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SHORT COMMUNICATION

Influence of voluntary control of masticatory side and rhythm on cerebral hemodynamics

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Abstract The aim of this study was to investigate the influence on cerebral hemodynamics of voluntary control of masticatory side and rhythm during gum chewing. Blood flow velocity in the middle cerebral artery was measured using transcranial Doppler ultrasonography to evaluate cerebral circulation in healthy volunteers. Heart rate and masseter muscle activity were recorded simultaneously. Volunteers performed three tasks: (1) free gum chewing, (2) gum chewing in which mastication was limited to the right side, and (3) gum chewing in which mastication was limited to the right side and rhythm was set at 1.0 Hz. Changes in cerebral circulation during pre-task, on-task, and post-task periods were analyzed using random effects model, and differences in cerebral circulation and muscle activity between tasks were analyzed using the Friedman test. In all tasks, on-task cerebral circulation was greater than pre-task. Muscle activity and masticatory rhythm varied between tasks, whereas the rate of increase in cerebral circulation did not differ significantly among tasks. These results suggest that cerebral circulation is activated during gum chewing, irrespective of voluntary control of masticatory side and rhythm.

Keywords Chewing · Cerebral hemodynamics · Voluntary control · Heart rate · Masseter muscle activity

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Introduction

Recently, various methods have been employed to investigate the influence of jaw movement on brain function. Brain mapping studies during gum chewing, tapping, and clenching have shown that not only the areas of cerebral cortex related to movement and sensation, but also the hippocampus and prefrontal cortex associated with memory are activated by jaw movements [1–4]. Furthermore, animal studies [5, 6] and epidemiological survey [7] demonstrated that the loss of teeth and decrease in chewing ability likely reduce the cognitive function and learning effect. These findings attract attention as collateral evidence for the hypothesis that daily chewing movement consistently stimulates the brain and thus has a positive effect on maintaining brain function. However, little information is available regarding the influence of chewing movement on cerebral circulation, let alone substantial evidence to support the hypothesis.

Activated areas in the brain exhibit more blood flow than areas at rest, because they need more energy for the increased metabolism due to changes in electric potential in brain cells and synthesis of neurotransmitters [8]. Brain mapping, which is based on this principle, has been used to elucidate the areas that are activated during jaw movement [1, 2, 9]. However, the low temporal resolution of brain mapping is unsuitable for quantitative analysis of overall changes in cerebral circulation associated with chewing.

Transcranial Doppler ultrasonography (TCD) [10], which employs the Doppler effect to measure blood flow velocity in major cerebral blood vessels, has recently found application in laboratory tests. With superior temporal resolution, this method provides the advantages of continuous real-time recording and ease-of-use, allowing evaluation of relationships between jaw movement and cerebral circulation [11, 12].

Using TCD, we have already demonstrated that gum chewing at a prescribed rate and on the prescribed chewing side results in activation of cerebral circulation, and that such activation is bilateral [13, 14]. However, given that chewing is a movement semi-automatically controlled by the pattern generator of the brainstem [15], voluntary control of chewing side and rhythm may considerably influence the activation of cerebral hemodynamics during chewing. The present study investigated the influence of such voluntary control of chewing movements on cerebral circulation by comparing changes in cerebral circulation during three different tasks: a task in which both chewing side and rhythm were prescribed, a task in which only chewing side was prescribed, and a third task in which neither chewing side nor rhythm was prescribed.

Materials and methods

Subjects

Subjects comprised 25 healthy volunteers (11 men, 14 women; mean (±standard error of the mean) age 27.3± 4.0 years) with no history of brain disease, craniomandibular disorder, or tooth loss, selected from among employees and students of the Faculty of Dentistry at Osaka University. Prior to initiation of the study, the study protocol was approved by the ethics committee of Osaka University, and written informed consent was obtained from each person after explaining the aims and methodology of the study.

Data recordings

In the present study, middle cerebral artery blood velocity (MCAV) was measured bilaterally to evaluate cerebral circulation using a TCD system (Multi Dop-T; DWL, Sipplingen, Germany), with 2-MHz ultrasound probes fixed anterosuperior to the left and right auricles using a designated headband (Marc 600; Spencer Technologies, Seattle, USA). Sample volumes were fixed at a diameter of 10 mm and depth of 48–60 mm, and MCAV was captured at each change in heart rate and recorded on a personal computer.

