Title: Influence of restricted mastication on swallowing function

Short title: Mastication restriction and swallowing

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Author's contributions

HH designed the study, contributed to the collection and analysis of data, and wrote the initial draft of the manuscript. AS designed the study, contributed to the collection, analysis, and interpretation of data, and assisted in the preparation of the manuscript. All other authors have contributed to data interpretation and critically reviewed the manuscript. All authors approved the final version of the manuscript.

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Abstract

Background: Swallowing is a semi-automatic muscular action that plays a critical role in our daily food intake routine. Dysphagia, caused by diseases, accidents, or aging, can be a major contributor to a reduced quality of life. Often, only symptomatic therapy options exist for dysphagia. Therefore, to develop improved treatment and prevention methods, a better understanding of the pathophysiology associated with dysphagia is needed.

Objective: This study aimed to investigate the intercorrelation between mastication and swallowing, specifically focusing on the effect of restricted mastication duration on swallowing function.

Methods: Thirty healthy men (25±3 years old, mean±SD) were instructed to masticate a gummy jelly for free mastication (G100), half, and one-quarter duration of G100. Masseter and digastric electromyograms (EMGs) were recorded as parameters, representing masticating and swallowing, respectively, along with the velocity of the thyroid cartilage ridge measured with an accelerometer. Masticatory efficiency was evaluated using a glucosensor. The root mean square (RMS) of muscle EMG activity, the number of masticatory cycles, time to peak and total duration of each masticatory cycle, swallowing duration and latency, and masticatory efficiency were analyzed.

Results: Restricting mastication duration reduced the number of mastication cycles and prolonged the time to peak and total duration of masticatory cycles, which increased masticatory muscle activity. On the other hand, shortened duration and latency of swallowing increased swallowing

muscle activity. Consequently, masticatory efficiency decreased.

Conclusion: Under restricted mastication conditions, habitual masticatory patterns could be optimized to achieve safe swallowing in healthy individuals.

Keywords: mastication, swallowing, dysphagia, electromyography, masseter muscles, thyroid cartilage

1 Introduction

Food intake represents a fundamental and daily biological activity, serving not only as a source of essential nutrients but also as a significant social event[1,2]. This process involves a complex chain of physiological events, encompassing mechanical muscle activity and the molecular breakdown and absorption of nutrients[3,4]. Oral food processing comprises five distinct phases: 1. Preceding phase (food recognition), 2. Preparatory phase (formation of a food bolus in preparation for swallowing), 3. Oral phase (transfer of the food bolus from the oral cavity to the pharynx), 4. Pharyngeal phase (movement of the food bolus from the pharynx to the esophagus), and 5. Esophageal phase (transfer of the food bolus from the esophagus to the cardia of the stomach)[5]. Mastication plays a crucial role in both mechanically preparing the food bolus and initiating digestion by introducing salivary enzymes to the food. Swallowing promptly follows, involving semi-automatic muscular actions of various organs, including the tongue and pharynx, facilitating the passage of the food bolus from the mouth through the pharynx, esophagus, and into the stomach. This coordinated process is tightly regulated by a complex network of nerves, including the trigeminal, facial, glossopharyngeal, vagus, and hypoglossal nerves[6].

Consequently, neurological disorders such as amyotrophic lateral sclerosis, Parkinson's disease, stroke, as well as oral injuries and cancers, can often lead to disruptions in normal oral food processing function[7–11]. The most prevalent condition is dysphagia, characterized by difficulty in

swallowing[12]. While often considered secondary to more severe symptoms of the aforementioned diseases, it can result not only in malnutrition but also in life-threatening situations such as asphyxia due to ingested food obstructing the airway or causing infections[13,14]. Furthermore, dysphagia and related eating difficulties significantly impact patients' quality of life, as eating is a common and socially important practice[15]. Unfortunately, the treatment of eating deficits is often challenging and primarily focuses on symptom management, ranging from muscle exercises to strengthen and improve coordination of oral muscles to the adoption of new approaches to mastication and swallowing, and, as a last resort, the application of a feeding tube[16,17]. While a substantial body of research has investigated the effects and causes of dysphagia and related conditions, much of it has concentrated on specific aspects of the process, such as swallowing in cases of dysphagia. Consequently, these processes are frequently examined in isolation. To advance the evaluation and treatment of these conditions, further research is necessary to understand the interrelationships between processes like mastication and swallowing.

Mastication and swallowing are primarily controlled by the masticatory central pattern generator (CPG) and swallowing CPG, located in the medulla oblongata[18,19]. These adaptive networks of neurons activate motor neurons, generating task-specific motor patterns, including the rhythmic movements of mastication and the precise act of swallowing[20]. Intriguingly, animal studies have demonstrated the influence of the masticatory CPG and rhythmic jaw movements on the neural

circuitry of the swallowing reflex[21–23]. This suggests a direct influence of rhythmic mastication cycles on the subsequent swallowing process. In this study, we investigate the effect of reduced mastication duration on both the masticatory process itself and the subsequent swallowing process.

