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Mastication accelerates Go/No-go decisional processing: An event-related potential study

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HIGHLIGHTS

- We investigated the effects of mastication on Go/No-go decisional processing using event-related potentials (ERPs) and reaction time (RT).
- Mastication affected N140 latency, P300 latency, RT, and the standard deviation of RT.
- Mastication accelerated both response execution processing in Go trials and response inhibition processing in No-go trials.

ABSTRACT

Objective: The purpose of the present study was to investigate the effect of mastication on Go/No-go decisional processing using event-related potentials (ERPs).
Method: Thirteen normal subjects underwent seven sessions of a somatosensory Go/No-go paradigm for approximately 4 min; Pre, and Post 1, 2, 3, 4, 5, and 6. The Control condition included the same seven sessions. The RT and standard deviation were recorded, and the peak amplitude and latency of the N140 and P300 components were analyzed.
Results: The RT was significantly shorter in Mastication than in Control at Post 1–3 and 4–6. The peak latency of N140 was earlier in Mastication than in Control at Post 4–6. The latency of N140 was shortened by repeated sessions in Mastication, but not by those in Control. The peak latency of P300 was significantly shorter in Mastication than in Control at Post 4–6. The peak latency of P300 was significantly longer in Control with repeated sessions, but not in Mastication.
Conclusions: These results suggest that mastication may influence response execution processing in Go trials, as well as response inhibition processing in No-go trials.
Significance: Mastication accelerated Go/No-go decisional processing in the human brain.

1. Introduction

Previous studies reported the effects of mastication on psychological tests related to arousal (Endo et al., 1982; Nageishi et al., 1993; Otomaru et al., 2003), energy expenditure and heart rate (Suzuki et al., 1992, 1994), choice reaction time (RT) (Chu, 1994), positive mood (Smith, 2009), and working memory (Wilkinson et al., 2002; Baker et al., 2004; Stephens and Tunney, 2004; Hirano et al., 2008). For example, Nageishi and colleagues (1993) investigated the effects of mastication on arousal using the UWIST test, which consists of three-dimensional scales, energetic arousal (active–tired), tense arousal (nervous–calm), and hedonic tone (pleasure–displeasure). They observed differences in the scores of these scales between the mastication and control groups. Suzuki and colleagues (1992) reported that mastication of a gum base with no odor or taste for 10 min increased mean energy expenditure by approximately 24.7%, from resting values, and heart rate increased during mastication by six to eight beats per minute. Wilkinson and colleagues (2002) set three experimental

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conditions, chewing, sham chewing, and quiet control ($N = 25$ per group), and they investigated the effects of mastication on simple and choice RTs, vigilance, spatial and numeric working memories, recall, and word and picture recognition. They showed that episodic and working memories as well as immediate and delayed word recall were better under the chewing condition than under the quiet Control condition.

Several studies using electroencephalography (EEG) attempted to clarify these effects by recording background activity (Endo et al., 1982; Masumoto et al., 1999; Morinushi et al., 2000). However, other studies reported no significant effect of gum chewing on memory (Tucha et al., 2004; Johnson and Miles, 2007) or background EEG (Suzuki et al., 1989; Masumoto et al., 1998). Thus, the effects of mastication have been contentious, and objective methods and indexes, instead of psychological and working memory tests, are needed to investigate these effects in more detail.

Our previous study used event-related potentials (ERPs) obtained by time-locked averaging EEG to evaluate the effects of mastication on the central nervous system (CNS) (Sakamoto et al., 2009a). Subjects performed four sessions of an auditory oddball paradigm, which included frequent (80%) and infrequent (20%) stimuli in a random series, and they were instructed to respond only to infrequent stimuli by pressing a button. The RT and ERPs were recorded in the four sessions: Pre (before chewing), and Post 1, Post 2, and Post 3 (after chewing). The RT and the peak latencies of the N100 and P300 components during the Mastication condition (chewing gum) were significantly shorter in Post 2 or Post 3 than in Pre. By contrast, these parameters were almost identical among sessions or significantly longer in Post 2 or Post 3 than in Pre in the Control (relaxing without chewing gum), Jaw Movement (sham chewing), and Finger Tapping (tapping the right index finger) conditions. This study suggests that mastication influences cognitive processing time as reflected by the RT and the latency of ERP waveforms. However, the precise mechanisms underlying the effects of mastication need to be clarified. We hypothesized that mastication influenced arousal. The level of arousal was adjusted according to neural activity in the brain stem (Moruzzi and Magoun, 1949), and the neural pathways basic to the cortical arousal response are known as the ascending reticular activating system (ARAS). We consider the ARAS to be affected by mastication because rhythmic mastication is generated by a central pattern generator (CPG) in the brain stem (Nakamura and Katakura, 1995; Yamada et al., 2005; Lund and Kolta, 2006).

We also focused on the effects of mastication on human motor preparation processing in another study by recording contingent negative variation (CNV) and movement-related cortical potentials (MRCPs) (Sakamoto et al., 2009b). CNV has been associated with both motor preparation and cognitive processes including expectancy, motivation, attention, and arousal (Brunia, 1998; van Boxtel and Brunia, 1994; Ikeda et al., 1996), and MRCPs are recorded preceding self-initiated voluntary movement to reflect the movement preparation process and not cognitive processing for an imperative stimulus (reviewed in Shibasaki and Hallett, 2006). As a result, the effects of mastication on CNV, but not MRCPs, were confirmed, suggesting that mastication mainly affects the nonmotor or cognitive aspects of CNV rather than motor preparation.

