치의과학석사 학위논문

A Preliminary Study of Increased Taste Sensitivity in Patients with Temporomandibular Disorders

측두하악장애 환자의 미각 역치에 관한 예비연구

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Abstract

A Preliminary Study of Increased Taste Sensitivity in Patients with Temporomandibular Disorders

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There have been several studies suggesting the overlap between specific brain regions involved in pain and taste perceptions, and the recent studies that the patients with chronic pain such as chronic back pain or fibromyalgia reported increased taste sensitivity. The aim of this study was to evaluate the gustatory function in the patient with temporomandibular disorder (TMD).

Nine TMD patients with no high levels of anxiety and depression, and 17 age- and gender-matched control volunteers were evaluated. Detection and recognition thresholds for sour and umami taste, and ratings of both suprathreshold taste intensities and pleasantness-unpleasantness perceptions for sweet, sour, salty, bitter, and umami stimuli were evaluated in each subject. Graded Chronic Pain (GCP) scale, Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), and both resting and stimulated whole salivary flow rates were measured.

The obtained results were as follows.

1. TMD patients showed significantly lower detection thresholds and recognition thresholds for umami taste than the control subjects.
2. TMD patients showed lower stimulated salivary flow rates than control

subjects.

3. The GCP scales of the subjects were significantly correlated with detection thresholds of umami taste.
4. The GCP scales of the subjects were significantly correlated with stimulated salivary flow rates.
5. The detection thresholds for umami taste were significantly associated with the existence of TMD after adjusting the age, gender, BDI, BAI, and unstimulated salivary flow rates.

Our results showed that the patients with TMD reported increased sensitivities for umami taste, and suggested the possibilities of gustatory function changes in chronic TMD patients.

Keywords : Temporomandibular disorder, Taste, Pain, Saliva, Umami

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A Preliminary Study of Increased Taste Sensitivity in Patients with Temporomandibular Disorders

Introduction

Temporomandibular disorder (TMD) is a clinical condition characterized by pain and dysfunction in the temporomandibular joints and the masticatory muscles. According to the report of the Korean National Health Insurance Service, the number of the patients claiming insurance for TMD was gradually increased from 0.14% to 0.17% between 2003 and 2005.[1] In the 2007 U.S. report, the average annual incidence of TMD was 3.5 %.[2] The prevalence of the subjective orofacial pains symptoms (jaw joint pain, face pain, oral sores, burning mouth, and tooth pain) in Korean elders was reported 42% and the rates of jaw joint pain of all orofacial pains symptoms was 15.5% in 2000.[3] Despite of increasing rate of TMD patients, the pathophysiology and etiology of TMD pain are unknown accurately. We know simply TMD pain characterized persistent, recurring or chronic natures. And TMD pains were appeared to be mostly related to psychological variables.

There have been several studies of sensory perceptions in TMD pains and chronic pain patients. Decreased pressure pain thresholds were reported in patients suffering chronic tension type headache, fibromyalgia, and myofascial temporomandibular pain.[4-6] And decreased heat pain tolerance threshold in the anterior tibialis region was reported in patients with arthrogenous TMD pain patients.[7] These results reveal increased pain sensitivity in chronic pains.

In the recent study of gustatory sensitivity in chronic back pain patients, chronic back pain patients significantly displayed lower detection thresholds of sour taste and higher overall suprathresholds of bitter, salty, sweet and sour tastes than controls. And a report suggested that both chronic back pain and gustatory processing appeared to be related to the overlapped brain regions such as the anterior insula, the medial prefrontal cortex, and the thalamus.[8,9]

Regarding gustatory processing, several brain functional magnetic resonance imaginig (fMRI) studies reported that various tastes stimulation activate the insular cortex, the perisylvian region, the anterior cingulated gyrus, the parahippocampal gyrus, the lingual gyrus, the caudate nucleus, the temporal gyri, and the thalamus.[10,11] Umami and sweet taste stimuli were also shown to activate the insular/opercular cortex, the caudolateral orbitofrontal cortex and a part of the rostral anterior cingulated cortex.[12]

And several studies reported chronic pain conditions appeared to be related to changes of specific brain structures although the involved regions of brain were different by the kind of chronic pains.[14-24] In the review article investigating changes of gray matter in brain of chronic pain patients, common atrophic sites of brain in highest order were the cingulated cortex, the orbitofrontal cortex, the insula and the dorsal pons,[13] which are aforementioned and overlapped cortex activated by taste stimuli. Thus brain regions related to gustatory processing were presumed adjacent or overlapped to brain regions related to chronic pain.[10-12,33,34]

However there are few studies on the possibilities of the association between TMD and taste perception and one retrospective study suggesting the relevance of TMD pain and taste disturbances.[25] In this study, the frequency of taste disturbances was greater in TMD pain patients (6%) than in controls (2%) and correlated with severity of TMD pain. However, severity of taste disturbance was evaluated by only self-reported two questions of Oral Health Impact Profile (OHIP) in this study. So objective further evaluations were thought be needed regarding taste disturbance in TMD patients.