2 Materials and method

2.1 Participants

Thirty participants (30 men, mean age±SD: 25±3 years old) participated in this study. These participants were recruited from both students and staff at Osaka Dental University. Inclusion criteria were 1) men, 2) age: ≤ 35 years, and 3) no diagnoses according to the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD)[24]. Exclusion criteria were: 1) removable denture wearers, 2) having severe periodontal disease, 3) being diagnosed with Sjögren's syndrome, 4) undergoing medical treatment, and 5) participating in other clinical studies. We ensured that all participants fully understood the study's purpose, content, and data usage, and obtained their written consent. This study adhered to the Declaration of Helsinki and received ethical approval from the Ethics Committee of Osaka Dental University (Approval No. 111146).

2.2 Test Food

In this study, a cylindrical glucose-containing gummy (Glucolam®, GC, Tokyo, Japan) was chosen as the test food. The gummy jelly weighted 2.3 g and had a size of 14 mm in diameter and 1 mm

thick.

2.3 EMG and accelerometer Recording

Electromyographic (EMG) activity in the right and left masseter muscles (MAR, MAL), as well as the anterior digastric muscle, was recorded during each task. Ag/Ag Cl surface electrodes (NM-316Y, Nihon Koden, Tokyo) were applied to the thickest part of each muscle at a distance of 15 mm between electrodes, as far as possible parallel to the running of the muscle fibers[25]. The ground electrode was affixed to the back of the right hand. The accelerometer (INTERCROSS2222, Intercross Corporation, Tokyo, Japan) was fixed with surgical tape on the skin of the thyroid cartilage ridge[26]. The EMG of the EMG-derived bipolar and the shock waveform of the vertical motion of the thyroid cartilage by the accelerometer were recorded simultaneously using a bio-signal measurement system (FE234, AD Instruments, NEW ZEALAND). The EMG signals were transferred to a personal computer (ProBook450G7, HP,) through an AD converter (Power Lab8/35, AD Instruments, NEW ZEALAND) at a sampling frequency of 2 kHz, with a high cutoff frequency of 50 Hz for the accelerometer and a low cutoff frequency of 15 Hz (Fig. 1).

2.4 Mastication and Swallowing Tasks

Participants were comfortably seated in a dental chair with their heads supported by a headrest, ensuring that the Frankfurt plane was parallel to the floor in the sitting position. After attaching surface electrodes and the accelerometer, participants were instructed to chew a gummy jelly freely

and signal when they were ready to swallow the bolus. The duration between the onset of mastication and the onset of swallowing was measured and defined as the free masticatory duration for the gummy jelly (G100). This task was repeated three times at G100, half duration of G100 (G50), and one quarter duration of G100 (G25), respectively.

2.5 Assessment of Masticatory Efficiency

For G100, G50, and G25, participants were asked to chew the same gummy jelly as in the previous task. After free mastication in G100, they rinsed their mouth with 10 ml of water and mixed the chewed gummy jelly with water[27]. Glucose concentration was measured using a glucose analyzer (GLUCO SENSOR GS-II, GC, Tokyo, Japan) in a standardized manner. Measurements in each duration were repeated three times, and the mean values were used for subsequent statistical analysis.

2.6 Outcome Parameters

Figure 2 presents the outcome parameters analyzed in this study. Mastication-related parameters included the number of total masticatory cycles, the duration and time to peak of each masticatory cycle, and the root mean square (RMS) of masseter EMG activity (Fig.2A). To determine the onset of a masticatory cycle, we considered the first timepoint when the EMG activity exceeded ±2SD of the baseline EMG activity. Similarly, we defined the offset of a masticatory cycle as the time point when the EMG activity fell to ±2SD of the baseline EMG activity. The masticatory duration was

calculated as the time between the onset and offset of a mastication cycle. The time from the onset of a masticatory cycle to its peak point was defined as the time to peak of a masticatory cycle. The number of masticatory cycles was calculated by counting them in each recording, including one before the onset of anterior digastric EMG activity as the last masticatory cycle. The mean RMS of masticatory EMG activity during mastication per cycle was computed by dividing the total RMS by the number of masticatory cycles. The mean activity of the anterior digastric muscles during swallowing as the RMS value of the swallowing muscle was calculated. The time from the onset to the end of the anterior digastric muscle activity during swallowing was defined as the swallowing duration. The time from the onset of the anterior digastric muscle activity during swallowing to the onset of the descending thyroid cartilage movement was referred to as the swallowing latency (Fig. 2B). For the total number of masticatory cycles, both masticatory and swallowing RMS, and glucose concentration, relative values in G50 and G25 were calculated based on those in G100.