Taking the finding of our two previous studies using P300, CNV, and MRCPs into consideration, we hypothesized that the effects of mastication may be found on cognitive processing rather than motor processing. However, the precise mechanisms underlying the effects of mastication have not yet been clarified because the definition of "cognitive processing" includes many factors such as stimulus detection, decision making, and response inhibition.

The present study was conducted to examine the effects of mastication on Go/No-go decisional processing by recording ERPs and behavioral data. This study had two objectives. The first was to clarify the effects of mastication on the ERP waveforms elicited by "target" and "non-target" stimuli during Go/No-go paradigms; we focused on response execution processing in Go (target) trials and response inhibitory processing in No-go (non-target) trials. In No-go trials, two large components, which show a negative deflection at approximately 140–300 ms (N2) after the stimulus onset and a positive deflection at approximately 300–600 ms (P3), were elicited relative to the ERPs recorded in Go trials (Jodo and Inoue, 1990; Kopp et al., 1996; Falkenstein et al., 1999, 2002; Roche et al., 2005). In the present study, we designed "target" and "non-target" stimuli with the same probability to avoid the effect of stimulus probability and minimize differences in response conflict between event types (Braver et al., 2001; Nakata et al., 2005a, b).

The second objective was to determine whether mastication affected "somatosensory" ERPs. Our previous study confirmed the effects of mastication on "auditory" ERPs during oddball paradigms (Sakamoto et al., 2009a). We assumed that such effects would not be dependent on sensory modalities including visual, auditory, and somatosensory, if mastication influenced the state of arousal via ARAS and accelerated cognitive processing. We previously identified No-go-related brain potentials following somatosensory (tactile) (Nakata et al., 2004, 2005a,b, 2006a,b, 2010a,b, 2012) and painful (noxious) stimuli (Nakata et al., 2009). In somatosensory Go/No-go paradigms, the amplitude of No-go-N140 (N140 evoked by No-go stimuli) was more negative than that of Go-N140 (N140 evoked by Go stimuli). The amplitude of No-go-P300 (P300 evoked by No-go stimuli) was also significantly larger than that of Go-P300 (P300 evoked by Go stimuli). A thorough literature search revealed that the effects of mastication on somatosensory cognitive processing have not yet been examined. Thus, the present study investigated whether mastication affected the amplitudes and/or latencies of somatosensory Go- and No-go-N140 and Go- and No-go-P300.

Here, we showed the significant effects of mastication on somatosensory ERP waveforms.

2. Methods

2.1. Subjects

Twenty normal right-handed subjects (11 males and nine females; mean age 25.5 years, range 21–34) participated in the present study. None of the subjects had a history of neurological or psychiatric disorder. Informed consent was obtained from all subjects; however, the aim of the experiment performed was not explained to avoid any effect of bias. The study was approved by the Ethical Committee of the National Institute for Physiological Sciences, Okazaki, Japan, and Nara Women's University, Nara City, Japan.

2.2. Experiment procedure

The experiment consisted of two conditions, Mastication and Control, each performed on a different day. Half of the subjects began with the Mastication condition and half with the Control condition. The Mastication condition comprised seven sessions of recordings: Pre, Post 1, Post 2, Post 3, Post 4, Post 5, and Post 6. Subjects performed a somatosensory Go/No-go paradigm for approximately 4 min each session. Subjects were asked to chew gum for 5 min at a relaxed self-pace after one session. There were six gum-chewing intervals (Fig. 1A) in total. The gum was removed from the mouth during the EEG-recording periods. A special gum base that was odorless and tasteless was prepared (CAT21 Chewing Pellet, NAMITEC Co., Ltd., Osaka, Japan), and it was made of

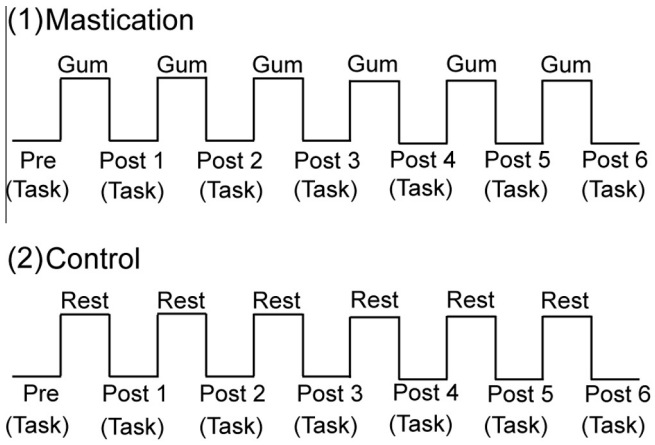

Fig. 1. Protocol for the Mastication and Control conditions. Subjects underwent seven sessions of a somatosensory Go/No-go paradigm under each condition. In Mastication, subjects were asked to chew a gum base that was odorless and tasteless during the intervals between sessions for 5 min. In Control, subjects were instructed to relax without gum chewing during the intervals.

polyvinyl acetate, wax, and polyisobutylene, based on Japan food hygiene laws. Each gum was packed. The Control condition included the same seven sessions (Pre, Post 1, Post 2, Post 3, Post 4, Post 5, and Post 6), but subjects were instructed to relax without chewing gum in each interval (Fig. 1B).

We stimulated the second or fifth digit of the left hand with ring electrodes. The electrical stimulus was a current constant square-wave pulse 0.2 ms in duration, and the stimulus intensity was 2.5 times, a sensory threshold that yielded no pain or unpleasant sensations. The anode was placed at the distal interphalangeal joint and the cathode at the proximal interphalangeal joint of the corresponding digit. The second digit was used for the Go stimulus at a probability of 0.5, and the fifth digit for the No-go stimulus at a probability of 0.5. The stimulus setting of Go and No-go was the same in all subjects. The interstimulus interval was 0.3 Hz.

