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Effects of thorough mastication on postprandial plasma glucose concentrations in nonobese Japanese subjects

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Abstract

Thorough mastication has the potential to affect postprandial plasma glucose concentrations by improving digestibility and absorption of nutrients. To evaluate the effects of mastication on postprandial plasma glucose concentration, we compared usual and thorough mastication in subjects with normal glucose tolerance (NGT group, n = 16) and subjects predisposed to type 2 diabetes (first-degree relatives of type 2 diabetic patients, subjects with impaired glucose tolerance, and type 2 diabetic patients) (predisposed group, n = 10) in a crossover trial of 52 test meals. Plasma glucose and serum insulin concentrations were measured for 3 hours postprandially, and the insulinogenic index (the ratio of incremental serum insulin to plasma glucose concentration during the first 30 minutes after meal) was calculated. In the NGT group, thorough mastication reduced the postprandial plasma glucose concentration at 90 minutes (5.8 ± 0.3 vs 6.5 ± 0.4 mmol/L, $P < .05$) and 120 minutes (5.4 ± 0.2 vs 6.3 ± 0.4 mmol/L, $P < .05$) and the area under the curve (AUC) from −15 to 180 minutes (19.1 ± 0.6 vs 20.6 ± 0.8 [mmol/L] · h, $P < .05$) without an increase in the AUC for insulin. In the predisposed group, thorough mastication significantly augmented plasma glucose and serum insulin concentrations and the AUCs compared with usual mastication. Thorough mastication elicited a significantly higher insulinogenic index than usual mastication in the NGT group (205.0 ± 27.6 vs 145.6 ± 17.7 pmol/mmol, $P < .05$), whereas the predisposed group showed significantly less early-phase insulin secretion than the NGT group. In the NGT group the postprandial plasma glucose concentration upon thorough mastication of meal was significantly lower, most probably because of the potentiation of early-phase insulin secretion. In the subjects predisposed to type 2 diabetes, thorough mastication did not potentiate early-phase insulin secretion and elicited a higher postprandial plasma glucose concentration.

1. Introduction

Fletcherism, the practice of chewing food slowly and thoroughly as an aid to digestion [1], was advocated by the American dietician Horace Fletcher (1849-1919). He found that prolonged mastication both inhibited overeating and contributed to reduced food intake [2]. Under laboratory conditions, it has been found that when people enjoy softer food, they masticate less and bite with less vigor [3]. Fast food such as hamburgers is highly palatable by clever seasoning and flavoring, but soft and airy and with a generally homogenous consistency, and is now so commonplace worldwide [4] that the physiological importance of thorough mastication is barely recognized.

The major physiological function of mastication is the mechanical disruption of food into small particles suitable for gastrointestinal absorption of nutrients [5]. Preabsorptive or cephalic-phase insulin release, a vagally mediated response, occurs within the first few minutes of food ingestion [6] and is thought to be required for normal postprandial glucose tolerance [7]. Thus, mastication plays a crucial role in determining the postprandial plasma glucose concentration. Modified sham feeding, in which food is chewed and tasted but not swallowed [8], has been shown to elicit cephalic-phase insulin release [9], but few studies have examined the relation between thorough mastication and postprandial plasma glucose concentra-

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tions. Read et al [10] found that thoroughly masticating food rather than merely swallowing it increased plasma glucose concentrations after the ingestion of 4 kinds of carbohydrate (sweet corn, potato, rice, and apple) in 6 healthy subjects, mostly because of improved digestibility and absorption. However, no variables other than the plasma glucose concentration during the early postprandial period were examined. The aim of the present study is to evaluate the effect of thorough mastication on postprandial plasma glucose concentrations. We used a mixed-nutrient meal of hamburger steak and rice as the test meal. Hamburger steak is a kind of processed meat, the frequent consumption of which is reported to increase the risk of type 2 diabetes [11]. The hamburger steak and rice used in this study were both readily swallowed without thorough mastication.