2.7 Statistics

The statistical analysis was performed with GraphPad Prism (Version 9, Japanese edition, GraphPad Software, USA). For the mastication-related factors, a two-way analysis of variance (2-way ANOVA) was performed with mastication duration (3 levels: G100, G50, and G25) and site (2 levels: MAL and MAR) as main factors for masticatory muscle RMS only. The D'Agostino and Pearson tests were used to test the normality of the data, and since all were parametric except for the

number of the masticatory cycles, a one-way ANOVA was performed. The number of masticatory cycles was non-normative, so the Friedman test was performed. The main factor in all ANOVAs was the mastication duration. When appropriate, depending on all analysis items, post-hoc Tukey's honestly significant difference test, Dunnett's test, or Dunn's test for multiple comparisons was performed for multiple comparisons. The significant level was set at $P < 0.05$.

3 Results

As shown in Figure 3A, the experimentally induced inhibition of mastication duration resulted in a notable decrease in the number of masticatory cycles. The Friedman test revealed a highly significant effect of mastication duration on the number of masticatory cycles ($P < 0.001$). Post-hoc analysis demonstrated that the number of masticatory cycles in G25 was significantly lower compared to both G50 and G100 ($P < 0.001$). Furthermore, G50 exhibited a significant reduction compared to G100 ($P < 0.001$).

Conversely, both the time to reach the peak of masticatory cycles and the duration of each masticatory cycle increased as a function of reduced mastication duration (Fig. 3B and 3C, respectively). One-way ANOVA indicated a significant effect of mastication duration on time to peak ($F = 3.222$, $P < 0.001$) and masticatory cycle duration ($F = 4.725$, $P < 0.001$). Tukey's post hoc

tests revealed a significant increase in time to peak at G25 compared to G50 and G100 ($P = 0.014$ and $P = 0.028$, respectively). Additionally, there was a significant increase in masticatory cycle duration at G25 compared to G50 and G100 ($P = 0.001$ and $P = 0.004$, respectively).

Examining muscle activity during mastication inhibition (Fig. 3D and 3E), a one-way ANOVA showed a significant effect of mastication duration on masticatory RMS ($F = 4.567$, $P = 0.017$), while no significant effect of site or interaction was observed (site: $F = 0.537$, $P = 0.4646$; interaction: $F = 0.136$, $P = 0.873$). Post-hoc testing demonstrated that masticatory RMS in G25 was significantly increased compared to G100 ($P = 0.006$).

Regarding the swallowing process, participants exhibited a decrease in both swallowing duration and swallowing latency when mastication duration was experimentally inhibited (Figure 4A and 4B, respectively). One-way ANOVA tests revealed a significant effect of mastication duration on swallowing duration ($F = 6.031$, $P = 0.001$) and on swallowing latency ($F = 2.016$, $P = 0.012$). Post-hoc analysis showed that swallowing duration at G25 was significantly shorter than those at G50 and G100 ($P = 0.032$ and $P = 0.003$, respectively). Similarly, swallowing latency at G25 was significantly shorter than that at G100 ($P = 0.002$).

Mastication duration also had a significant effect on swallowing RMS values, as confirmed by one-way ANOVA ($F = 2.619$, $P = 0.001$)(Fig. 4C and 4D). Tukey's post hoc test revealed that swallowing RMS at both G25 and G50 was significantly increased compared to G100 ($P < 0.001$ and $P = 0.012$,

respectively).

Finally, one-way ANOVA indicated that mastication duration had a significantly decreasing effect on mastication efficiency (Fig. 4E) ($F = 2.150$, $P = 0.007$). Post-hoc testing showed that masticatory efficiency at G25 was significantly lower compared to G50 and G100 ($P < 0.001$). Moreover, G50 exhibited a significant reduction compared to G100 ($P < 0.001$).

4 Discussion

This study demonstrated several compensatory adaptations in oral food processing when mastication duration is restricted. As expected, a shortened experimental mastication duration led to a reduction in the number of masticatory cycles. Intriguingly, within this smaller number of masticatory cycles, prolonged total duration and increased time to peak for each cycle were observed, resulting in heightened masticatory EMG activity. Additionally, under the conditions of restricted mastication, a shortened swallowing duration and latency were noted, along with a significant increase in swallowing EMG activity. This heightened muscle activity likely serves as a compensatory mechanism to facilitate the swallowing of incompletely masticated food bolus.

Typically, the initiation of swallowing is triggered when the food bolus is ready to be swallowed during the preparatory phase[28]. Our findings suggest a potential involvement of trigeminal afferents receiving input from mastication muscles in initiating swallowing. Indeed, a past

study has reported similar findings of shortened swallowing latency and increased clenching activity before swallowing[29]. Furthermore, the size of the food bolus just before swallowing was consistent across individuals, even when the number of masticatory cycles and mastication duration differed[29]. This suggests that the initiation threshold for swallowing depends, at least in part, on the size of the chewed food bolus[30].