Hence we thought TMD patients might show different taste perceptions or taste pleasantness. Chronic TMD pain condition might be associated to the brain regions related to the other chronic pains or gustatory processing. The aim of this study was to evaluate the gustatory changes in the temporomandibular disorder pain patients.

Methods

1. Subjects

Nine patients with temporomandibular disorders (6 women and 3 men) visited in

the Department of Oral Medicine of Seoul National University Dental Hospital and 17 healthy control volunteers (9 women and 8 men) with no pain or musculoskeletal disorders in orofacial regions were evaluated. The patients were diagnosed as TMD according to the Research Diagnostic Criteria for Temporomandibular disorder (RDC/TMD).[26] The mean ages were 25.2±6.1 years (ranged 17-36 years) in TMD patients and 29.8±2.0 years (ranged 27-33 years) in control subjects. Age, gender, and suprathreshold taste intensity for 6-n-propylthiouracil (PROP) were matched in patients and control groups. And the Graded Chronic Pain (GCP) status of RDC/TMD Axis II was evaluated for each TMD patient. And the patients with high disability groups (grade III or IV) were selected for the study.

The patients with neuromuscular disorders, endocrine disorders, severe depression state or severe anxiety state, history of trauma or pain in other site in prior 6 months, and taking medicines which could affect this study were excluded.

The Symptom Checklist-90-Revision (SCL-90-R), the Beck Depression Inventory (BDI), and the Beck Anxiety Inventory (BAI) were examined in all the subjects because the effects of the psychological disorders were ruled out. Following their results were identified in normal ranges, we examined their several taste thresholds and their salivary flow rates.

All analyses were conducted on the data obtained from participants at the time of their initial evaluation, and this study was approved by the Institutional Review Board of Seoul National University Dental Hospital (CRI 12020). The informed consent was obtained from each subject.

2. Psychological evaluation

(1) The Symptom Checklist-90-Revision (SCL-90-R)

The SCL-90-R is considered of 90 questions for evaluating 9 primary symptoms dimensions and 3 global distress indices. The subjects were asked how much the symptom of each item bothered or distressed them during the past week. All items were scored ranging 0 (not at all) to 4 (extremely). The scale scores were recorded as standardized T-scores.[27,28] In our study, the subjects with high score (T-score > 60) of Depression and Anxiety dimensions were excluded.

(2) The Beck Depression Inventory (BDI)

The Beck Depression Inventory (BDI) was administered to each subject for measuring the severity of depression. The BDI is a 21-question multiple-choice self-report instrument. Each answer was scored ranging 0 (I do not feel sad) to 3 (I am so sad or unhappy that I can't stand it).[29] The scores 0 to 9 indicate minimal depression, 10–18 indicate mild depression, 19 to 29 indicate moderate depression, and 30 to 63 indicate severe depression.[30] We excluded the patients showing moderate to severe depression.

(3) The Beck Anxiety Inventory (BAI)

The Beck Anxiety Inventory (BAI) is a 21-question multiple-choice self-report questionnaire, for measuring the severity of anxiety. Each answer was scored gradually ranging 0 (not at all) to 3 (severely). The BAI has a maximum score of 63. The scores 0 to 7 mean minimal level of anxiety, 8 to 15 mean mild anxiety, 16 to 25 mean moderate anxiety, and 26 to 63 mean severe anxiety. We excluded the patients showing severe anxiety.[31]

3. Graded Chronic Pain Status

The patients were evaluated the severity of chronic pain using GCP status. GCP status is a 7-question self-report inventory, for rating the intensity of current pain and the interference period of usual activity because of facial pain in the last 6 months.

The patients filled the RDC/TMD Axis II questionnaire. If the patients had no TMD pain in prior 6 months, their GCP status was Grade 0. If the disability point was less than 3, the GCP status was low disability including Grade I and Grade II. Finally as the disability point was 3 to 6, regardless of characteristic pain intensity, patients' GCP status would be high disability including Grade III and Grade IV.[6] The patients with high disability were selected for the study.