2. Subjects and methods

2.1. Subjects

A total of 26 volunteers (17 men and 9 women; mean age, 38.9 ± 11.5 [SD] years [range, 25-71 years]; mean body mass index [BMI], 21.8 ± 2.8 kg/m^2 [range, 16.8-26.8 kg/m^2]) participated in the study. Sixteen had normal glucose tolerance (NGT), 6 were first-degree relatives of type 2 diabetic patients, 2 had impaired glucose tolerance (IGT), and 2 had mild type 2 diabetes mellitus without pharmacotherapy. None of the subjects were taking medication known to influence glucose concentration. Subjects were classified into 2 groups, one with NGT (NGT group) and the other with a predisposition to diabetes (predisposed group), which comprised IGT, mild type 2 diabetes, and first-degree relatives of type 2 diabetic patients, and underwent 1 session of each mastication procedure. Fourteen of the 16 NGT subjects and all 10 subjects in the predisposed group underwent 75-g oral glucose tolerance test (OGTT). Subjects with fasting plasma glucose (FPG) of less than 5.6 mmol/L and HbA_{1c} of less than 5.0% and/or with FPG of less than 6.1 mmol/L and 2-hour glucose of less than 7.8 mmol/L in OGTT by 1998 World Health Organization diagnostic criteria [12] were classified as NGT. IGT and type 2 diabetes also were defined according to World Health Organization criteria. Table 1 shows the clinical characteristics of the NGT and the predisposed groups. The study protocol was approved by the Ethics Committee of the Faculty of Medicine, Kyoto University, and was conducted in accordance with the Declaration of Helsinki. All subjects gave written informed consent.

Table 1
Clinical characteristics of the 26 subjects

	NGT group	Predisposed group
n (male/female)	16 (9/7)	10 (8/2)
Definition	16 NGT	6 First-degree relatives, 2 IGT, 2 type 2 diabetes
Age (y)	35.6 ± 2.1	44.1 ± 4.4
BMI (kg/m^2)	21.2 ± 0.6	23.0 ± 1.0
HbA_{1c} (%)	4.6 ± 0.1	5.4 ± 0.4
FPG (mmol/L)	5.2 ± 0.1	5.8 ± 0.2
Fasting insulin (pmol/L)	57.4 ± 5.0	49.5 ± 4.3
Total cholesterol (mmol/L)	5.1 ± 0.2	5.0 ± 0.2
HDL cholesterol (mmol/L)	1.8 ± 0.1	1.5 ± 0.1
Triglyceride (mmol/L)	1.0 ± 0.1	1.0 ± 0.1

Data are means (of 2 sessions) ± SE. There were no significant differences between the NGT and the predisposed groups. HDL indicates high-density lipoprotein.

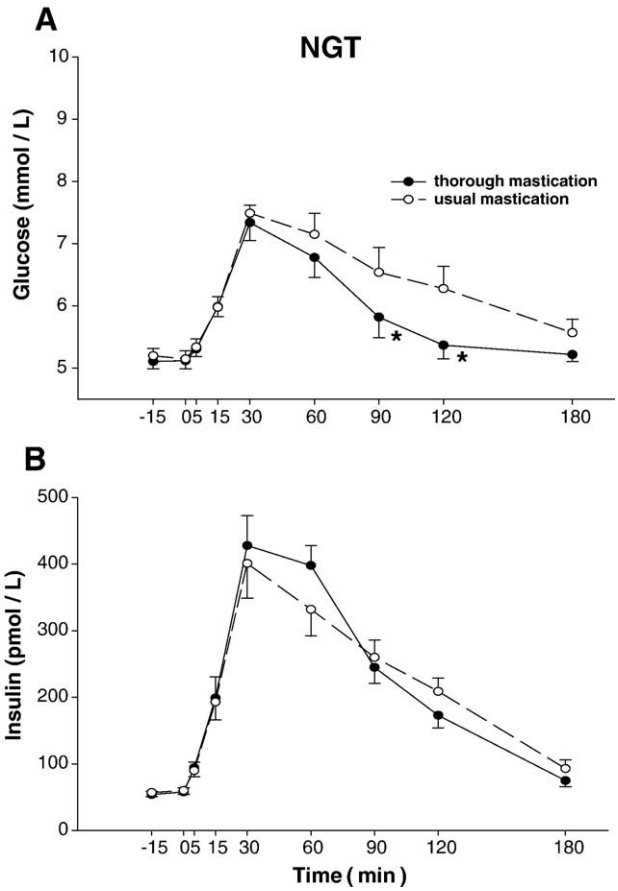

Fig. 1. Plasma glucose (A) and serum insulin (B) concentrations in the NGT group at various time points in usual and thorough mastication. Data are means ± SE, n = 16, *P < .05.