In support of this, the longer masticatory cycles, extended time to peak, and increased masticatory EMG activity observed in our study likely act as a compensatory mechanism to generate a normal food bolus by generating greater bite force. This altered masticatory pattern is likely to affect the threshold for initiating swallowing by interfering with the signaling from the trigeminal circuit to the neurons responsible for triggering swallowing.

Both the masticatory CPG and the swallowing CPG are rhythm-generating structures located in the medulla oblongata, identified as controllers of rhythmic movements in mastication and swallowing, respectively[18,19]. These centers are believed to regulate motor functions and muscle activity across multiple organs[31]. Animal studies have provided evidence of a neural circuit linking the masticatory CPG and the swallowing reflex[21–23]. Rhythmic jaw movements elicited by stimuli inhibit the peripherally evoked swallowing reflex. Additionally, transcranial magnetic stimulation (TMS) has revealed higher pharyngeal motor evoked potentials (MEPs) following a swallowing task compared to a mastication task[32], indicating an inhibitory effect of mastication on the pharyngeal

swallowing reflex[32]. These findings collectively illustrate how various processes involved in oral food processing are adapted and coordinated to ensure safe and efficient swallowing when normal mastication is disrupted in healthy individuals.

As a next step, we intend to apply these established experimental protocols to assess similar physiological dynamics of oral food processing in patients with neurodegenerative diseases, such as amyotrophic lateral sclerosis (ALS) and Parkinson's disease (PD), both of which have been associated with impaired oral food processing conditions[33–38]. Currently, these patients often require symptomatic treatment following the evaluation of swallowing function through endoscopic swallowing examinations[39]. Symptomatic treatment may include percutaneous endoscopic gastrostomy as a final resort[40]. However, the indication for percutaneous endoscopic gastrostomy is reviewed from both medical and ethical perspectives[41]. Presently, preoperative testing is limited, and patient and caregiver decision-making plays a crucial role. Based on the findings of this study, further investigations into the progression of dysphagia and assessments of oral function to facilitate safe oral food processing in such patients could offer new indicators for predicting dysphagia and provide a less invasive preoperative testing option.

There are certain methodological limitations to consider in this study. Firstly, saliva plays a vital role in oral food processing by contributing to food bolus formation[42]. Adequate saliva secretion enhances viscosity and cohesion, promoting stable and safe swallowing[43]. While our study

used a test jelly food that was assumed to be minimally affected by saliva compared to other foods like bread and cookies, we did not assess saliva secretion. Consequently, further research is needed to understand how and if saliva is involved in the observed compensatory mechanisms during oral food processing. Another limitation is the exclusion of women in our study, as only men were included. In future patient studies, while the prevalence of both ALS and PD has been considered higher in men[44,45], recent research suggests the importance of considering sex-specific factors in these diseases[46,47]. Therefore, it will be crucial to collect data from women to support patient studies and explore potential differences in masticatory and swallowing compensation between the sexes.

5 Conclusion

The mastication-related factor of shortened mastication duration affected swallowing function in the form of increased muscle activity and shortened swallowing duration. This indicates that a new coordinated mastication and swallowing movement may have been formed in healthy adult men.

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Figure legends

Figure 1: Block diagram of the experimental setup. MAR: Right masseter muscle, MAL: Left masseter muscle.

Figure 2: Representative example of recorded waveforms. A) Masseter EMG activity. RMS: Root mean squares. R: masseter RMS, S: Masticatory duration, T: Time to peak of a masticatory cycle. The onset and offset of each cycle were defined based on +2SD of the baseline value. B) Digastric EMG activity and velocity of thyroid cartridge. U: digastric RMS, V: Swallowing duration, W: Swallowing latency, X: the point when the velocity indicates 0, which is considered as the timing of swallowing.

Figure 3: A) Relative change in the number of masticatory cycles (%). B) Time to peak (s). C) Masticatory cycle duration (s). D) Representative waveforms of masticatory RMS in G100, G50, and G25. E) Relative change in masticatory RMS values (%). *: $P < 0.05$, **: $P < 0.01$, ***: $P < 0.001$. The error bars indicate SEM. N = 30.