Subjects were instructed to keep their eyes open and look at a small fixation point positioned in front of them at a distance of approximately 1.5 m. The subjects had to respond by pushing a button with their right thumb (contralateral to the stimulated side) as quickly as possible after presentation of the Go stimulus. The subjects were also asked not to respond to the No-go stimulus. One run comprised 60 epochs of stimulation, which included 30 epochs for the second digit and 30 for the fifth digit. As a practice run, the subjects were instructed to perform the task for 10 stimuli before the recordings.

We previously confirmed the effects of stimulated sites during somatosensory Go/No-go paradigms (Nakata et al., 2006b, 2010b). Our findings showed that the peak amplitudes of N140 and P300 were larger in No-go trials than in Go trials, even when the second and fifth digits were used for No-go and Go trials, respectively, which indicated that the Go/No-go effect was independent of the stimulated sites of digits.

2.3. EEG recordings and analysis

EEGs were recorded with Ag/AgCl disk electrodes placed on the scalp at Fz, Cz, Pz, C3, and C4, according to the International 10–20 System. Each scalp electrode was referenced to linked earlobes. The ground electrode was placed at Fpz. To eliminate eye movements or blinks exceeding 100 μV, an electrooculogram (EOG) was recorded bipolarly with a pair of electrodes placed 2 cm lateral to the lateral canthus of the left eye and 2 cm above the upper edge of the left orbit. Impedance was maintained at <5 kΩ. All EEG signals were collected on a signal processor (Neuropack MEB-2200 system, Nihon-Kohden, Tokyo, Japan). The analysis epoch for ERPs was 600 ms including a prestimulus baseline period of 60 ms. The band-pass filter was set at 0.1–50 Hz, and the sampling rate was 1000 Hz. The peak amplitudes and latencies of N140 and P300 were measured at 110–180 and 260–450 ms, respectively. The peak latencies for the individual ERP components were determined using a measuring scale on the Neuropack system with visual inspection. Amplitudes were measured from baseline to peak.

To analyze the N140 and P300, the peak amplitude and latency data were subjected to an analysis of variance (ANOVA) with repeated measures using Condition (Mastication vs. Control), Trial (Go vs. No-go), Session (Pre, Post 1–3, and Post 4–6), and Electrode (Fz, Cz, and Pz) as within-subject factors. Data on Post 1, Post 2, and Post 3 were averaged after determining each peak amplitude and latency, and defined as Post 1–3. The same averaging was performed for Post 4, Post 5, and Post 6, and defined as Post 4–6. The significant main effect of Trial and/or interaction including a Trial factor indicated the existence of differences between Go-ERPs and No-go-ERPs. The data of four subjects were excluded because they did not match the criteria for submission to ANOVA with repeated measures for the following reasons: the peak latency of P300 was not determined at 260–450 ms in one subject, the mean RT was markedly later in one subject than in the other subjects, one subject slept during the experiment, and the ERP data in one subject involved unexplained noise.

Behavioral data on the mean RT, the standard deviation (SD) of RT, and commission and omission errors were subjected to a two-way ANOVA with repeated measures using Condition and Session as within-subject factors. Whether Mauchly's sphericity assumption was violated was tested for all repeated-measures factors with more than two levels. If the result of Mauchly's test was significant and the assumption of sphericity was violated, the Greenhouse–Geisser adjustment was used to correct the sphericity by altering the degrees of freedom using a correction coefficient epsilon. Statistical tests were performed using computer software (SPSS for windows ver. 16.0, SPSS). The significance was set at $p < 0.05$.

3. Results

3.1. Behavioral data

Fig. 2A shows the mean RT with standard error (SE), and the averaging data for Post 1–3 and Post 4–6. A significant Condition–Session interaction was found for RT ($F(2,30) = 3.477$, $p < 0.05$). This interaction revealed a difference in the mean RT between the Mastication and Control conditions with repeated sessions. Further analyses of the effects of Condition on Session showed that RT was significantly shorter in Mastication than in Control at Post 1–3 ($F(1,15) = 7.656$, $p < 0.05$) and Post 4–6 ($F(1,15) = 5.212$, $p < 0.05$), but not at Pre. In addition, further analyses of the effects of Session on Condition revealed that RT was significantly shorter with repeated sessions in Mastication ($F(2,30) = 6.443$, $p < 0.01$), but not in Control.

Fig. 2B shows the SD of RT with SE. A significant Condition–Session interaction was found for the SD of RT ($F(2,30) = 4.723$, $p < 0.05$). This interaction indicated a difference in the SD of RT between the Mastication and Control conditions with repeated sessions. Further analyses of the effect of Condition on Session showed that the response variability (i.e., the SD of RT) was smaller in Mastication than in Control at Post 1–3 ($F(1,15) = 6.043$, $p < 0.05$) and Post 4–6 ($F(1,15) = 13.659$, $p < 0.01$), but not at Pre. Further analyses of the effects of Session on Condition revealed that response variability was significantly smaller with repeated sessions in Mastication ($F(2,30) = 9.850$, $p < 0.01$), but not in Control.