2.2. Experimental protocol

The study was a crossover experiment that included 52 sessions. After overnight fasting for at least 12 hours, the subjects began each eating session at 8:00 AM. A butterfly needle was inserted into an antecubital vein to draw blood samples at −15 minutes and was kept open by a slow drip of physiological saline. Immediately after a blood sample was drawn at 0 minute, the test meal of 130 g hamburger steak of 962 kJ (230 kcal) (Tokiwa Kanpo Pharmaceutical, Osaka, Japan) and 100 g rice of 649 kJ (155 kcal) (Hagoromo Foods, Shizuoka, Japan), with a total energy content of 1611 kJ (385 kcal) comprising 51%, 15%, and 34% carbohydrate, protein, and fat, respectively, began. Each

food item was sealed in a retort pouch and heated in a standard microwave oven for 2 minutes before the meal. The hamburger steak and rice were divided into 8 equal portions. Each subject underwent both mastication procedures. In the "usual mastication" sessions, the subjects took 16 teaspoonfuls of food, chewing each teaspoonful for 10 seconds before swallowing. In the "thorough mastication" sessions, each teaspoonful was swallowed only after 30 seconds of chewing. The rate of mastication was maintained at about 1 cycle per second in each session. Thus, thorough mastication involved 3-fold more bites than usual mastication. As the difference in the time taken eating might be a confounding factor, the subjects in usual mastication paused for 20 seconds after every 10 seconds, during which they were permitted to drink nonenergetic water, equalizing the duration of all meals at 8 minutes. The succession of mastication procedure was randomized for each subject. The average duration of the experiment was 9.9 days for male subjects. Female subjects participated only during the follicular phase of the menstrual cycle, with the interval fixed at 4 weeks to reduce variations in insulin sensitivity [13].

Blood samples for glucose and insulin were withdrawn at −15 and 0 minute before each meal and at 5, 15, 30, 60, 90, 120, and 180 minutes after each meal.

2.3. Analytical methods

Plasma glucose was measured by the glucose oxidase method using a Hitachi Automatic Analyzer 7170 (Hitachi, Tokyo, Japan). Serum insulin was measured in duplicate using LS regand Eiken insulin (Eiken, Tokyo, Japan) by automatic chemiluminescence enzyme immunoassay analyzer BCS 600 (SRL, Tokyo, Japan). The cross-reactivity to proinsulin, C-peptide, and split insulin was 0.01%, 0%, and 0%, respectively.

2.4. Data analysis

Values are expressed as mean ± SE unless otherwise noted. Statistical analysis was performed using StatView 5.0 (Abacus Concepts, Berkeley, CA). The area under the curve (AUC) was calculated according to the trapezoid rule. FPG and fasting serum insulin concentrations are the average of 2 premeal values (−15 and 0 minute). The insulinogenic index (II) [14], the ratio of the incremental serum insulin to plasma glucose concentration during the first 30 minutes after glucose ingestion calculated by OGTT (II_{OGTT}), has been commonly used as a measure of early-phase insulin secretion [15-18] since it was proposed by Seltzer et al [19] in 1967. In this study, the II during the first 30 minutes after meal tolerance test (MTT) (II_{MTT}) was calculated as the serum insulin concentration (30 − 0 minute)/plasma glucose concentration (30 − 0 minute) (pmol/mmol), and II_{MTT} and II_{OGTT} were compared. To estimate differences between 2 means, Student paired t test was performed with paired variates. To compare unpaired variates, Student unpaired t test with equal variances or Welch test with unequal variances was used. Multiple comparisons between differences among individual time points were done by analysis of variance (repeated measures) followed by Student t test with Bonferroni correction. Pearson r was used to evaluate univariate correlations. $P < .05$ was considered statistically significant.