Figure 4: A) Swallowing duration (s). B) Swallowing latency (s). C) Representative waveforms of swallowing RMS in G100, G50, and G25. D) Relative change in masticatory RMS values (%). E)

Relative change in masticatory efficiency (%). *: $P < 0.05$, **: $P < 0.01$, ***: $P < 0.001$. The error bars indicate SEM. N = 30.

figure 1

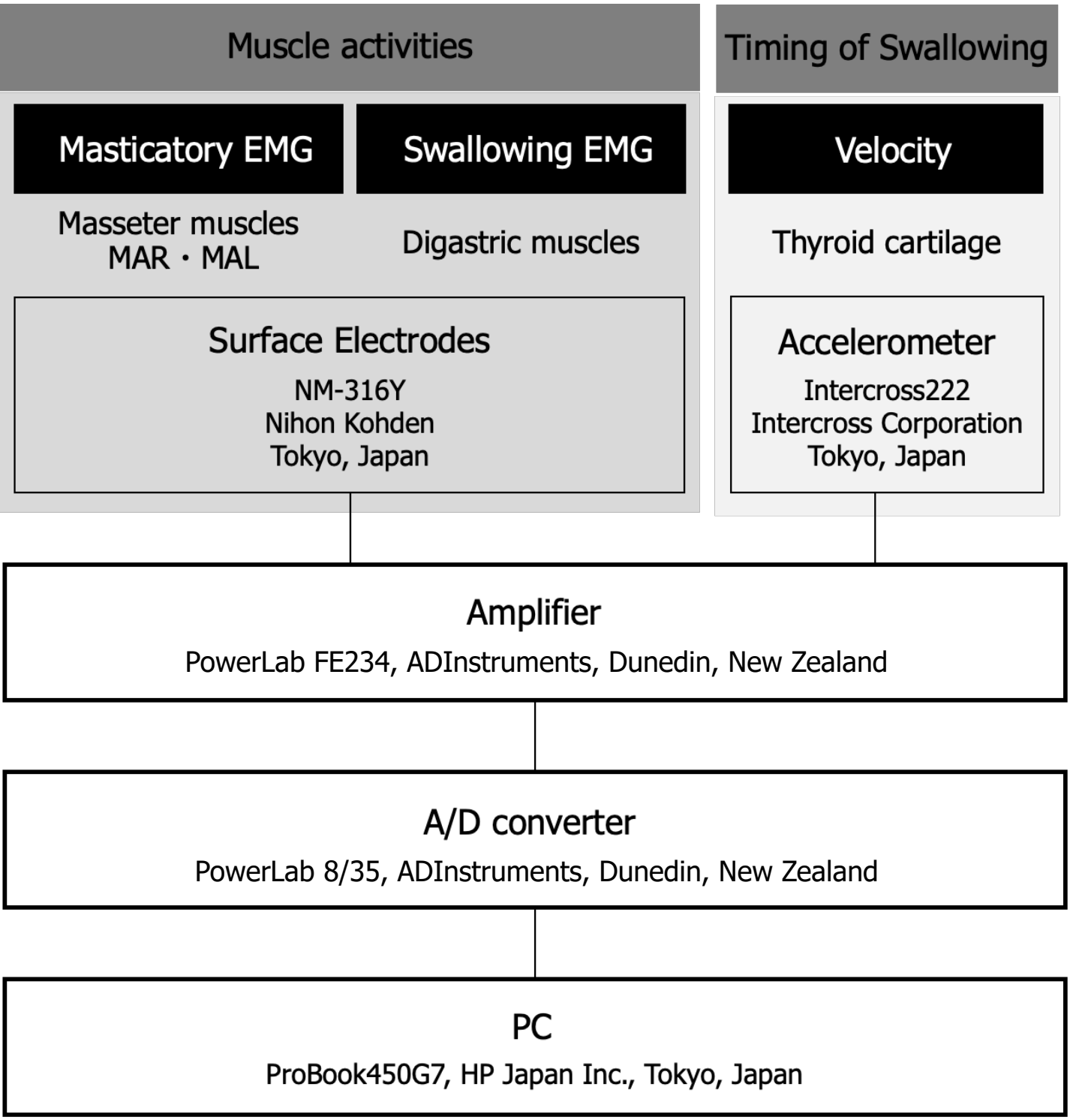
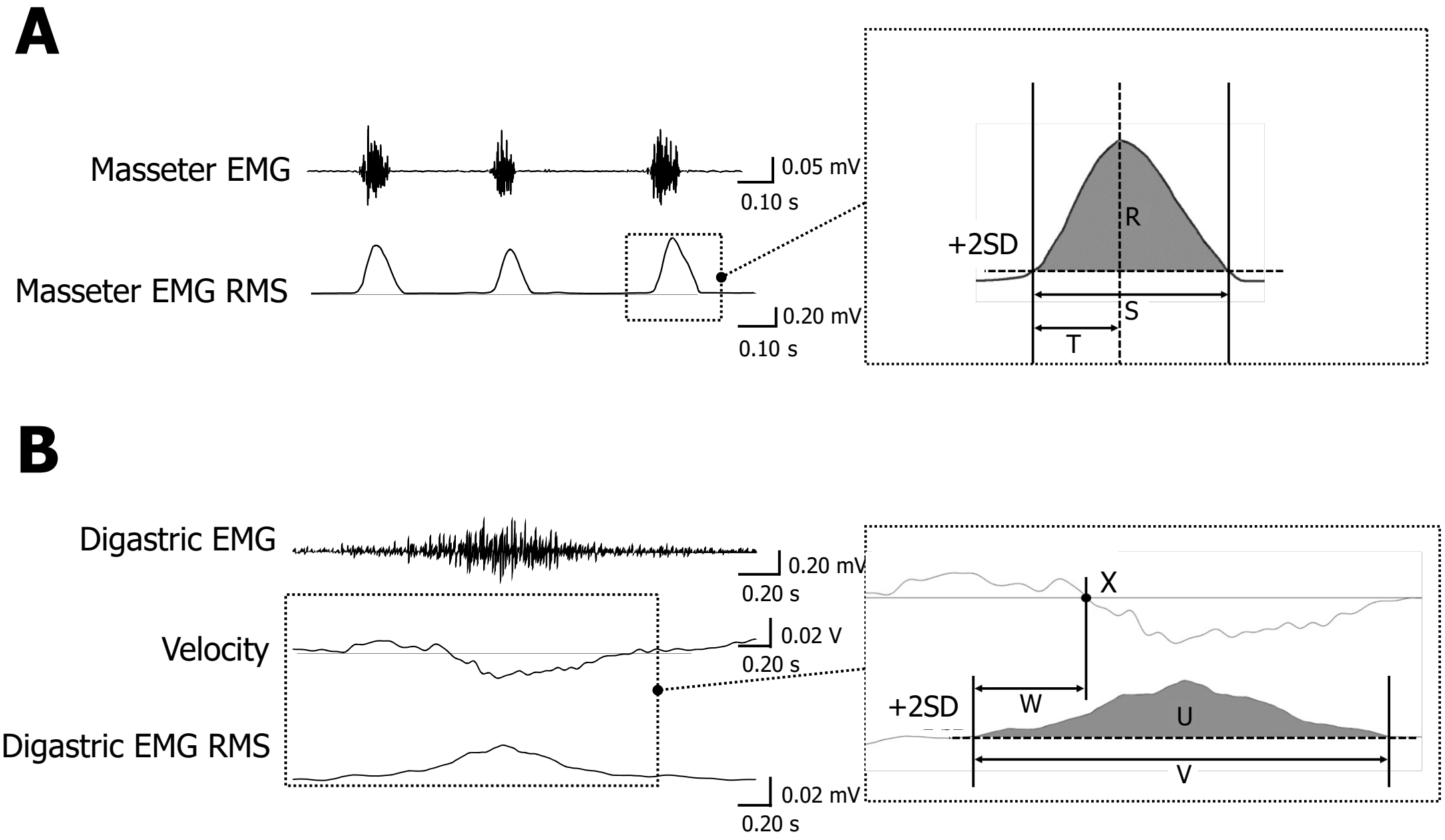

