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Influence of Sourness on Higher Brain Functions

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Abstract

We investigated whether change of emotion related to sourness during chewing causes higher brain functions by using mental arithmetic test.

Subjects comprised 120 healthy individuals. The mental arithmetic test was performed under four conditions: chewing lemon-flavored gum (Standard gum, as a delicious gum); gum with 6 times the citric acid component of the Standard gum (Strong-sour gum, as an unpleasant gum); the Standard gum with citric acid component removed (Without-sour gum); and no chewing (Control). After chewing gum, subjects completed a subjective sensory evaluation about taste and deliciousness.

The number of answers was lowest while chewing Without-sour gum compared to chewing the other gums or control. No significant correlation was found between performances of the mental arithmetic test and subjective sensory evaluation, except for a weak negative correlation with taste.

These results suggest that the sourness might have influence on higher brain functions.

Keywords: Taste; Flavor; Perception; Higher brain function; Sourness

Introduction

Chewing is an essential behavior in daily life. In addition to the well-known functions in digestion and absorption, the emotion generally experienced while eating (chewing) is tightly linked to hedonic (emotional) systems in the human brain [1]. The hedonic aspect of chewing is greatly affected by the taste and flavor properties of food [2]. Chewing palatable foods (e.g., gum with good taste and flavor) can induce positive emotions [3]. The underlying neural mechanisms begin with detection via taste and odorant chemoreceptors. Sensory signals are subsequently processed individually in the gustatory and olfactory neural circuits of the brain and finally integrated as a sensation of flavor in the insular and orbitofrontal cortical areas [4]. This cortical "flavor" information is further transmitted to the brain reward system, including the nucleus accumbens, midbrain dopamine areas, amygdala and hypothalamus [5,6]. Moreover, chewing can relieve stressful conditions that result in the release of various hormones and neurotransmitters [7,8].

We have been focusing on correlations between the taste and flavor from eating food (delicious/unpleasant tasting) and autonomic nerve activity [9]. We also conducted a sensory test (Visual Analog Scale (VAS)) after subjects chewed gum created with combinations of various tastes and flavors, and evaluated the taste and flavor of subjects while chewing. The results showed that when subjects chewed the gum that they felt to be the most tasteful and flavorful, blood flow in bilateral cerebral hemispheres was mostly increased [9]. This indicated that cranial cells are activated by the perception of ingesting tasteful and/or flavorful food. During mastication, mass sensory inputs flow into the brainstem through the trigeminal nerve, enhancing activity of the brainstem reticular formation, and the arousal level increases to a clearly awakened state [10]. A functional magnetic resonance imaging study by Hirano et al. [11] found that chewing may improve or recover the process of working memory. Furthermore, brain mapping methods have clarified that neuronal activity in an extensive region of the brain increases during gum chewing [12,13].

Specifically, chewing a «sweet delicious gum» was suggested to cause a strong expression of «pleasant» emotions and activate the reward-related cortex (subcallosal region, caudomedial orbitofrontal cortex, insula/operculum, striatum, and midbrain) [5,14]. On the other hand, Small et al. [15] performed positron emission tomography to evaluate brain blood flow when liquids combining various tastes and flavors were dropped into the oral cavity, finding that stimulation by mismatched combinations of tastes and flavors (e.g., sour taste and coffee flavor) increased blood flow more than matched combinations of tastes and flavors (e.g., sweet taste and strawberry flavor). These results are very interesting, with both «good taste» and «bad taste» foods showing increases in blood flow, and a subjective perception of taste/flavor and higher brain function may not show a simple linear correlation. For example, sourness taste is known to evoke emotions of bad tasting [16], meanwhile, it may stimulate the brain and increase cerebral blood flow.