4. Salivary flow rates

We examined the salivary flow rates of all the subjects to know the influence of

disturbance in salivary secretion. For measuring unstimulated whole saliva, each subject spitted his/her whole saliva in a 15mL disposable plastic tube for 10 minutes. For measuring stimulated whole saliva, each subject chewed the paraffin wax and swallow his/her saliva for 2 minutes, and then each subject was instructed to chew the paraffin wax continuously and spit their whole saliva in a 15mL disposable plastic tube for 5 minutes.

5. Taste thresholds and intensities

(1) Taste solutions

Detection and recognition thresholds for citric acid and monosodium glutamate (MSG) were measured in each subject. Citric acid solutions of 25 grades (sour, $1.3x10^{-5}$M to $1.35x10^{-2}$M, differed by 0.125 log units) and monosodium glutamate (MSG) solutions of 25 grades (umami, $7.5x10^{-5}$M to $7.5x10^{-2}$M, differed by 0.125 log units) were prepared.[32]

Suprathreshold pleasantness and general-labeled magnitude scale (g-LMS) which reflects taste intensity were determined by using citric acid (sour, 0.032 M), sucrose (sweet, 0.5 M), sodium chloride (salty, 1 M), quinine-HCl (bitter, 0.001 M), and MSG (umami, 0.032 M) solutions. And 1g 6-n-propylthiouracil (PROP) was added to 1L of distilled water.[8,33]

Each solution was presented as 10mL in a 120mL disposable paper cup for whole mouth stimulation.

(2) Detection threshold

We used modified single-staircase procedure to decide detection threshold.[34] On the first step 10mL distilled water in one cup and 10mL citric acid solution in the other cup were provided to the subject in order. The subject sipped each of them for 5 seconds and then spitted them. The subject was asked that the tastes of liquids of the two cups were different. If the subject answered the tastes were not different, on the second step a higher concentration of citric acid solution was provided. If the answer of the subject was the two tastes were different each other, on the second step the same concentration of the solution was provided and then if the subject also answered the tastes were different each other, then on the third step the

lower concentration of the citric acid solution was provided to the subject. In this way, eight reversals were needed to complete the test. Average concentration for the last four reversals was determined to the detection threshold.

Like the procedure for determining of the detection threshold of sour taste (citric acid), the same procedure for determining of the detection threshold of umami taste (MSG) was followed.

(3) Recognition threshold

As the detection threshold of citric acid was determined, the subject was asked whether they could identify the taste of the solution. We gave cups of increasing concentration to each subject until he or she could recognize the taste. If the subject answered correctly (i.e. sour or Shin (신) which means sour in Korean) or his or her answer was similar to sour taste (i.e. Sikeuman (시큼한) which means like 'sour' in Korean or lemon taste), the concentration was taken as the recognition threshold.

Like the procedure for determining of the recognition threshold of citric acid, the same procedure for determining of the recognition threshold of MSG was followed. If the subject answered correctly (i.e. umami or Gamchilmat (감칠맛) which means umami in Korean) or similarly (i.e. Neukkihan (느끼한) which means greasy in Korean, Dalkeunhan (달큰한) which means like a little sweet in Korean, Zzapzzalhan (짭짤한) or Ganganhan (간간한) which mean like a little salty in Korean, seasoning taste), the concentration was taken as the recognition threshold.

(4) Suprathreshold pleasantness and taste intensity

After determining detection threshold and recognition threshold, taste pleasantness and g-LMS taste intensity were also determined. The subjects sipped each five solution for 5 seconds and then spitted them. Then they determined the suprathreshold pleasantness and the g-LMS taste intensity. Also the subjects sipped PROP solutions for 5 seconds and then spitted them. Then they determined the g-LMS taste intensity.

Rating of taste pleasantness is a 21-point scale (-10 to +10 ; -10=extremely unpleasant, 0 =neutral, +10=extremely pleasant).[8] So the subjects were asked how

pleasant they were when they sipped the solutions and they determined the rating of taste pleasantness of each solution.

To evaluate taste intensity of each solution, the g-LMS was used. The g-LMS is like a ruler divided of the scale of 100 units on the vertical line of 230mm. The labels were barely detectable at 1.4, weak at 6, moderate at 17, strong at 34.7, very strong at 52.5, and strongest imaginable sensation of any kind at 100. We placed a g-LMS recording paper in front of each subject and made the subject point out their rating of taste intensity.

6. Statistical analyses

Differences between TMD patients and healthy controls in age, BDI, BAI, salivary flow rates, and g-LMS of PROP were analyzed by Independent T-test. And evaluation of gender matching between TMD patients and healthy controls was analyzed by Chi-square test.