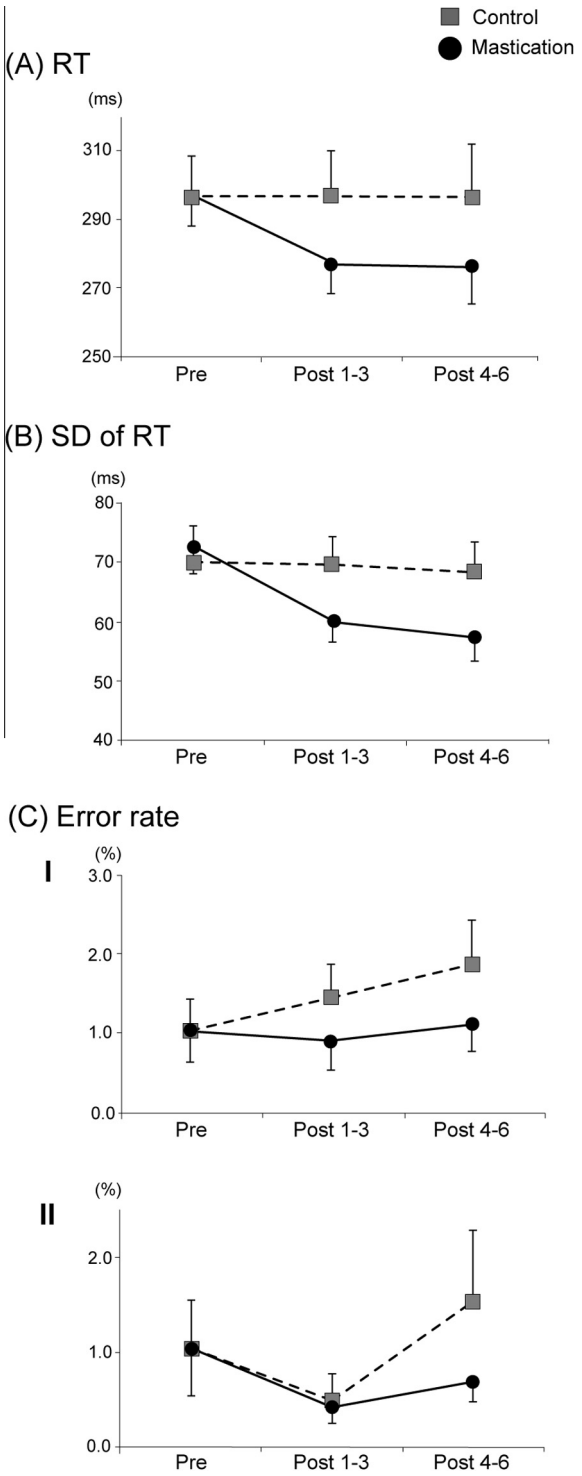

Fig. 2. (A) The mean reaction time (RT) for the Mastication and Control conditions. Black circles indicate RT in Mastication, and gray squares show RT in Control. The bars indicate standard errors. (B) The mean standard deviation (SD) of RT for the Mastication and Control conditions. (C-I) The mean commission error for the Mastication and Control conditions. (C-II) The mean omission error for Mastication and Control.

Fig. 2C-(I) shows the commission error rate with SE. The mean values of commission error were larger in Control than in Mastication. However, no significant main effects or interactions were noted. Fig. 2C-(II) shows the omission error rate with the standard error. No significant main effects or interactions were noted.

3.2. N140 component

Fig. 3 shows the grand-averaged ERP waveforms in Pre during Control. Clear waveforms were recorded from all subjects in all sessions; therefore, the N140 and P300 components were determined at all electrodes.

The results of ANOVA for the peak amplitude of N140 showed a significant main effect of Session (Greenhouse–Geisser correction; $F(1.393,20.902) = 8.941$, $\varepsilon = 0.697$, $p < 0.01$), Electrode (Greenhouse–Geisser correction; $F(1.326,19.891) = 29.338$, $\varepsilon = 0.663$, $p < 0.001$), and Session–Electrode interaction ($F(4,60) = 7.026$, $p < 0.001$). Further analyses of the effects of Session on each Electrode collapsing the effects of Trial and Condition revealed a significant main effect on Fz ($F(2,30) = 7.650$, $p < 0.01$), Cz (Greenhouse–Geisser correction; $F(1.428,21.426) = 12.379$, $\varepsilon = 0.714$, $p < 0.01$), and Pz (Greenhouse–Geisser correction; $F(1.344,20.155) = 4.937$, $\varepsilon = 0.672$, $p < 0.05$), suggesting that the peak amplitude of N140 decreased with repeated sessions at all electrodes (Figs. 4A and 5, and Supplementary Table S1).

The same ANOVA for the peak latency of N140 showed a significant main effect of Electrode (Greenhouse–Geisser correction; $F(1.140,17.099) = 17.807$, $\varepsilon = 0.570$, $p < 0.001$), and Condition–Session–Electrode interaction ($F(4,60) = 3.238$, $p < 0.05$). Further analyses of the effects of Condition on each Session and Electrode collapsing the effects of Trial showed significant differences in the latency of N140 at Pz for Pre between Mastication and Control ($F(1,15) = 6.209$, $p < 0.05$), at Fz for Post 4–6 ($F(1,15) = 6.537$, $p < 0.05$), indicating that the peak latency of N140 was earlier in Mastication than in Control. Further analyses of the effects of Session on each Condition and Electrode collapsing the effects of Trial revealed significant differences in the latency of N140 during Mastication at Fz ($F(2,30) = 3.966$, $p < 0.05$), indicating that the latency of N140 was shortened with repeated sessions in Mastication, but not in Control (Figs. 4B and 5, and Supplementary Table S2).