In general, prolonged exposure to stressful conditions is considered to lead to a loss of neurons, particularly in the hippocampus. Glucocorticoids secreted during stress may contribute to neuron loss. The depression caused by the stress associated with the hippocampal atrophy typically involves significant hypersecretion of glucocorticoids [17]. Steroids show a variety of adverse effects in the hippocampus, including overt neuron loss. The loss of cerebral nerve cells is associated with changes to higher brain functions [17]. Mental arithmetic is used as a gauge of the level of brain function, and also has the advantage of being able to be conducted while chewing gum. There is a general consensus that in humans, higher brain functions are activated during calculation tasks [18].

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The present research used a mental arithmetic test to evaluate the influence on higher brain functions when chewing gum that included taste components contained appropriate acidity, as compared to gum including taste components includes excessive strong sourness, thereby investigating whether changes in the sourness of food changes higher brain functions in a short period of time.

Methods

This research was conducted with the approval of the ethics board of Hyogo College of Medicine (approval no. H24-1318). The study was carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

Test subjects

Test subjects were 120 non-smoking adults (60 men, 60 women; mean (SD: Standard Deviation) age, 29.5 ± 10.3 years) with healthy jaws and teeth who could continuously chew gum and were staff or students at Hyogo College of Medicine. Test subjects were given a thorough explanation of the contents of the study in advance, and only those who provided voluntary consent were included as subjects. The experiment was conducted at least 3 h after eating.

Foods used in the experiment

Commercially available lemon-flavored gum (Free zone; Lotte, Tokyo, Japan; Standard gum) was used as the "standard sourness» food in the experiment. To investigate the influence of changes in the amount of citric acid, we also used a gum with 6 times the citric acid content of the standard gum (Strong-sour gum), and a gum with the sourness components removed (Without-sour gum). Before the experiment, we adjusted the hardness of the gum so that adjusting the sourness components would not change the hardness of the gum, and then unified the volumes of the 3 types of gum. Test subjects were blinded to the type of gum provided, and the appearance of all three gums was identical. Production of the gums was outsourced to an external company (Nagaoka Sangyo, Nishinomiya, Japan).

Experiment protocol

The experimental tasks were limited to 2 attempts per subject. The reason for this 2-attempt limit was that a learning effect was found in the mental arithmetic test. Performance of mental arithmetic tests twice in one day in a pilot study showed that results in the second experimental task were better than in the first experimental task. Test subjects were randomly allocated to one of 6 groups (Figure 1A). Each group was then separated into 2 sub-groups, for a total of 12 groups. The 12 groups all underwent different experimental procedures. The groups were adjusted so that all groups had a 1:1 ratio of males to females using stratified randomization.

The mental arithmetic questions consisted of addition, subtraction, multiplication and division of whole numbers, each comprising no more than 2 digits. The mental arithmetic test was a written test. Three sheets of A4 paper containing 100 questions each were given to the subject, who was then instructed to answer the questions in the order they appeared, to go to the next sheet after completing one sheet, and to ask for another sheet when completing the third sheet or any subsequent sheet. The first-time and second-time tasks contained separate problems, and all 120 participants answered the same mental arithmetic test problems.

The experiment protocol is shown in Figure 1B. A total of 4 patterns of experimental task were undertaken with the mental arithmetic test: while chewing each of the 3 types of gum (Standard, Strong-sour and Without-sour); and while chewing nothing (Control). After entering the experiment room, the test subject sat in a chair and received an explanation regarding the flow of the experiment from an operator. Next, we had the test subject write their information (height, weight, date of birth) on a sheet of paper and provided instructions regarding how to complete a VAS answer sheet, as well as how to perform the mental arithmetic test. The subject rested for 9 min, and from 1 min before starting the experiment, we played the sound of a metronome set to a 70 cycles/min rhythm and instructed the test subject to time the speed of chewing to match the metronome rhythm. The reason for setting the chewing rhythm to 70 cycles/min was that the results of a preceding study showed that around 70 cycles/min was the free-chewing speed [19]. No instructions were given regarding which side of the mouth to chew with. Chewing was also started 1 min before the mental arithmetic test, and the mental arithmetic test was conducted for a further 5 min after that. Test subjects were instructed to time their chewing with the sound of the metronome. Controls who were not chewing were under the same environment (including the metronome sound) as the other tasks except for gum chewing. After the mental arithmetic test was complete, the test subject completed VASs regarding taste (terribly bad taste=0, fantastically good taste=100), flavor (terribly bad flavor=0, fantastically good flavor=100), and deliciousness (not at all delicious=0, fantastically delicious=100). After chewing, the test subject rinsed their mouth with mineral water, rested for 10 min, and then conducted the 2nd task.