Differences between TMD patients and healthy controls in each taste thresholds were analyzed by ANCOVA with g-LMS PROP as a covariate.

Correlations among age, pain duration, graded chronic pain status, salivary flow rates, and each taste perception value were analyzed by Pearson's correlation analyses.

The associations between age, salivary flow rate, existence of TMD, psychological measures, and each taste perception for umami taste were estimated using multivariate linear regression analysis.

Results

1. Characteristics of the study population

Clinical characteristics and psychological profiles of each patient were shown in table 1. The mean age, gender ratio, and mean g-LMS for PROP were not significantly different between TMD patients group and control group. And mean pain duration of TMD patients was 28.1 ± 29.4 months. BDI and BAI of TMD patients were 10.6 ± 4.4 and 6.1 ± 6.2.

Table 1. Characteristics of the study population

	Age (years)	Pain duration (months)	BDI	BAI	g-LMS for PROP	Gender (Male, %)
TMD patients	25.2 ± 6.1	28.1 ± 29.4	10.6 ± 4.4	6.1 ± 6.2	45.2 ± 26.4	33.3
Controls	29.8 ± 2.0	0	9.7 ± 2.2	4.8 ± 3.5	26.2 ± 21.6	47.1
P-values	0.057[a]	0.001[a]	0.595[a]	0.503[a]	0.060[a]	0.500[b]

BDI : Beck Depression Inventory
BAI : Beck Anxiety Inventory
g-LMS for PROP : General-labeled magnitude scale for 6-n-propylthiouracil
[a] P-values were obtained from Independent *t*-test.
[b] P-value was obtained from Chi-square test.

2. Comparison of taste perception values between TMD patients and controls

TMD patients showed significantly lower detection thresholds ($p<0.05$) and lower recognition thresholds ($p<0.05$) for umami tastes than control subjects.

And TMD patients showed significantly higher g-LMS scales for bitter taste than controls ($p<0.05$).

There was no significant change of taste pleasantness between TMD group and control group. Also no significant difference was shown in detection thresholds and recognition thresholds of sour taste stimuli between TMD patients group and control group. (Table 2)

3. Salivary flow rates of the TMD patients and the controls

TMD patients showed significantly lower stimulated salivary flow rates than the control subjects ($p<0.05$) and GCPs and stimulated salivary flow rates showed negative correlation ($p<0.05$). Correlation between pain duration and stimulated salivary flow rates was not significant. (Table 3 and 4)

However unstimulated salivary flow rates were not significantly different between TMD patients and controls. (Table 3)

Table 2. Comparison of taste perception values (Mean±SD) between TMD patients & controls

		TMD patients	Controls	P-values
Detection thresholds	Sour	4.00 ± 2.50	3.71 ± 1.57	0.149
	Umami	2.56 ± 1.67	4.94 ± 2.38	0.002
Recognition thresholds	Sour	5.56 ± 3.01	5.12 ± 1.58	0.280
	Umami	5.22 ± 2.11	6.53 ± 1.77	0.001
Taste pleasantness	Sweet	4.56 ± 3.64	5.12 ± 3.14	0.070
	Salty	-6.22 ± 1.48	-6.24 ± 2.08	0.842
	Bitter	-6.50 ± 3.10	-6.12 ± 2.06	0.470
	Sour	-4.22 ± 3.93	-6.71 ± 2.64	0.108
	Umami	-0.22 ± 2.49	-1.82 ± 1.67	0.159
g-LMS scales	Sweet	49.67 ± 23.30	35.18 ± 15.42	0.112
	Salty	68.11 ± 15.23	53.29 ± 16.53	0.109
	Bitter	52.33 ± 28.04	42.94 ± 24.95	0.033
	Sour	55.89 ± 18.58	49.65 ± 24.52	0.643
	Umami	16.56 ± 14.21	15.41 ± 11.85	0.505

P-values were obtained from ANCOVA (as g-LMS PROP as a covariate)

Table 3. Comparison of the salivary flow rates (Mean ± SD) between TMD patients and control groups

	TMD patients	Controls	P-values
Unstimulated (mL/min)	0.33 ± 0.18	0.92 ± 0.41	0.112
Stimulated (mL/min)	0.92 ± 0.41	1.56 ± 0.54	0.005

P-values were obtained from independent T-test.

4. Correlations among age and each parameter of taste perception

The detection thresholds of umami stimuli showed significantly negative correlation with GCPs ($r=-0.401$, $p<0.05$). The detection thresholds of sour stimuli

showed significantly positive correlation with pain duration ($r=0.389$, $p<0.05$). And the detection thresholds and the recognition thresholds of umami tastes showed significantly negative correlations with the g-LMS of PROP ($r=-0.596$, $p<0.01$; $r=-0.660$, $p<0.01$). (Table 4)

The taste pleasantness for sweet taste showed negative correlations with the detection thresholds and the recognition thresholds for sour stimuli ($r=-0.455$, $p<0.05$; $r=-0.412$, $p<0.05$).