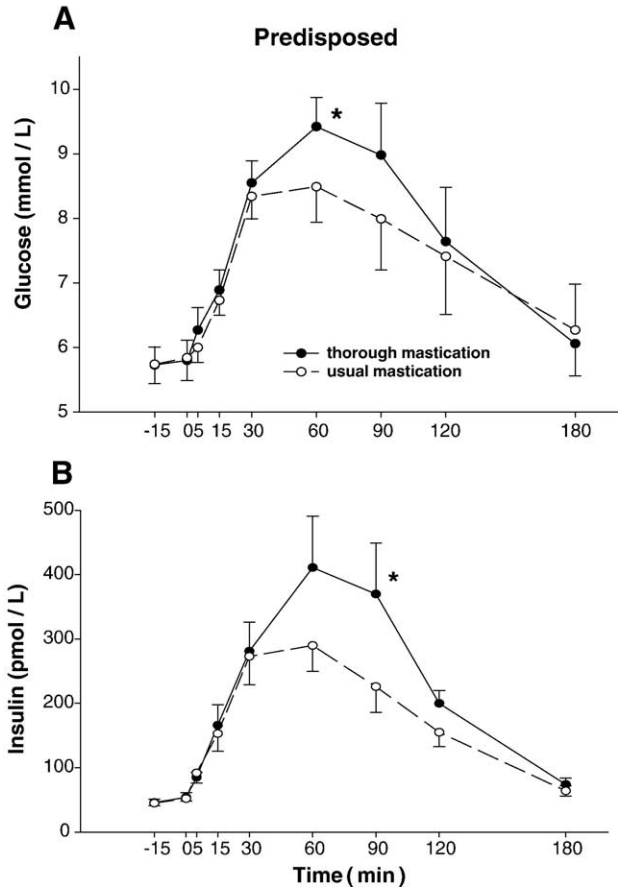

Fig. 2. Plasma glucose (A) and serum insulin (B) concentrations in the predisposed group at various time points in usual and thorough mastication. Data are means ± SE, n = 10, *$P < .05$.

Table 2
Comparison of the total AUCs (−15 to 180 minutes) for glucose and insulin in the NGT and the predisposed groups

	Glucose AUC ([mmol/L] · h) (−15 to 180 min)	Insulin AUC ([pmol/L] · h) (−15 to 180 min)
NGT group		
Usual mastication	20.6 ± 0.8	722.5 ± 60.3
Thorough mastication	19.1 ± 0.6*	722.5 ± 50.9
Predisposed group		
Usual mastication	23.7 ± 1.7	574.7 ± 65.3
Thorough mastication	24.9 ± 1.5**	755.5 ± 91.8**

Data are means ± SE.
* $P < .05$, significantly different from usual mastication in each group.
** $P < .01$, significantly different from usual mastication in each group.

3. Results

All 26 subjects completed all sessions of the test meals. Fig. 1 shows the plasma glucose and serum insulin concentrations in the NGT group in usual and thorough mastication. The plasma glucose concentration in both masticatory procedures increased in the first 30 minutes to 7.4 and 7.3 mmol/L, respectively. On the other hand, plasma glucose in thorough mastication decreased more rapidly than in usual mastication and was significantly reduced at 90 and 120 minutes (90 minutes, 5.8 ± 0.3 vs 6.5 ± 0.4 mmol/L, $P < .05$; 120 minutes, 5.4 ± 0.2 vs 6.3 ± 0.4 mmol/L, $P < .05$) (Fig. 1A). The AUC for glucose in the NGT group from −15 to 180 minutes was significantly less in thorough mastication than in usual mastication ($P = .017$) (Table 2). Insulin secretion was increased in thorough mastication from 5 minutes to nearly 90 minutes (the major difference occurring at 60 minutes: 397.5 ± 29.4 vs 332.2 ± 39.5 pmol/L) (Fig. 1B). The AUC for insulin in the NGT group from 90 to 180 minutes was significantly less in thorough mastication than in usual mastication (228.9 ± 20.1 vs 268.3 ± 23.0 [pmol/L] · h, $P = .044$). The total AUCs for insulin in the 2 mastication procedures were the same (Table 2).