Statistical analysis

The number of questions answered, ratio of incorrect answers, and number of correct answers were calculated from the results of the mental arithmetic test. A two-sample t-test was conducted to compare the 2 groups (first task vs. second task). To investigate the influence of differences in tasks on results of the mental arithmetic test, statistical analysis was conducted using two-way repeated-measures analysis of variance (4 tasks × 2 repeats). In tasks where significant differences were observed, differences due to task differences were evaluated using multiple comparison testing (Fisher's protected least significant difference). Regarding the relationship between subjective feelings during gum chewing and results of the mental arithmetic test, evaluations to find the partial correlation coefficient with age and task order as the control variable were conducted, and values of $P<0.05$ were considered significant.

Results

Experimental condition

A comparison of first time: second time number of answers (mean ± SD, 118.0 ± 43.5:112.3 ± 44.5) for the mental arithmetic test did not show any significant difference ($P=0.28$, paired t-test). A comparison of first time: second time ratio of incorrect answers (mean ± SD, 4.8 ± 3.0:5.1 ± 3.3) likewise did not show a significant difference ($P=0.51$, paired t-test). In other words, no difference would seem to exist between the difficulty levels of mental arithmetic tests.

Examination of the influence of the experiment procedure on the mental arithmetic test showed that subjects taking the mental arithmetic test while chewing the Without-sour gum answered significantly fewer answers the second time compared to the first time ($P=0.004$, t-test). A significant increase in the ratio of incorrect answers was also seen