The g-LMS taste intensities of sweet, salty, bitter, and sour stimuli were significantly correlated each other ($p<0.01$), and the g-LMS of bitter taste showed significant correlation with the g-LMS of PROP ($r=0.506$, $p<0.01$). However the g-LMS taste intensity of umami stimulus was not significantly correlated with other taste stimuli or PROP. (Table 4)

5. Taste perception and age

Detection threshold ($r=0.475$, $p<0.05$) and recognition threshold for umami tastes ($r=0.426$, $p<0.05$) showed significantly positive correlations with ages. And the subjects' age showed negative correlations with pleasantness for umami tastes ($r=-0.570$, $p<0.05$). Also the subjects' age showed significantly negative correlation with the g-LMS suprathresholds of sweet tastes ($r=-0.480$, $p<0.05$). (Table 4)

6. Association of umami tastes perceptions with the existence of TMD

From the multivariate linear regression analyses adjusted for the age, gender, BDI, BAI, and unstimulated salivary flow rates, the detection threshold for umami taste were significantly associated with the existence of TMD ($\beta=-0.606$, $p<0.05$). From the multivariate linear regression analyses, umami taste pleasantness was significantly associated with age ($\beta=-0.624$, $p<0.05$) and unstimulated salivary flow rates ($\beta=0.441$, $p<0.05$).

Table 4. Pearson's correlation coefficient among age, salivary flow rates and each parameter of taste perception

		Age	Detection thresholds		Recognition thresholds		G-LMS suprathresholds						Salivary flow rates	
			Sour	Umami	Sour	Umami	Sweet	Salty	Bitter	Sour	Umami	PROP	UWS	SWS
Age		1	0.081	0.475*	0.101	0.426*	-0.480*	-0.226	-0.328	-0.191	-0.042	-0.326	0.112	0.263
GCP		-0.329	0.235	-0.401*	0.259	-0.215	0.248	0.307	0.042	0.099	-0.036	0.199	-0.334	-0.482*
Pain duration		-0.345	0.389*	-0.316	0.368	-0.051	0.162	0.058	0.115	0.024	0.017	0.236	-0.166	-0.365
Taste Pleasant-ness	Sweet	-0.116	-0.455*	-0.298	-0.412*	-0.275	0.216	0.082	0.304	0.085	0.465	-0.090	-0.033	-0.008
	Salty	0.011	-0.058	0.006	-0.054	0.137	-0.111	0.369	0.088	-0.040	0.060	-0.017	0.108	-0.123
	Bitter	0.092	0.124	0.354	-0.088	0.135	-0.211	0.343	-0.062	-0.180	-0.431	-0.031	-0.150	-0.227
	Sour	-0.035	0.024	-0.173	-0.035	-0.120	-0.275	0.072	0.118	0.018	-0.097	0.775**	-0.227	-0.246
	Umami	-0.570**	0.087	-0.065	0.035	0.044	0.063	-0.213	0.319	-0.041	0.098	0.282	0.286	-0.028
g-LMS supra-thresholds	Sweet	-0.480*	-0.013	-0.278	-0.011	-0.338	1	0.687**	0.674**	0.692**	0.085	0.325	0.055	0.034
	Salty	-0.226	-0.089	-0.181	-0.169	-0.230	0.687**	1	0.586**	0.627**	0.038	0.101	-0.171	-0.120
	Bitter	-0.328	-0.139	-0.352	-0.164	-0.364	0.674**	0.586**	1	0.720**	0.194	0.506**	0.165	0.157
	Sour	-0.191	-0.012	-0.187	-0.006	-0.329	0.692**	0.627**	0.720**	1	0.114	0.180	0.159	0.118
	Umami	-0.042	0.122	-0.279	-0.110	-0.379	0.085	0.038	0.194	0.114	1	0.236	-0.252	-0.070
	PROP	-0.326	-0.327	-0.596**	-0.248	-0.660**	0.325	0.101	0.506**	0.180	0.236	1	0.159	-0.104

* Correlation is significant at 0.05 level.
** Correlation is significant at 0.01 level.