3.3. P300 component

Significant main effects of Session (Greenhouse–Geisser correction; $F(1.298,19.465) = 15.101$, $\varepsilon = 0.649$, $p < 0.001$), Electrode (Greenhouse–Geisser correction; $F(1.356,20.343) = 52.688$, $\varepsilon = 0.678$, $p < 0.001$), Condition–Session interaction ($F(2,30) = 4.217$, $p < 0.005$), Session–Electrode interaction (Greenhouse–Geisser correction; $F(2.386,35.786) = 3.669$, $\varepsilon = 0.596$,

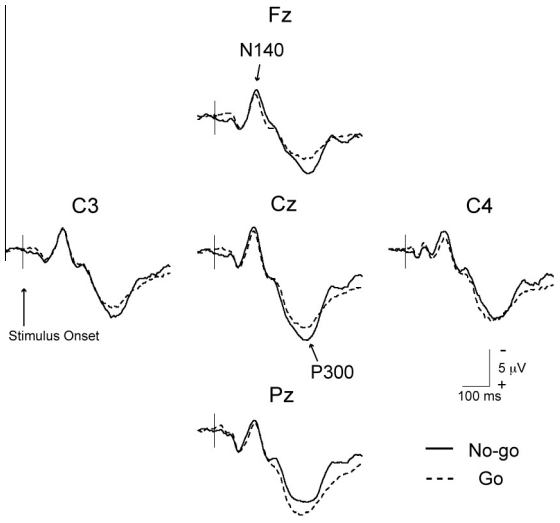

Fig. 3. Grand-averaged somatosensory ERP waveforms evoked by Go and No-go stimuli for Mastication in Pre sessions.

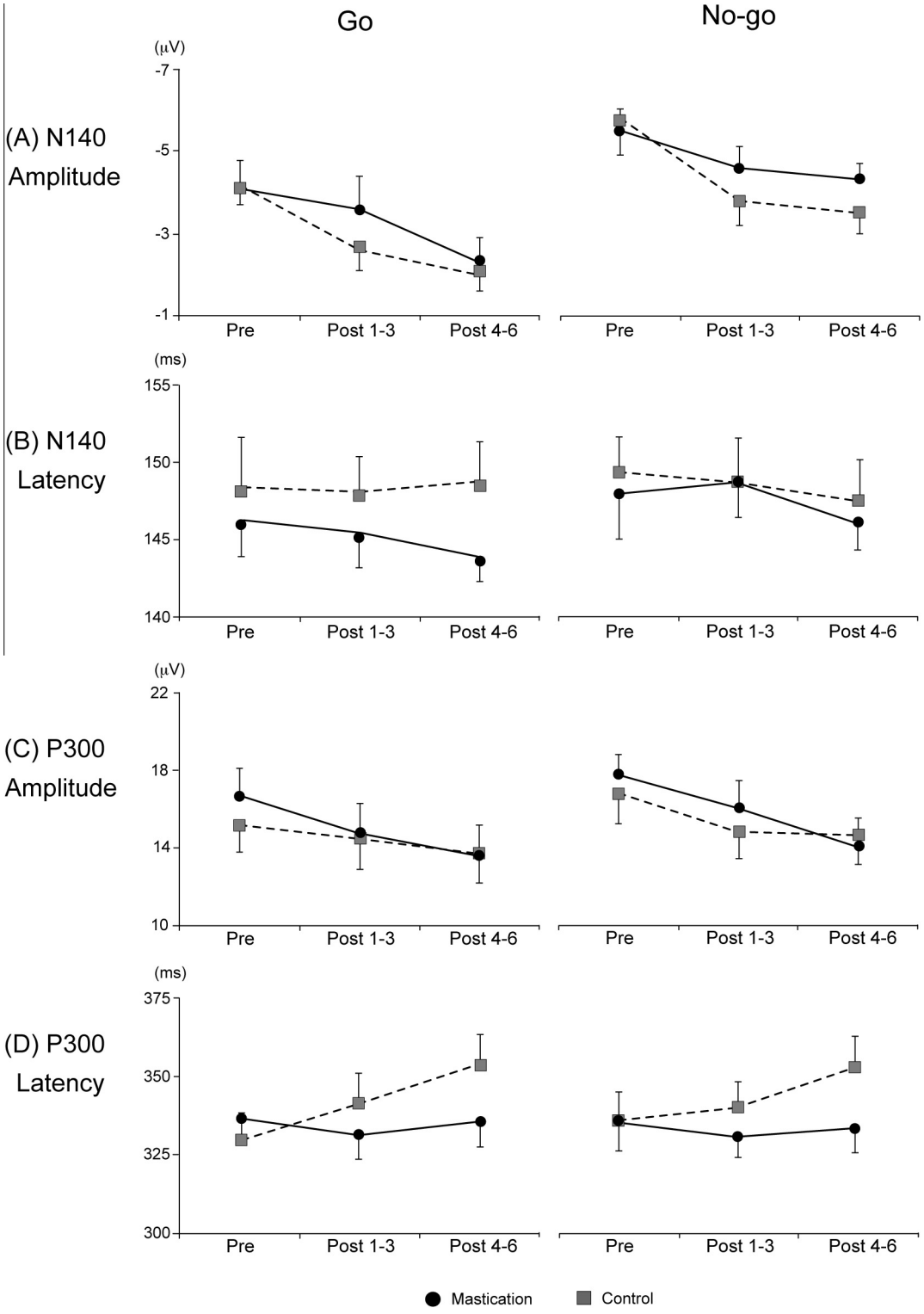

Fig. 4. (A) The mean amplitude of N140. The vertical lines indicate SE. (B) The mean latency of N140. (C) The mean amplitude of P300. (D) The mean latency of P300. Data were collapsed across Fz, Cz, and Pz.