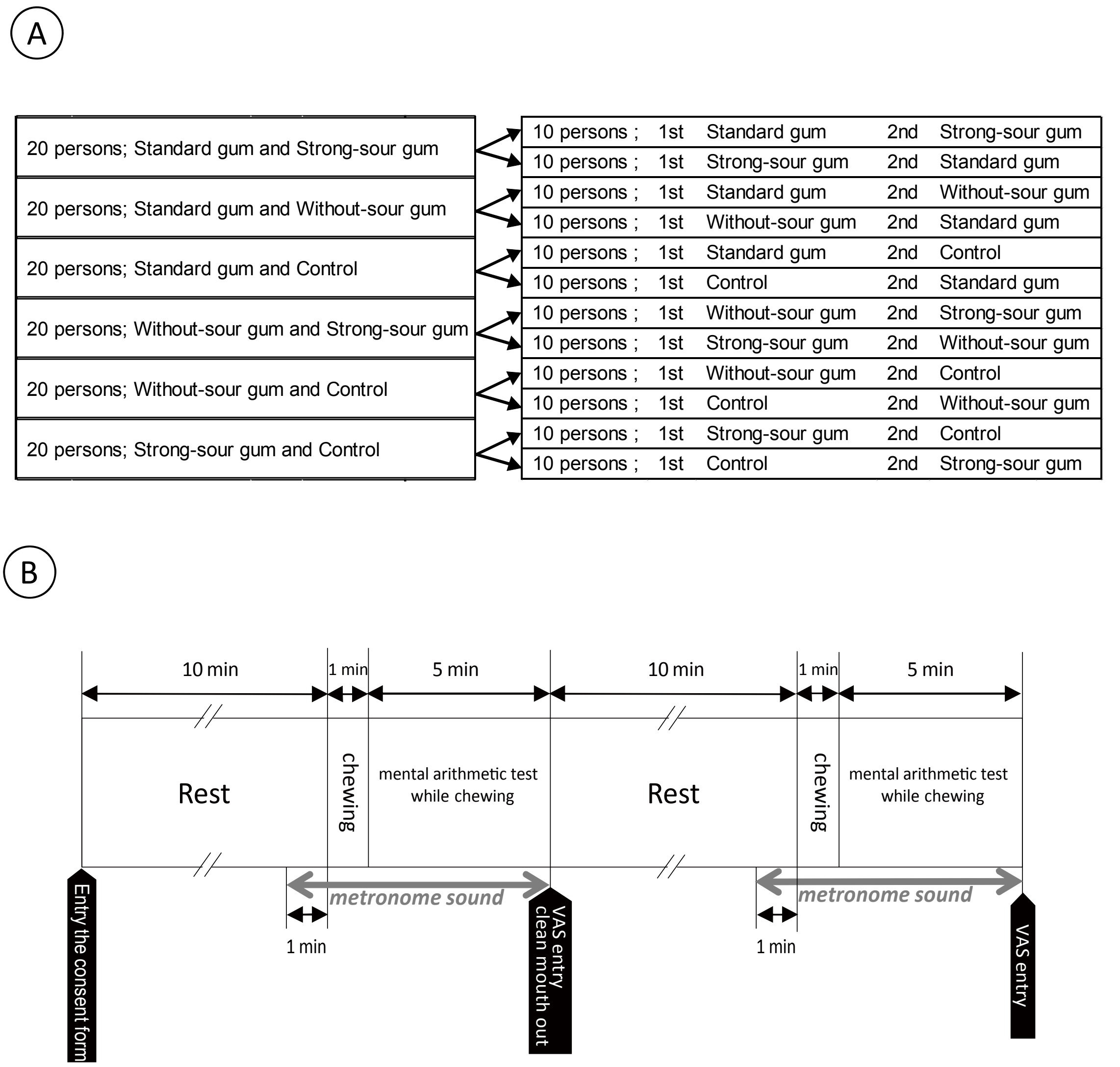

Figure 1: Division of test subjects into groups and experiment protocol. (A) Division of the 120 test subjects into 12 groups according 4 tasks (mental arithmetic while chewing standard gum, strong-sour gum or without-sour gum, or without chewing (Control)) and 2 attempts for each subject. Standard gum, a sweet, lemon-flavored gum (as delicious gum); Strong-sour gum, 6 times the citric acid content of the Standard gum (as unpleasant gum); Without-sour gum, the Standard gum with citric acid components removed; Control, no chewing. (B) Experimental protocol. The experiment in one subject.

(P=0.01). The Control group answered significantly more questions the second time than the first time (P=0.02, t-test). Based on these results, when conducting multivariate analysis, adjustment using the weighted least squares method was conducted to exclude the influence of task order.

Experiment conditions and influence on results

Mean ages of control, without-sour, strong-sour and standard-sour group subjects were 29.3 ± 9.7, 29.8 ± 11.4, 29.5 ± 9.5 and 30.1 ± 11.2 years, respectively. Mean Body Mass Index (BMI) for the control, without-sour, strong-sour and standard-sour group subjects were 23.3 ± 5.2, 2.6 ± 4.9, 21.7 ± 3.9 and 21.9 ± 4.2 kg/m^2, respectively. No differences in age or BMI were seen by type of gum (P=0.98, P=0.17, respectively; Kruskal-Wallis test).

Sensory evaluations (VAS scores) after chewing the gum are shown in Figure 2. VAS values of the Strong-sour gum were lower in all 4 categories compared to the other 2 types of gum. On the other hand, the perceived taste of Strong-sour gum showed a wide variation in VAS scores, and was clearly influenced by individual preferences. The Standard gum was reported as the most delicious, and VAS scores showed high ratings. Although the flavors involved the same lemon flavor among all gums, the Strong-sour gum had a significantly lower VAS score than the other gums, suggesting that the perceived smell was strongly influenced by subjective feelings.

An evaluation of the influence of the different tastes on the mental arithmetic test is shown in Figure 2. The number of questions answered was lower while chewing Without-sour gum compared to the other 3 tasks (P<0.05). No significant difference in the ratio of incorrect answers was seen among the 4 groups.