The data on the predisposed group are shown in Fig. 2. During the first 30 minutes, both plasma glucose and serum insulin concentrations showed a similar pattern in the 2 mastication procedures. At 60 minutes, there was a significantly higher glucose response in thorough mastication than in usual mastication (9.4 ± 0.45 vs 8.4 ± 0.55 mmol/L, $P < .05$) (A), as well as a significantly higher insulin response at 90 minutes (370.9 ± 78.9 vs 226.0 ± 40.2 pmol/L, $P < .05$) (B). The AUCs for both glucose ($P = .008$) and insulin ($P = .002$) in the predisposed group were increased significantly in thorough mastication compared with usual mastication (Table 2).

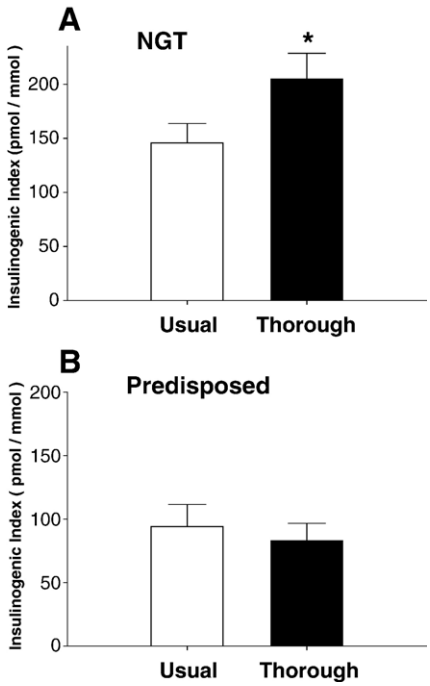

Fig. 3. II_{MTT} in the NGT group (n = 16) (A) and the predisposed group (n = 10) (B) during the first 30 minutes after meal in usual and thorough mastication. Data are means ± SE, *$P < .05$.

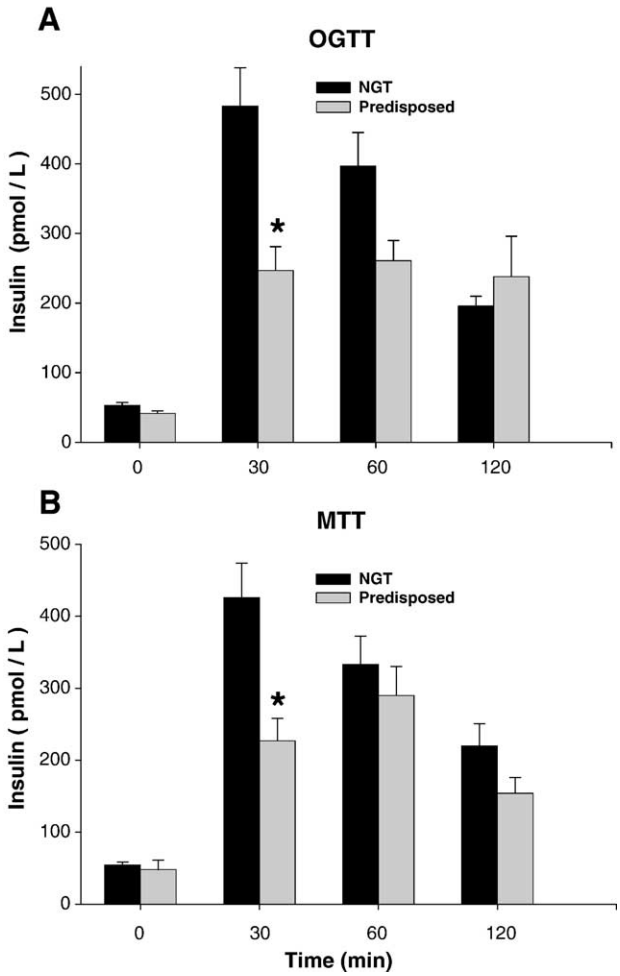

Fig. 4. Serum insulin concentrations in the NGT group (black bars, n = 14) and the predisposed group (gray bars, n = 10) measured by OGTT (A) and MTT in usual mastication (B) at 4 time points. Data are means ± SE, *$P < .05$.