Table 5. Multivariate linear regression analysis for each perception of umami taste as age, gender, the existence of TMD, psychiatric measures and unstimulated salivary flow rates

Dependent variable	Independent variable	Coefficient	Standardized coefficient (β)	P-value
Detection threshold	Age	-0.037	-0.067	0.828
	Gender	-1.237	-0.253	0.277
	The existence of TMD	-1.510	-0.606	0.043
	BDI	0.159	0.202	0.367
	BAI	0.080	0.149	0.485
	Salivary flow rates	-0.866	-0.111	0.593
Recognition threshold	Age	0.052	0.115	0.731
	Gender	-1.241	-0.312	0.221
	The existence of TMD	-0.700	-0.345	0.269
	BDI	0.036	0.056	0.815
	BAI	-0.026	-0.059	0.798
	Salivary flow rates	-0.953	-0.150	0.508
Taste pleasantness	Age	-0.297	-0.624	0.020
	Gender	-0.244	-0.058	0.755
	The existence of TMD	0.452	0.209	0.361
	BDI	0.004	0.006	0.972
	BAI	0.145	0.309	0.081
	Salivary flow rates	2.978	0.441	0.015
G-LMS suprathreshold	Age	1.079	0.382	0.261
	Gender	9.394	0.374	0.145
	The existence of TMD	2.429	0.189	0.538
	BDI	-0.458	-0.113	0.639
	BAI	-0.915	-0.329	0.164
	Salivary flow rates	-12.260	-0.305	0.185

Adjusted R^2 ; Detection threshold=0.192, Recognition threshold=0.042, Taste pleasantness=0.478, G-LMS suprathreshold=0.048

Discussion

In our study, we matched the g-LMS scales of PROP in TMD patients and control subjects since PROP sensitivity might be affected by the number and diameter of fungiform papillae, salivary levels of specific proline-rich proteins and the presence of specific genes such as TAS2R38 which encode taste receptors better. [35,36] So we could rule out peripheral effects on the taste results.

And the g-LMS was used to evaluate the taste intensity of each solution. The g-

LMS provides labeling scales with ratio properties and reduces ceiling effects of taste intensity so taste sensitivity can be reflected more accurately.[37-40] Also the gLMS was suggested that the valid tool for taste comparison through nontasters, medium tasters, and supertasters.[39]

We also measured unstimulated and stimulated salivary flow rates of both TMD patients and controls to know effects of salivary flow to taste perception. There wasn't significant difference of unstimulated salivary flow rates between TMD patients and control subjects. So we presumed that in our study the results of taste perceptions were not affected by the unstimulated salivary flow rates of the subjects.

Meanwhile TMD patients showed significantly lower stimulated salivary flow rates than controls. And as the intensity and duration of TMD pain were increased (as GCPs and pain duration), stimulated salivary flow rates also increased, although regarding pain duration result was not significant. All the patients and the controls didn't take any drug during this study and they were not in severe depression or anxiety state on the psychiatric measures. So we hypothesized that the TMD patients felt too painful to chew gum enough to stimulate salivary flow or their masticatory muscles could not work well for a long time resulting in functional atrophy. As a result, their glands including parotid glands couldn't work well.[41] As previously stated, unstimulated salivary flow rates of TMD patients were not significantly different from control subjects.

Regarding the study of salivary flows in orofacial pain patients, there is a study comparing the salivary flows of orofacial pain patients and controls. They used cottons placed on the mouth floor for 5 minutes then measured weights of the cotton wads. The result was that salivary flows in orofacial pain patients were lower than controls. However 78% of patients and 69.6% of controls were on chronic medication and some patients were taking amitriptyline (35.3%), anti-hypertensive drugs (15.9%) and other drugs in this study.[42]

Our study was the first experimental study revealing the relevancy of TMD and taste perceptions. Our controlled study showed TMD pain patients had more intense gustatory perception (lower detection and recognition thresholds) of umami stimuli than healthy people. In addition, as pain severity of TMD patients (measured by GCPs)[43] increased, the detection thresholds of umami stimuli

significantly decreased. These results might support the previous study of increased taste perception in chronic pain.[8] However in our study the detection threshold of sour taste showed positive correlation with pain duration. So we presumed that pain severity (measured by GCP status) rather than pain duration might be related to increased pain perception. Also we thought further studies with more subjects suffering from longer pain durations might be needed.

The detection thresholds, the recognition thresholds, and the taste pleasantness for umami stimuli were correlated with the g-LMS of PROP. These results mean supertasters might be involved to increased sensitivity in gustatory perceptions for umami tastes, which might involved in TMD patients as the results of our study.