Results of an examination of the relationship between subjective analysis of chewing time and results of the mental arithmetic test are shown in Table 1. The partial correlation coefficient between the

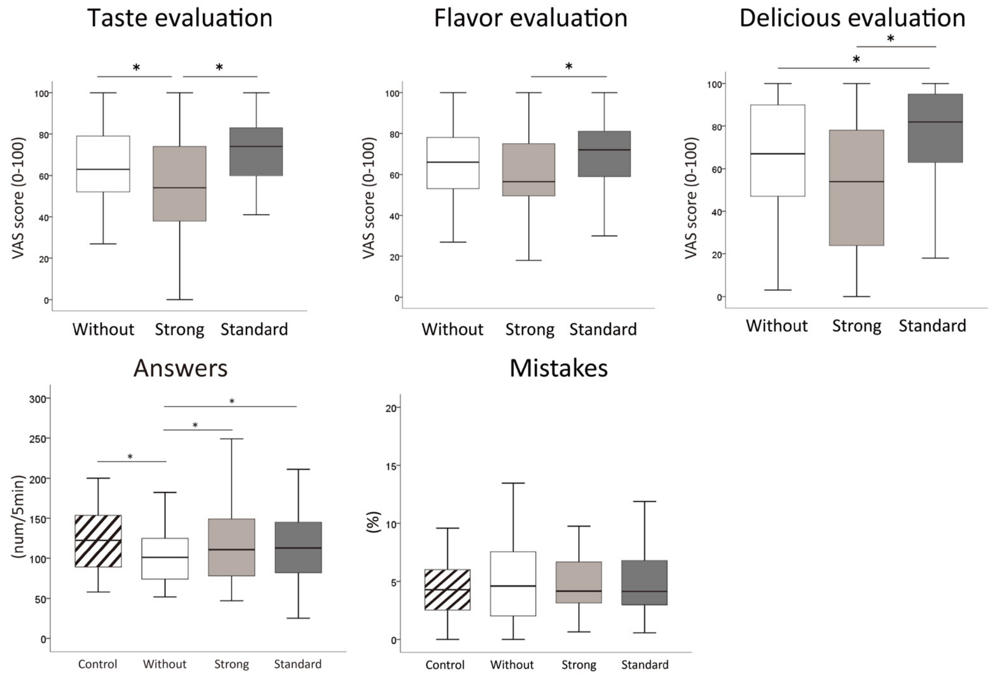

Figure 2: Emotional change and results of mental arithmetic test by 4 tests. Taste, VAS score for taste (0-100); Odor, VAS score for odor; Delicious, VAS score for delicious/bad taste; Answers, number of answers given in 5 min; Mistakes, rate of incorrect answers among all answers (%).horizontal line, median; box, 25th to 75th percentiles; whiskers, 5th and 95th percentiles; *P<0.05, Fisher's PSLD.

		Odor	Delicious	Answer (No.)	Mistake (%)
Taste	R	0.74	0.83	-0.16	-0.16
	P-value	P<0.001	P<0.001	0.03	0.03
Odor	R	-	0.64	-0.11	-0.09
	P-value	-	P<0.001	0.16	0.26
Delicious	R	-	-	-0.08	-0.11
	P-value	-	-	0.29	0.14
Answer(num)	R	-	-	-	0.92
	P-value	-	-	-	P<0.001

R: Partial correlation coefficient for each test; Taste, Visual Analog Scale (VAS) score for taste (terribly bad taste=0, fantastically good taste=100); Flavor, VAS score for flavor (terribly bad flavor=0, fantastically good flavor=100); Preference, VAS score regarding preference (dislike=0, like=100); Delicious, VAS score regarding deliciousness (not at all delicious=0, fantastically delicious=100); Answers, number of answers in the mental arithmetic test; Mistakes (%), rate of incorrect answers in the mental arithmetic test

Table 1: Correlation between subjective sensory evaluation and mental arithmetic test.

number of answers and the mistake rate was higher (0.92, P<0.001). The 4 subjective evaluations each showed strong positive correlations, and a positive correlation was identified between how the taste/flavor was perceived and how the deliciousness was felt. In contrast, the only significant correlation found between results of the mental arithmetic test and subjective evaluation was a weak negative correlation with taste.

