunits [31]. In Drosophila, PPK 25, a subunit of the DEG/ENaC family, amplifies olfactory signals [32]. These results indicate an interaction between olfactory function and amiloride-sensitive salt taste reception, suggesting that ENaC may also play an important role in human olfactory function. In the present study, the male group with hypogeusia to salty taste had significantly lower UPSIT-J scores for five odorants (strawberry, mint, smoke, rose, and onion), whereas the female group showed significant differences for three odorants (chocolate, grape, and soap). Although the cause of the sex difference is unknown, we believe that these results provide important insights into the relationship between olfactory and gustatory functions.

Notably, in the present study, salt intake was not associated with olfactory function in men; however, salt intake was significantly higher in the hyposmia group than in the control group. Excessive salt intake can also lead to hypertension. Consequently, the risk of heart disease, stroke, and dementia increases. The number of patients with hypertension is increasing worldwide, highlighting the importance of salt reduction [33]. In Japan, compared to women, men are less likely to cook meals after marriage and are strongly influenced by the saltiness preferences of their wives who cook the meals [34, 35]. Therefore, early detection of a woman's decreased sense of smell may lead to the detection of hypogeusia to salty taste, which in turn may lead to salt reduction for her and her family. However, early intervention is challenging because elevated taste thresholds are often considered a preference, and gustatory testing is less common than olfactory identification testing. If an elevated salt taste perception threshold can be detected early, excessive salt intake may be prevented using the olfactory identification test, which is important for dementia, thereby reducing the risk of developing various diseases, including hypertension.

This study has some limitations. All participants in this study were interested in their health and may be healthier than other community members. Second, the average daily salt intake of Aomori residents is 11.3 g for men and 9.7 g for women, which is higher than those in other regions [36]. Additionally, in this study, olfactory function tests were performed only for patients over 50 years of age. These selection biases should be considered when targeting the general population.

5. Conclusion

In the present study, we investigated the relationship between olfaction and gustation functions based on the results of a large-scale health examination. We identified sex-related differences in olfactory identification ability and gustatory function. Among the four taste qualities examined, increased salty recognition threshold was the most strongly associated with olfactory identification ability. This study suggests that olfactory tests may be useful in predicting an increase in salty perception threshold, which may lead to decreased salt intake for a healthy life.

Author contributions

All authors (1) made substantial contributions to the study concept, data analysis, or interpretation; (2) drafted the manuscript or revised it critically for important intellectual content; (3) approved the final version of the manuscript to be published; and (4) agreed to be accountable for all aspects of the work.

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Conflict of interest

The authors declare no conflicts of interest associated with this manuscript.

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Figure legends

Figure 1. Sex differences in the taste test (mean). (A) Detection threshold and (B) cognition threshold

$^{*}p < 0.05$, $^{**}p < 0.01$, Mann–Whitney U-test

Figure 2. Differences in the University of Pennsylvania Smell Identification Test series modified for the Japanese market (UPSIT-J) scores between the hypogeusia to salty taste

and normal groups. (A) Men and (B) women

$^{*}p < 0.05$, $^{**}p < 0.01$, χ^2 test