Muscle activities
Timing of Swallowing
Masticatory EMG
Swallowing EMG
Velocity
Masseter muscles
MAR・MAL
Digastric muscles
Thyroid cartilage
Surface Electrodes
NM-316Y
Nihon Kohden
Tokyo, Japan
Accelerometer
Intercross222
Intercross Corporation
Tokyo, Japan
Amplifier
PowerLab FE234, ADInstruments, Dunedin, New Zealand
A/D converter
PowerLab 8/35, ADInstruments, Dunedin, New Zealand
PC
ProBook450G7, HP Japan Inc., Tokyo, Japan

figure 2


A
Masseter EMG
Masseter EMG RMS
0.05 mV
0.10 s
0.20 mV
0.10 s
+2SD
R
S
T
B
Digastric EMG
Velocity
Digastric EMG RMS
0.20 mV
0.20 s
0.02 V
0.20 s
0.02 mV
0.20 s
X
+2SD
W
U
V

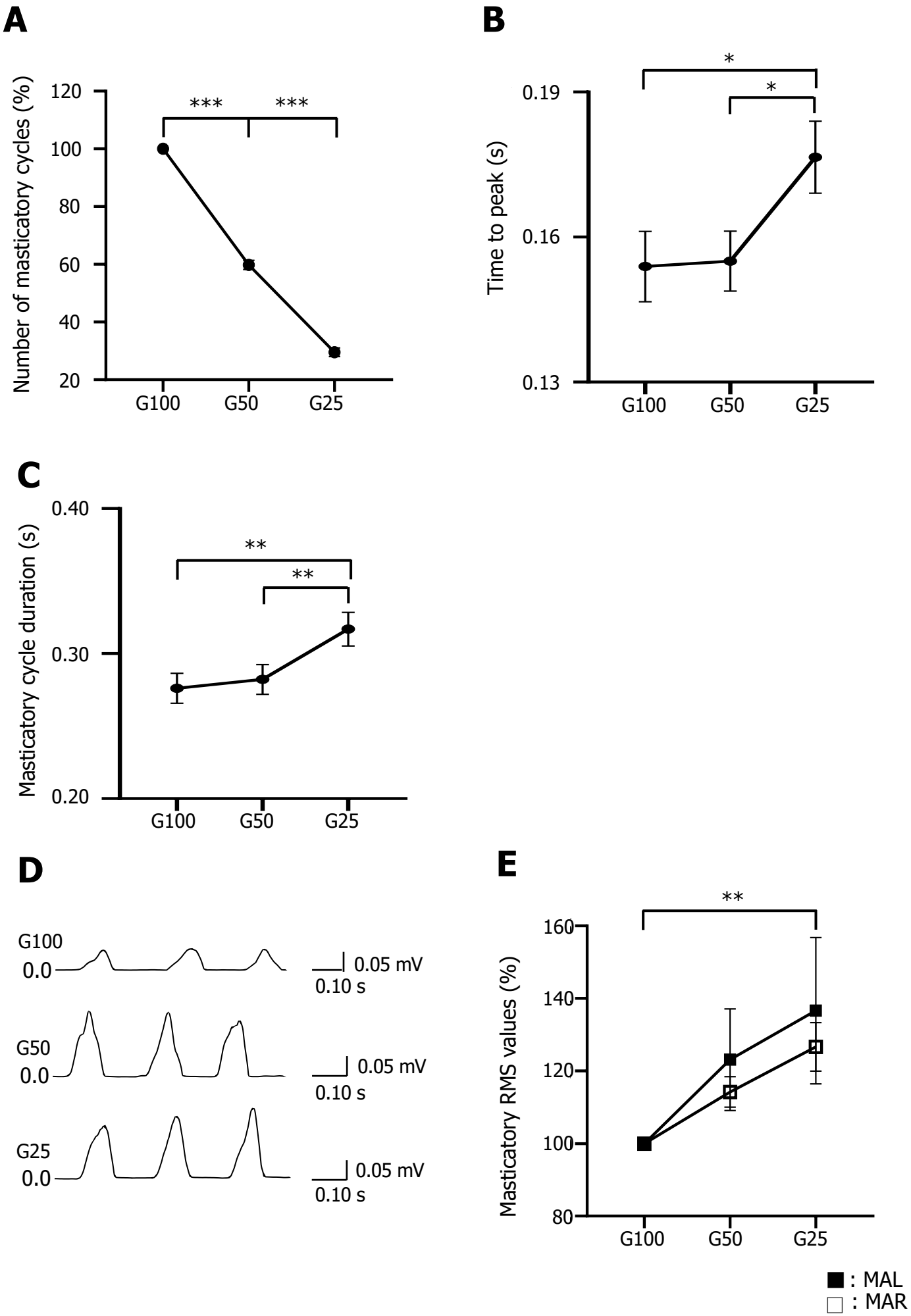
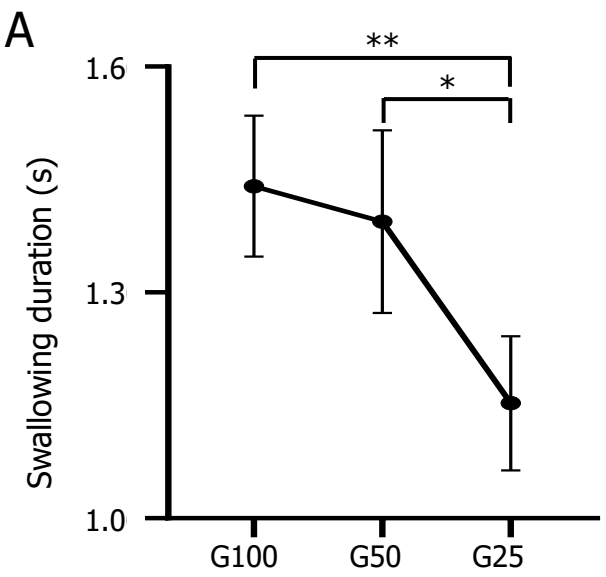
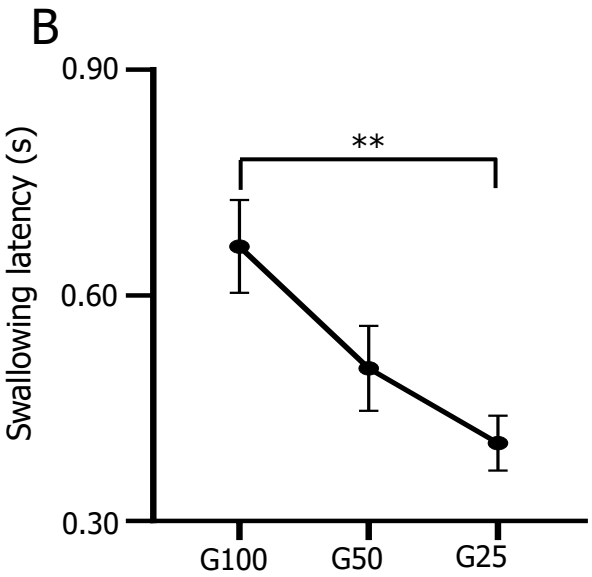
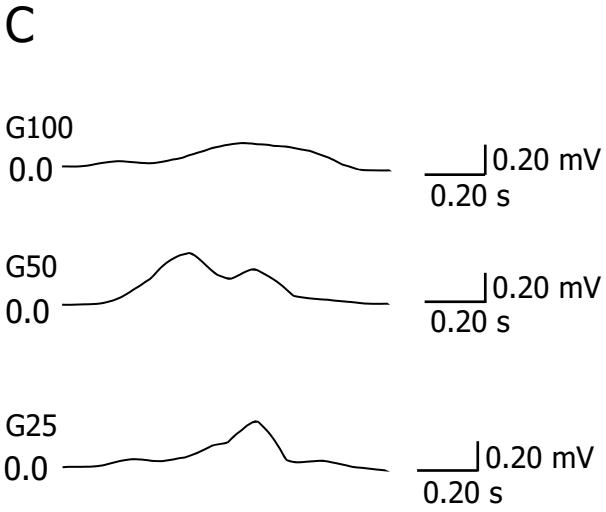