Taste is the sensation produced by substances reacting chemically with receptors of taste buds.[44] The tastes can be differentiated by taste buds through detecting interactions such as G protein-coupled receptors regarding umami, sweet, and bitter tastes or alkali metal or hydrogen ions entering taste buds regarding salty and bitter taste.[45] And the etiology of supertasters have been thought to be related to the TAS2R38 gene, which is encoding bitter taste receptor TAS2R38, and an increased number of fungiform papillae. Supertasters are also known to be react sensitively to PROP or phenylthiocarbamide (PTC) solutions.[35]

Several brain functional magnetic resonance imaginig (fMRI) studies reported that various tastes stimulation activate the insular cortex, the perisylvian region, the anterior cingulated gyrus, the parahippocampal gyrus, the lingual gyrus, the caudate nucleus, the temporal gyri, and the thalamus.[10,11] In a fMRI study, umami and sweet taste stimuli were also shown to activate the insular/opercular cortex, the caudolateral orbitofrontal cortex, and a part of the rostral anterior cingulated cortex.[12]

Central mechanisms of chronic pains, including chronic orofacial pain, have been explained by several theories such as disturbance of the descending inhibitory system and central sensitization or neuroplasticity and other consideration of chronic pain mechanism might be the biopsychosocial model.[48] Thus there have been several studies trying to reveal connections between chronic pains and brain structures.[14-24] In the review article investigating changes of gray matter in brain of chronic pain (chronic back pain, phantom pain, chronic head pain, migraine, fibromyalgia, and irritable bowel syndrome) patients, common atrophic sites of

brain in highest order was the cingulated cortex, the orbitofrontal cortex, the insula, and the dorsal pons.[13] Anterior cingulated cortex interacts with other structures including the orbitofrontal cortex, the amygdala, and the PAG so that effects pain modulation and analgesia.[49,50] In other words, the decrease of gray matter in the anterior cingulated cortex or the orbitofrontal cortex or the amygdala could lead to dysfunction in effective antinociception. These changes were transient at first, but became permanent with continuing pathologic changes, then could explain the part of the shift from acute pain to chronic pain.[13] Unlike other several chronic pains, however, there is no study investigating relation of chronic orofacial pain and brain structure itself using any brain imaging.

Interestingly the earlier referred structures showed overlapping with the activated sites by taste stimuli including sweet and umami stimuli in fMRI brain study.[12] Thus we thought that this overlapping supports that chronic TMD pain patients show different perceptions of taste stimuli such as umami taste and these structures might be involved in chronic TMD pain and gustatory processing. The limbic structures, including the amygdala, the hippocampus, the cingulated gyrus, and the cingulum, which are controlled by the hypothalamus, can modify many internal bodily functions (wakefulness, sleep, excitement, attentiveness, and rage), evaluate pain experiences, and contain certain centers or nuclei that are responsible for specific emotions and behaviors (fear, rage, helplessness, sadness, and depression).[39] Thus the biopsychosocial model as a etiology of chronic TMD pain could be also explained by our results.

There are studies on the hypersensitivity of the olfactory or gustatory functions in chronic pains. In the study of chronic back pain, chronic back pain patients significantly displayed lower detection thresholds of sour taste and higher overall g-LMS rating of bitter, salty, sweet, and sour tastes than controls.[8] Regarding chronic back pain and gustatory processing, the authors highlighted three brain regions, the anterior insula, the medial prefrontal cortex, and the thalamus.[8,9,14] Also there is a study on the olfactory and gustatory function in irritable bowel syndrome which is a kind of chronic pains. The result was that the irritable bowel syndrome patients had better odor identification and odor discrimination than controls but non-significant different taste perception compared to normative data. Because the taste solution was classified only four levels of each solution, they appeared to

need to be classified precisely.[51] Though the results of our study, chronic back pain study and irritable bowel syndrome study were different regarding tastes, they reached the similar conclusions of increased chemesthesis and hypersensitivity in chronic pains.

Also connecting substance between chronic pain and hypersensitivity on gustatory function (in supertasters) have to be considered. In recent neurophysiological studies, brain-derived neurotrophic factor (BDNF) have been considered. BDNF is a member of the neurotrophic factor family which includes nerve growth factor and neurotrophin-3. These are known to play important roles on nerves to sensory organs, such as taste buds. In a review article of BDNF and chronic pain, the changes of BDNF expression in the dorsal root ganglion neurons and spinal cord involved in the pathophysiological mechanisms of chronic pain.[46] In the rodent model, overexpression of BDNF appeared to lead to elevated levels of phosphorylated TrkB proteins in taste buds cells, resulting in larger taste buds, increased taste cell number, and gustatory innervations promotion.[47]

Therefore these reports and our results appeared to support the central etiology of chronic pains such as TMD, chronic back pain, and irritable bowel syndrome.