$p < 0.05$), and Trial–Electrode interaction ($F(2,30) = 57.535$, $p < 0.001$) were observed for the peak amplitude of the P300. Further analyses of the effects of Session on each Condition collapsing the effects of Trial and Electrode showed differences in the peak amplitude of P300 among Mastication (Greenhouse–Geisser correction; $F(1.389,20.842) = 17.269$, $\varepsilon = 0.695$, $p < 0.001$) and Control ($F(2,30) = 6.451$, $p < 0.01$), suggesting that the peak amplitude of P300 decreased with repeated sessions. Further analyses of the effects of Session on each Electrode collapsing the effects of Trial and Condition revealed a decrease in the peak amplitude of P300 with repeated sessions at Fz (Greenhouse–Geisser correction; $F(1.467,21.998) = 10.440$, $\varepsilon = 0.733$, $p < 0.01$), Cz (Greenhouse–Geisser correction; $F(1.239,18.588) = 12.175$, $\varepsilon = 0.620$, $p < 0.01$), and Pz (Greenhouse–Geisser correction; $F(1.290,19.356) = 16.222$,

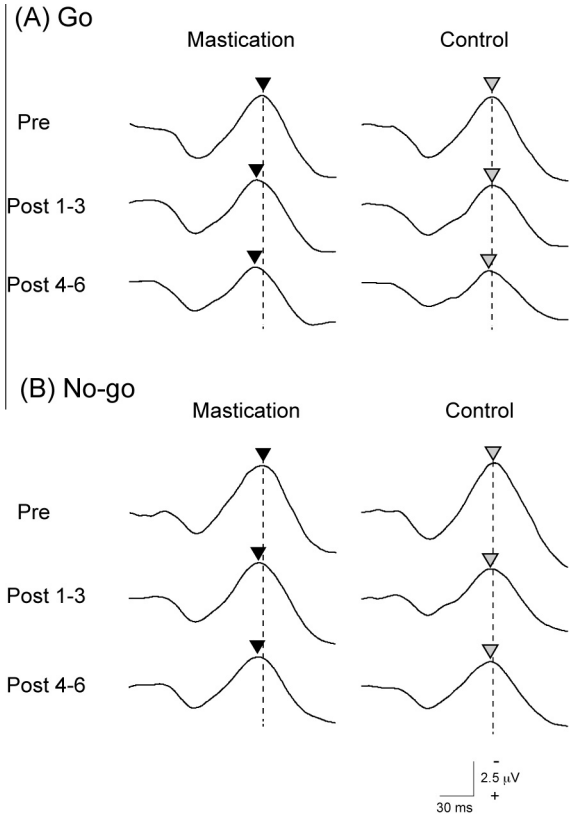

Fig. 5. (A) Grand-averaged waveforms of the Go-N140 component at Cz in Mastication and Control across all subjects. The figures on the left show the waveforms in Mastication, with black triangles indicating the peak latency of Go-N140. The dotted line indicates the peak latency of Go-N140 in Pre. Of note, latency was clearly shorter in the Post than in the Pre sessions. The figures on the right show the waveforms in Control, with gray triangles indicating the peak latency of Go-N140. The dotted line indicates the peak latency of Go-N140 in Pre. The peak latencies were similar among sessions. (B) Grand-averaged waveforms of the No-go-N140 component at Cz in Mastication and Control across all subjects. The figures on the left show the waveforms in Mastication, with black triangles indicating the peak latency of No-go-N140. The dotted line indicates the peak latency of No-go-N140 in Pre. The figures on the right show the waveforms in Control, with gray triangles indicating the peak latency of No-go-N140. The dotted line indicates the peak latency of No-go-N140 in Pre.