Fig. 3 shows the II measured by MTT for the 2 mastication procedures in the NGT (A) and the predisposed group (B). In the NGT group, II_{MTT} in thorough mastication was significantly higher than in usual mastication (205.0 ± 27.6 vs 145.6 ± 17.7 pmol/mmol, $P = .02$) (Fig. 3A). On the other hand, there was no significant difference in II_{MTT} between the 2 mastication procedures in the predisposed group (B).

Fig. 4 shows the serum insulin concentrations at 4 time points in OGTT (A) and MTT in usual mastication (B) in the NGT group (n = 14) and the predisposed group (n = 10) in subjects who underwent both OGTT and MTT. The

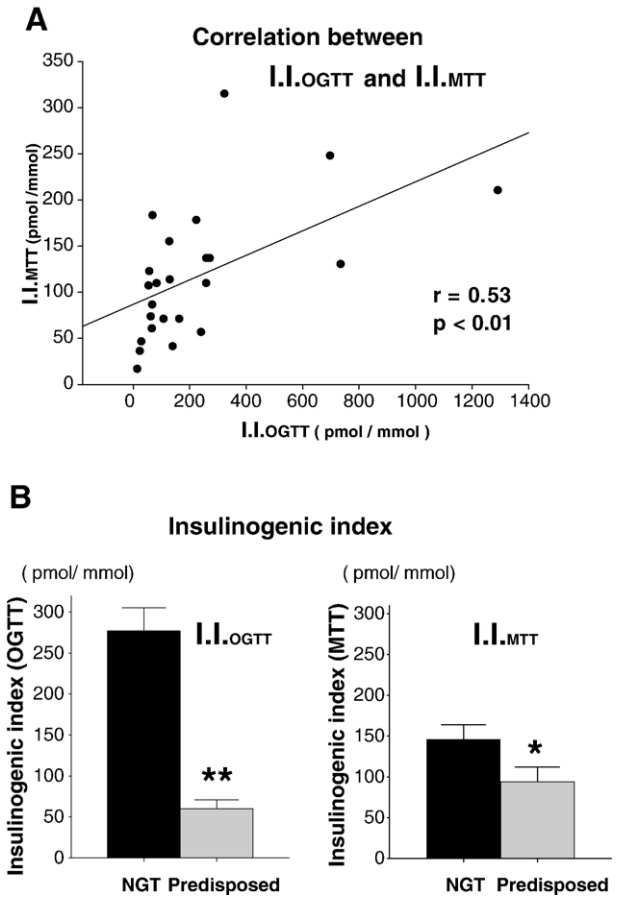

Fig. 5. A, Correlation between the II estimated from OGTT and MTT in usual mastication in 24 subjects who underwent both OGTT and MTT. B, II_{OGTT} (II during the first 30 minutes after OGTT) and II_{MTT} (II during the first 30 minutes after MTT) in usual mastication in the NGT group (n = 14) and the predisposed group (n = 10). Data are means ± SE, $*P < .05$, $**P < .01$.

serum insulin concentrations in the NGT and the predisposed groups showed a general similarity in both OGTT and MTT. The fasting serum insulin concentrations in both groups were similar in both tests. The peak serum insulin concentration occurred at 30 minutes in the NGT group and at 60 minutes in the predisposed group in both tests. The serum insulin concentration at 30 minutes was significantly higher in the NGT group than in the predisposed group in both tests (OGTT, 482.9 ± 55.2 vs 246.8 ± 34.4 pmol/L, $P < .05$; MTT, 426.2 ± 48.1 vs 227.4 ± 30.9 pmol/L, $P < .05$). There was no significant difference in the serum insulin concentration between the 2 groups at 60 and 120 minutes in both tests.