In our study, however, the number of the subjects was small. Therefore further studies including many subjects have to be performed. And we considered that the setting of solution density ranges for detection and recognition thresholds was based on the study for healthy people.[32] In our study, the detection thresholds of a few TMD patients were recorded as the minimum level 1. It means they might have lower thresholds than the evaluated thresholds. So the detection thresholds of some TMD patients have to be evaluated more precisely. Thus in future studies, the ranges of taste solution levels will be needed to be adjusted to lower levels or additional levels.

And recently, with the development of fMRI, there have been several studies of chronic pains and brain structures.[13-24] In addition, different chronic pain conditions were likely to be involved in different sites of brain.[13] Unlike other chronic pains, however there is no imaging study revealing relation of chronic orofacial pain and brain structures or brain processing. Therefore studies on the relationships between chronic orofacial pain and brain structures or brain processing using neuroimaings will be needed in the future.

Conclusions

There have been several studies suggesting the overlaps between specific brain regions involved in taste and pain perception. And the recent studies of the patients with chronic pain reported increased taste sensitivity. The aim of this study was to evaluate the gustatory function in the patient with TMD.

G-LMS of PROP as a covariate, TMD pain patients showed significantly lower detection thresholds and recognition thresholds for umami stimuli than the control subjects. And the GCP scales of the subjects were significantly correlated with detection thresholds of umami taste. The suprathreshold taste intensities of sweet, salty, bitter, and sour stimuli were significantly correlated each other but the taste intensity of umami stimulus was not significantly correlated with other taste stimuli in our subjects. TMD pain patients showed lower stimulated salivary flow rates than control subjects and the GCP scales were significantly correlated with stimulated salivary flow rates. From the multivariate linear regression analyses adjusted for the age, gender, BDI, BAI, and unstimulated salivary flow rates, the detection thresholds for umami taste were significantly associated with the existence of TMD.

Our results showed that the patients with TMD reported increased sensitivity for umami taste, and suggested the possibilities of gustatory function changes in chronic TMD patients.

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요약

측두하악장애 환자의 미각 역치에 관한 예비연구

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지도교수 정 진 우

미각과 통증 인지에 관련된 특정 뇌 영역이 겹친다고 제시한 여러 연구가 있었으며, 최근 만성 요통이나 섬유근통과 같은 만성통증 환자에서의 미각 예민성 증가가 보고된 바 있다. 본 연구의 목적은 측두하악장애 환자에서의 미각 역치를 평가하여 만성 턱관절 통증과 미각과의 관련성을 알아보는데 있다. 불안이나 우울 등의 심리학적 증상을 동반하지 않는 9 명의 측두하악장애 환자와 성별과 연령을 일치시킨 17 명의 건강한 대조군을 대상으로 만성통증척도(Graded Chronic Pain), Beck 우울지수(Beck Depression Inventory, BDI), Beck 불안지수(Beck Anxiety Inventory, BAI)와 비자극성 및 자극성 전타액분비율을 조사하였으며, 신맛과 감칠맛(umami taste)에 대한 감지역치(detection threshold)와 인식역치(recognition threshold), 단맛, 짠맛, 신맛, 쓴맛,

감칠맛에 대한 초역치 미각강도(suprathreshold taste intensity) 및 미각 유쾌성과 불쾌성(pleasantness-unpleasantness perception), PROP 의 초역치 미각강도를 평가한 결과 다음과 같은 결론을 얻었다.

1. PROP 의 초역치 미각강도 공변량분석에서 측두하악장애 환자는 대조군에 비하여 유의하게 낮은 감칠맛(umami taste) 감지역치와 인식역치를 보였다.
2. 측두하악장애 환자는 대조군에 비하여 낮은 자극성 타액분비율을 보였다.
3. 실험 대상의 만성통증척도는 감칠맛에 대한 감지역치와 유의한 상관성을 보였다.
4. 실험 대상의 만성통증척도는 자극성 타액분비율과 유의한 상관성을 보였다.
5. 연령, 성별, BDI, BAI, 비자극성 타액분비율을 조절한 다중회귀분석결과 감칠맛에 대한 감지역치는 측두하악장애 유무와 유의한 관련성을 보였다.

본 연구의 결과는 측두하악장애 환자에서의 미각과 통증 감각과의 관련가능성을 제시하고 있으며, 향후 만성 통증을 호소하는 측두하악장애 환자에서의 추가적인 연구가 필요할 것으로 판단된다.

주요어: 측두하악장애, 미각, 통증, 타액, 감칠맛

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