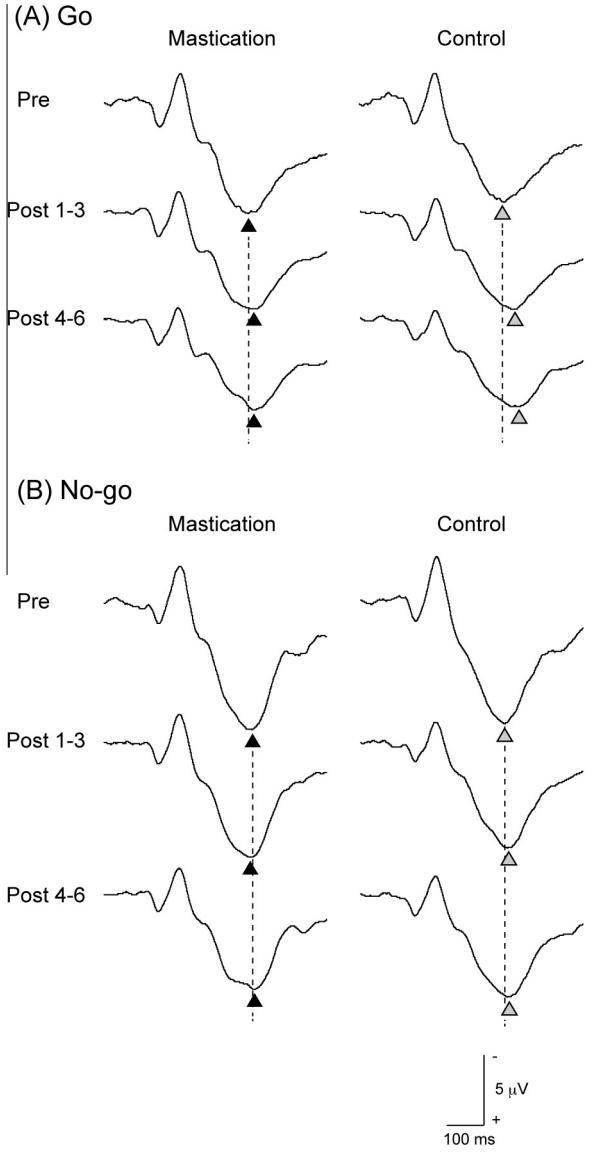

Fig. 6. (A) Grand-averaged waveforms of Go-P300 at Cz for the Mastication and Control conditions. The figures on the left show the waveforms in Mastication, with black triangles indicating the peak latency of Go-P300. The dotted line indicates the peak latency of Go-P300 in Pre. The peak was almost the same among sessions. The figures on the right show the waveforms in Control, with gray triangles indicating the peak latency of Go-P300. The dotted line indicates the peak latency of Go-P300 in Pre. The peak was longer in the Post than in the Pre sessions. (B) Grand-averaged waveforms of No-go-P300 at Cz for the Mastication and Control conditions. The figures on the left show the waveforms in Mastication, with black triangles indicating the peak latency of No-go-P300. The dotted line indicates the peak latency of No-go-P300 in Pre. The peak was almost the same among sessions. The figures on the right show the waveforms in Control, with gray triangles indicating the peak latency of No-go-P300. The dotted line indicates the peak latency of No-go-P300 in Pre. The peak was slightly longer in the Post than in the Pre sessions.

$\varepsilon = 0.645$, $p < 0.001$). Further analysis of the effect of Trial on each Electrode collapsing the effects of Condition and Session demonstrated that the peak amplitude of No-go-P300 was significantly larger than that of Go-P300 at Fz ($F(1,15) = 41.420$, $p < 0.001$) and Cz ($F(1,15) = 6.735$, $p < 0.05$), and significantly smaller at Pz ($F(1,15) = 11.918$, $p < 0.01$) (Figs. 4C and 6, and Supplementary Table S3).

The results of ANOVA for the peak latency of P300 revealed a significant main effect of Condition ($F(1,15) = 7.214$, $p < 0.05$) and Session (Greenhouse–Geisser correction; $F(1.345,20.169) = 6.370$, $\varepsilon = 0.672$, $p < 0.05$), and Condition–Session interaction ($F(2,30) = 4.664$, $p < 0.05$). Further analyses of the effects of Condition on each Session collapsing the effects of Trial and Electrode showed that the peak latency of P300 was significantly shorter in Mastication than in Control at Post 4–6 ($F(1,15) = 11.604$, $p < 0.01$), and slightly shorter at Post 1–3 ($F(1,15) = 4.459$, $p = 0.052$). Further analyses of the effects of Session on each Condition collapsing the effects of Trial and Electrode showed the peak latency of P300 to be significantly longer among Control with repeated sessions ($F(2,30) = 7.868$, $p < 0.01$), but not among Mastication (Figs. 4D and 6, and Supplementary Table S4).

4. Discussion

We measured ERPs, RT, the SD of RT, and behavioral error rates during somatosensory Go/No-go paradigms in the present study to evaluate the effects of mastication on human Go/No-go decisional processing.

As behavioral data, RT was significantly shorter in Mastication than in Control at Post 1–3 and Post 4–6, but not at Pre, and was significantly shorter with repeated sessions in Mastication, but not in Control (Fig. 2A). RT is an important measure for under-

standing sensorimotor performance in humans (Schmidt and Lee, 2000), and it is defined as the time from stimulus onset to the response, including components such as stimulus evaluation and response selection (Doucet and Stelmack, 1999). Therefore, our findings concerning the modulation of RT in Mastication indicate that sequential processing from stimulus input to response output was accelerated with mastication. Moreover, response variability (i.e., the SD of RT) was significantly smaller in Mastication than in Control at Post 1–3 and Post 4–6, but not at Pre, and was significantly smaller with repeated sessions in Mastication, but not in Control (Fig. 2B). Response variability has been identified as an important factor for evaluating the speed and accuracy of movement. It is often calculated as the SD of RT (Segalowitz et al., 1997; Johnson et al., 2005), indicating the variability of the time from the stimulus onset to the response, which includes components such as stimulus evaluation and response selection. Our results indicated that mastication decreased response variability with repeated sessions. In contrast to the shortened RT and SD of RT, behavioral error rates did not differ between Mastication and Control (Fig. 2C). Our results were similar to a previous study evaluating the differences in reaction, alerting, and conflict times between Mastication and Control (Hirano et al., 2013). Hirano and colleagues showed that cognitive processing presented as RT was accelerated after mastication, whereas behavioral effects shown as alerting and conflict times were not observed (Hirano et al., 2008). As our Go/No-go paradigms were simple to perform for the participants, behavioral data involving behavioral error rates may not have been affected by mastication.

The first objective of this study was to investigate the effect of mastication on ERPs for both the "target (Go)" and "non-target (No-go)" stimuli. Our results showed that the peak latency of N140 was significantly earlier in Mastication than in Control at Fz for Post 4–6, and the latency of N140 was shortened with repeated sessions in Mastication, but not in Control. No significant differences were observed in the amplitudes or latencies of Go-N140 and No-go-N140 between Mastication and Control (Fig. 4A and b, and Supplementary Tables S1 and S2). The peak latency of P300 was significantly shorter in Mastication than in Control at Post 4–6, and the peak latency of P300 was significantly longer among Control with repeated sessions, but not among Mastication. No significant differences were observed in the latencies of Go-P300 or No-go-P300 between Mastication and Control (Fig. 4C and D, and Supplementary Tables S3 and S4). Taken together, these results demonstrated that mastication affected the ERP waveforms elicited by both the "target" stimulus and the "non-target" stimulus. In other words, the effects of mastication on response execution processing were apparent in Go trials and inhibitory processing in No-go trials. In addition, an effect was observed on the latencies of N140 and P300, but not on the amplitudes of N140 and P300. Thus, the effects of mastication appeared to affect the speed of response execution and inhibitory processing. As the present study prepared a special gum base that was odorless and tasteless, these factors could be ruled out.