Fig. 5 shows the correlation between II_{OGTT} and II_{MTT} in usual mastication (A) and the IIs (B). II_{MTT} was significantly correlated with II_{OGTT} in the 24 subjects who underwent both tests ($r = 0.53$, $P < .01$) (A). II_{OGTT} (276.6 ± 28.0 vs 60.1 ± 11.3 pmol/mmol, $P = .004$) and II_{MTT} (145.8 ± 17.8 vs 94.0 ± 17.6 pmol/mmol, $P = .046$) were significantly higher in the NGT group than in the predisposed group (B).

4. Discussion

In this study, we compared the effects of thorough mastication on postprandial glucose and insulin secretion in subjects with NGT and subjects predisposed to type 2 diabetes. Thorough mastication was especially effective in reducing the postprandial plasma glucose concentrations in the NGT group, probably because of greater early-phase insulin secretion.

Surprisingly, the AUC for glucose was significantly less in thorough mastication compared with usual mastication, without an increase in the AUC for insulin. Mastication breaks food into small pieces, stimulates salivation, and mixes food with salivary enzymes, improving hydrolysis of carbohydrates in the mouth and stomach [10] and enhancing glycemic and insulinemic responses. Thus, thorough mastication should be expected to increase both postprandial plasma glucose and serum insulin concentrations. However, regardless of the mastication procedure, the plasma glucose and serum insulin concentration reached a peak at 30 minutes in the NGT group. In addition, II_{MTT} in thorough mastication was significantly higher than in usual mastication. Apparently, NGT subjects have sufficient early-phase insulin secretory capacity to lower the plasma glucose concentration after the more rapid absorption of glucose in thorough mastication. Thorough mastication was especially effective in NGT subjects in potentiating insulin secretion from 5 minutes (the cephalic-phase) to 90 minutes, resulting in lower plasma glucose concentrations after 30 minutes. Insulin secretion from 90 to 180 minutes was thus reduced, resulting in the same AUC for insulin in the 2 mastication procedures in the NGT group. Thus, the present study suggests that people with NGT can reduce postprandial plasma glucose concentrations by masticating food thoroughly.

In contrast to the NGT group, thorough mastication was not effective in reducing the postprandial plasma glucose concentration in the predisposed group. Compared with usual mastication, the glycemic response in thorough mastication was significantly enhanced at 60 minutes, and the insulinemic response was enhanced at 90 minutes. In addition, the AUCs for both glucose and insulin in thorough mastication were significantly greater than in usual mastication. In addition, in contrast to the NGT group, there was no significant difference in the II between the 2 mastication procedures in the predisposed group. The fact that thorough mastication did not potentiate insulin secretion in the predisposed group during the first 30 minutes suggests inability of the beta-cells to respond promptly to glucose stimulation. Thorough mastication might be expected to promote satiation with reduced food intake in ordinary life. Food intake can be reduced by a number of monoamines acting on noradrenaline, serotonin, dopamine, and histamine receptors within the hypothalamus [20]. The rate of 40 masticating cycles per minute has been shown to increase the firing rate of serotonergic neurons in cats [21]. Moreover, thorough mastication enhances satiation

independently of energy expenditure by activating neuronal histamine in the hypothalamus [22]. Accordingly, thoroughly masticating food might also benefit similarly predisposed individuals in daily life.

Early-phase insulin secretion is known to be disturbed in patients with type 2 diabetes, IGT, and normoglycemic first-degree relatives of patients with type 2 diabetes [14,23-27], so first-degree relatives of type 2 diabetic patients were included in the predisposed group. Early-phase insulin secretion in both OGTT and MTT was significantly less in the predisposed group than in the NGT group. Thus, the correlation between II_{MTT} and II_{OGTT} observed in the present study suggests that II_{MTT} calculated by the same formula as II_{OGTT} can be used as an index of early-phase insulin secretion. The II_{MTT} in the NGT and the predisposed groups of the present study were clearly different, most probably because of the difference in early-phase insulin secretion, which may underlie the altered postprandial plasma glucose concentrations. Early-phase insulin secretion is commonly referred to in both OGTT and MTT analyses [15-18]. Although the relation between the first-phase insulin response to intravenous glucose challenge and the early insulin response to oral glucose has been investigated recently [28-30], further studies are required to distinguish first- and second-phase insulin secretion sufficiently for in vivo comparison of mastication procedures. Because the plasma glucose concentrations increased gradually in this study, we used the term *early-phase insulin secretion*.