A
Number of masticatory cycles (%)
120
100
80
60
40
20
***
***
G100
G50
G25
B
Time to peak (s)
0.19
0.16
0.13
*
*
G100
G50
G25
C
Masticatory cycle duration (s)
0.40
0.30
0.20
**
**
G100
G50
G25
D
G100
0.0
0.05 mV
0.10 s
G50
0.0
0.05 mV
0.10 s
G25
0.0
0.05 mV
0.10 s
E
Masticatory RMS values (%)
160
140
120
100
80
**
G100
G50
G25
■ : MAL
□ : MAR

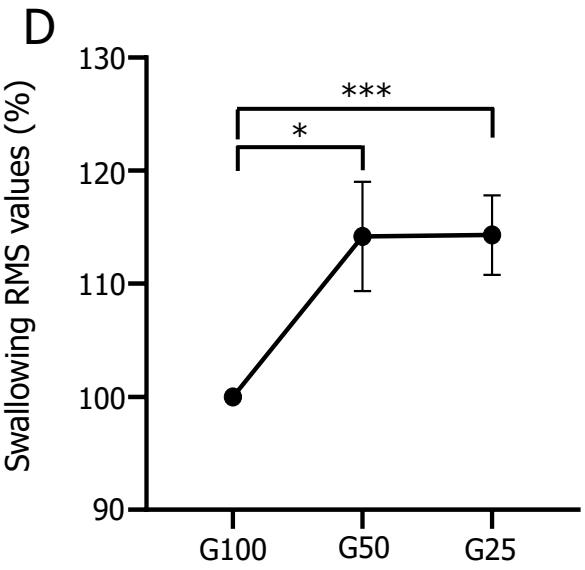
figure 3

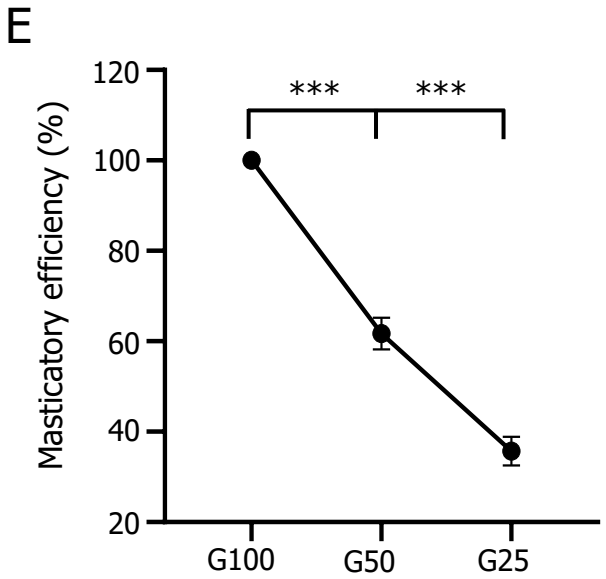
figure 4


A
**
*
1.6
1.3
1.0
Swallowing duration (s)
G100
G50
G25


B
**
0.90
0.60
0.30
Swallowing latency (s)
G100
G50
G25


C
G100
0.0
0.20 mV
0.20 s
G50
0.0
0.20 mV
0.20 s
G25
0.0
0.20 mV
0.20 s


D
***
*
130
120
110
100
90
Swallowing RMS values (%)
G100
G50
G25


E
***
***
120
100
80
60
40
20
Masticatory efficiency (%)
G100
G50
G25