As discussed in Section 1, we hypothesized that mastication influenced arousal. The level of arousal was previously shown to be adjusted by neural activity in the brain stem (Moruzzi and Magoun, 1949), and the neural pathways basic to the cortical arousal response are known as ARAS. We consider the ARAS to be affected by mastication because rhythmic mastication is generated by the CPG in the brain stem (Nakamura and Katakura, 1995; Yamada et al., 2005; Lund and Kolta, 2006). Many studies have reported that the CPG is driven not only by mastication but also by cyclic movements such as stepping, walking, and pedaling (Dietz, 2003; Yuste et al., 2005; Zehr et al., 2007). ERP-based studies demonstrated that the peak latency and/or amplitude of the P300 changed after these exercises (Polich and Kok, 1995; Nakamura et al., 1999; Yagi et al., 1999; Magnié et al., 2000; Hillman et al., 2003; Kamijo et al., 2004, 2007). Magnié and colleagues and Yagi and colleagues also indicated that the level of arousal has an important influence on ERP waveforms. If our hypothesis is correct, the waveforms of ERPs during somatosensory Go/No-go paradigms may be affected by stepping, walking, and pedaling. CPG has been detected in mammals such as monkeys and cats during stepping, walking, and mastication. These movements can be performed involuntarily, and they can be maintained for a long time (e.g., 30 min). By contrast, it is very difficult for mammals and even humans to perform finger tapping for 30 min, whereas stepping, walking, and mastication can easily be performed. This evidence reflects CPG driving. In our previous study (Sakamoto et al., 2009a), jaw movement without gum and finger tapping did not facilitate RT or P300. These movements are not as commonly performed in daily life as gum chewing, walking, and pedaling, even if jaw movement without gum chewing and finger tapping are rhythmic movements. Thus, jaw movements without gum chewing and finger tapping may not have precisely driven CPG, and caused fatigue rather than arousal. However, this is highly speculative; therefore, the effects of other cyclic movements should be examined.

The second objective of the present study was to clarify the effects of mastication on "somatosensory" ERPs. Our previous study confirmed the effects of mastication on "auditory" ERPs during oddball paradigms (Sakamoto et al., 2009a, b), and it showed that the latencies of auditory N100 and P300 components were significantly shorter in Mastication than in Control. These results suggested that such effects may not be dependent on sensory modalities including auditory and somatosensory. The somatosensory N140 component was generated from several regions including the secondary somatosensory cortex (SII), insula, cingulate cortex, and medial temporal area (Inui et al., 2003; Kida et al., 2006), and a negative potential generated from the prefrontal cortex was recorded at approximately 160 ms in No-go trials only, and overlapped with the N140 (Sasaki et al., 1993; Nakata et al., 2005a). In the present study, as the latency of N140 was affected by mastication, we speculate that neural activity relating to the sources of N140, which was associated with somatosensory processing and prefrontal activity, may be accelerated by the effects of mastication. Previous studies investigated the generator of the somatosensory P300 component or P3b elicited in the standard oddball paradigm using equivalent electrical dipole modeling, intracerebral recordings, and magnetoencephalography (MEG) (Yamaguchi and Knight, 1991; Tarkka et al., 1996; Valeriani et al., 2001; Huang et al., 2005). These studies demonstrated that somatosensory P3b activity originated from multiple cerebral regions, such as the dorsolateral prefrontal cortex (DLPFC), premotor area (PM), supplementary motor area (SMA), primary sensorimotor area (SMI), posterior parietal cortex (PPC), inferior parietal lobule (IPL), temporoparietal junction (TPJ), insula, medial temporal region, anterior cingulate cortex (ACC), and hippocampal area. A neuroimaging study using functional magnetic resonance imaging (fMRI) recently reported significantly different activated regions between Mastication and Control during a cognitive test (Hirano et al., 2013). Hirano and colleagues showed higher activations after chewing in the middle and superior frontal gyri, PM, insula, parietal operculum, ACC, posterior cingulate cortex (PCC), and thalamus (Hirano et al., 2008). Based on the brain regions examined in their study, overlapped regions with the generator sources of N140 and P300 may be more accelerated after mastication, such as the insula and cingulate cortex. However, the present study could not conclude in detail which brain regions were affected by mastication.

As a limitation of the present study, the differences observed in the peak latency of P300 across sessions may have reflected differ-

ences in the relative amplitudes of the subcomponent because P300 activity originates from multiple cerebral regions. However, the present study could not apply the independent component analysis or dipole analysis such as low-resolution electromagnetic tomography (LORETA) and brain electric source analysis (BESA) because of the small number of recording electrodes. Therefore, we herein could not directly address which brain regions were mainly influenced by the effects of mastication. Further studies are needed to clarify the precise mechanisms underlying the effects of mastication, for example, by using multichannel EEG recordings.

Furthermore, the effects of mastication may also have differed among subjects. These effects may be related to the frequency of chewing gum in daily life or under stressful conditions. In other words, a relationship may exist between the typical use of chewing gum and shortening of the ERP responses. Unfortunately, we did not record the frequency of chewing gum by the subjects in daily life. Thus, this possibility should be clarified in future studies.

In conclusion, the present study used somatosensory Go/No-go paradigms, and investigated the effects of mastication on RT, the SD of RT, and commission and omission errors as behavioral data, and Go- and No-go-N140 and Go- and No-go-P300 components. The effects of mastication were confirmed on RT and the SD of RT, and the latencies of N140 and P300. These results indicate that mastication accelerates Go/No-go decisional processing, including response execution processing in Go trials and response inhibition processing in No-go trials.

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Conflict of interest: None of the authors have potential conflicts of interest to be disclosed.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.clinph.2014.12.034.

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