Discussion

Regarding experimental foods

Cognitive functions, including those involved in mental arithmetic [20], have been shown to be sensitive to variations in nutrient intake, levels of glucose in the blood, interactions of glucose with other nutrients, e.g., proteins and fats [20,21] and hormones involved in glucose regulation, e.g., cortisol [22].

The gum used in this study as the Standard gum was a commercially available gum, while the Strong-sour gum had 6 times the citric acid content of the Standard gum. Sourness and bitterness are known to evoke emotions of «bad tasting» [16]. Standardization of conditions other than sourness (sweetness, taste, and gum base) among the 3 types of gum offered the advantage of being able to maintain a consistent hardness for the gums. When preparing the test foods for this study, we set commercially available gum as the standard gum and endeavored to create a test gum with the same hardness and flavor as the standard. Because the purpose of the mental arithmetic test while chewing was to clarify the influence of sourness changes on higher brain functions, this research needed to utilize gum as the test food to allow subjects to continue chewing gum for long periods.

Although we prepared the test foods on the presumption that the amount of chewing muscle force expended would be the same when chewing all gums, no significant differences were observed in the «Flavor» and «Like» item responses between Strong-sour gum and Without-sour gum (Figure 2). This means we were unable to prepare test foods in the manner intended. Strong-sour gum resulted in greater secretion of saliva than Without-sour gum (sourness is known to promote saliva secretion [23,24]), and when the sweet taste components and lemon flavor that had been included in the test gum began to dissolve into saliva delivered during chewing, a perception of deliciousness may still have been obtained with Strong-sour gum. In other words, even though the test foods contained the same flavor substances, the reduced sourness may have resulted in less of the taste components being dissolved, making it more difficult to consider the taste.

Regarding results

The occurrence of a difference in the results of the mental arithmetic test due to the order of tasks was also predicted to influence the learning effect for this test. The fact that the Controls who did not chew gum answered a significantly greater number of questions the second time compared to the first time was presumed to be due to the influence of a learning effect for the mental arithmetic test. Test subjects in this study, as staff and students of Hyogo College of Medicine, can be conjectured to not be involved in performing mental arithmetic on a daily basis and thus may not have been used to it. On the other hand, subjects chewing Without-sour gum showed a greater number of answers the first time compared to the second time (mean ± SD first time: second time=117.4 ± 36.7:91.7 ± 36.6; P=0.01). Such results may potentially have been influenced by the lack of sourness. Citric acid has been said to have stimulatory effects on the brain [25]. The amounts of citric acid contained in Standard gum and Strong-sour gum differed, but stimulated the sense of taste as well as stimulating higher brain functions, and thus may have contributed to the difference in mental arithmetic test results between gums.

Limitations of the research

The purpose of this research was to evaluate the influence of sourness changes during chewing on short-term mental arithmetic abilities, but the Controls who were not chewing anything answered the greatest number of questions. Test subjects did not seem used to the act of "chewing", and the test subjects also did not seem accustomed to testing using a mental arithmetic test, which may in turn have influenced performance. We therefore cannot reject the possibility that test subjects were distracted by gum chewing and use of any test gum may draw attentional resources away from the cognitive task.

Conclusion

Within the limitations of this study, these results suggest that differences in sourness can influence short-term higher-order brain function during chewing. In addition, subjective emotional changes during chewing might have little influence on higher brain functions.

Implications

The results of this research suggest that the presence of citric acid in gum can influence the results of mental arithmetic tests. Citric acid is a food found in easily obtainable vinegar, as well as being found in foods commonly found on dinner tables. The amount of citric acid contained in foods and ways to absorb it resulting in influences on higher function may facilitate the development of health foods in the future.

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