Thorough mastication was found to reduce the postprandial plasma glucose concentration mainly in the NGT group. Although the most important substance in physiological regulation of insulin release is glucose, incretin hormones (gastric inhibitory peptide [GIP] and glucagon-like peptide 1 [GLP-1]) also play important roles in postprandial insulin secretion in healthy subjects [7]. GIP and GLP-1 are released from the gut to the portal vein and are diluted when entering the systemic circulation. Only 10% to 15% of GLP-1 reaches systemic circulation and the pancreas in the intact form [31,32]. In the present study, thorough mastication elicited at most a 1.2-fold increase in the peripheral serum insulin concentration at 60 minutes in the NGT group compared with usual mastication. In a rodent study, intraportal injection of a pharmacological dose of GLP-1 was reported to evoke a peak of only a 2-fold increase in the peripheral insulin response to portal glucose compared with the control condition [33]. Accordingly, the slight change in GIP and GLP-1 in systemic circulation that may correspond to the difference in peripheral serum insulin concentrations in the NGT group would be difficult to detect by peripheral blood sampling. Further studies are required to determine whether differences in the rate of mastication affect incretin concentrations. In addition, other hormones, including glucagon, growth hormone, and cortisol, and other nutrients (amino acids) are also involved in insulin secretion upon meal ingestion [30,34]. We also measured the plasma arginine concentration. Insulin secretion is stimulated by amino acids after the digestion of protein in meal [35]. The AUC of incremental arginine from 0 to 120 minutes in thorough mastication was significantly greater than in usual mastication (data not shown). Thus, increased absorption of arginine in thorough mastication is at least partly responsible for the increased insulin secretion in NGT subjects.

The pancreas has rich innervation from both the sympathetic and parasympathetic nervous system. Sympathetic fibers are found primarily in the splanchnic nerve, whereas parasympathetic fibers are found in the vagus nerve [36]. According to the study of Rasmussen et al [37] and our previous report [38], neural factors play important roles in the normal pattern of insulin secretion. There are 2 neural stages before the late enteric stage when nutrients are absorbed [37]. During the cephalic phase in thorough mastication, the release of acetylcholine is considered to be stimulated more strongly than in usual mastication through activation of vagal-efferent fibers. Thus, during the early enteric phase, when the neurons of the enteric nervous system are activated by nutrients entering the intestine [37], thorough mastication may promote stronger release of cholecystokinin by augmenting gastric emptying. Accordingly, acetylcholine and cholecystokinin might contribute to potentiating early-phase insulin secretion in thorough mastication in the NGT group. In contrast, in the predisposed group, potentiation of early-phase insulin secretion in thorough mastication was not observed, most likely because of the poor response of the beta-cell to neural stimulation.

In addition, mastication mixes food particles with saliva. In studies comparing normal and diabetic subjects, the flow rate of saliva, the volume of saliva secreted per minute, is diminished significantly in diabetic patients [39]. Diabetic neuropathy may well account for this decrease [40]. Because the concentration of amylase in diabetic subjects has been reported to be lower [40], higher [39], and similar [41] to healthy subjects, whether improved exposure of food particles to amylase in saliva affects postprandial plasma glucose concentrations in persons with NGT remains to be determined.

Although the predisposed group was composed of 3 subgroups, first-degree relatives of type 2 diabetic patients, IGT, and type 2 diabetes, it was clearly distinguished from the NGT group in terms of early-phase insulin secretion. However, further investigation of the effect of thorough mastication in each of the subgroups with more samples would be informative.

In conclusion, in the present study, thorough mastication elicited lower postprandial plasma glucose concentrations than usual mastication in the NGT group, most probably because of the potentiation of early-phase insulin secretion. In contrast, in the predisposed group, thorough mastication did not potentiate early-phase insulin secretion and elicited higher postprandial plasma glucose concentrations.

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