Heart rate per second was recorded using a pulse oximeter (Surface Monitor 9900MK; Kohken Medical, Tokyo, Japan) attached to the left index finger and analyzed with a personal computer. For evaluation of masticatory muscle activity, bilateral electromyography (EMG) of the masseter muscles was recorded using an evaluation system of mandibular movement (K6-I; Myo Tronics, Taren Point, Australia) and Duo-trode surface Ag/AgCl electrodes (conducting surface diameter, 14 mm; Myo Tronics, Seattle, WA). EMG data were recorded at a sampling rate of 240 Hz and amplified at a time constant of 0.06 s. Analog data from K6-I were converted using an A/D converter (AD12-8; Contec, Osaka, Japan), full-wave-rectified and then integrated on a personal computer. For evaluation of muscle activity, maximum voluntary contraction (MVC) during clenching with maximum effort for 2 s by each subject was defined as 100% MVC and masseter muscle activity during each task was expressed in relation to this value as %MVC. Chewing frequency was obtained from the peaks of the integrated EMG waveform.

Chewing tasks

Measurements were performed in a shielded room with room temperature set at 25°C. Subjects sat upright with both feet touching the floor, and the head and neck were stabilized with the chair headrest to maintain the Frankfort plane parallel to the floor. Subjects were instructed to rest the arms on the armrests of the chair and to keep the eyes lightly closed while wearing an eye mask to avoid any light stimulation. Each subject chewed two sticks of chewing gum with sugar and odor, (Free Zone; Lotte, Tokyo, Japan) for 5 min, under the following three conditions: (1) free gum chewing, no control of chewing side or rhythm; (2) right gum chewing, mastication limited to the right side, but rhythm not controlled; and (3) right rhythmic gum chewing, mastication limited to the right side and rhythm set at 1.0 Hz using a metronome. Gum sticks were inserted into the oral cavity of the subject by the experimenter immediately before start of chewing and were removed by the experimenter after completion of chewing. For each task, 300 s during pre-task rest, 300 s during on-task and 300 s during post-task rest were measured continuously. Breaks of >5 min were arranged between measurements. The Latin square method was employed to randomize tasks, and each subject performed one sequence of the three tasks per day on two consecutive days, for a total of two sequences.

Data analysis

Representative values of right and left MCAV, heart rate, and right and left masseter muscle activities were calculated at 5-s intervals, with the time of task start defined as 0 s. For each measurement, maximum value (E_{max}), time to E_{max} (T_{max}), and area under the effect curve (AUEC) in on-task and post-task periods were calculated (Fig. 1). Two-factor analysis of variance with the random effects model was employed for comparison of data between pre-task and on-task periods and between on-task and post-task periods, between left and right MCAV. The Friedman test was employed for comparisons of on-task MCAV, heart rate and masseter muscle activity among tasks, and when significant differences were observed, a multiple comparison test with Bonferroni correction was performed. SPSS 12.0J for Windows software (SPSS Japan, Tokyo, Japan) was used for statistical analysis. Values of $P<0.05$ were considered statistically significant.

Results

Waveforms were obtained by averaging all data concerning the rate of change in MCAV, heart rate, and masseter muscle activity for pre-task, on-task, and post-task periods (Fig. 2). MCAV increased rapidly, peaked 114.1–147.6 s after the task began (rate of increase, 15.0–18.2%), and remained at the elevated level until decreasing after completion of the task. Heart rate increased rapidly, peaking 105.1–119.5 s after the task began at 108.5–116.0 beats/min, and decreasing gradually. Masseter muscle activity peaked immediately after the task began (7.4–15.5 s) at 44.0–63.9% MVC, then decreasing rapidly and reaching a value of 3–4% MVC on task completion (Table 1).

In all tasks, MCAV was significantly higher in the on-task period than in the pre-task period, suggesting that cerebral circulation was activated by gum chewing. For MCAV on the right and left, no significant differences in increase rate were noted between any tasks. Likewise, no differences in MCAV were observed between left and right sides in any task. In the post-task period, left MCAV was significantly higher for free gum chewing than for right gum chewing at 1.0 Hz, but no such difference was found with right MCAV (Table 2).

Heart rate was significantly higher in the on-task and post-task periods compared to that in the pre-task period, but no significant difference was noted among tasks (Fig. 3). No difference between left and right masseter muscle activities was observed during free gum chewing, while the right masseter muscle showed significantly higher values in the on-task period with right gum chewing and right rhythmic gum chewing. Significant differences in muscle activity were observed between free chewing and right rhythmic gum chewing, but these differences occurred only in the left masseter muscle (Fig. 4).

Chewing frequency was significantly higher with free gum chewing (75.5±0.4 times/min, $P<0.001$) and right gum chewing (79.2±0.4, $P<0.001$) as compared to right rhythmic gum chewing (60.4±0.1).

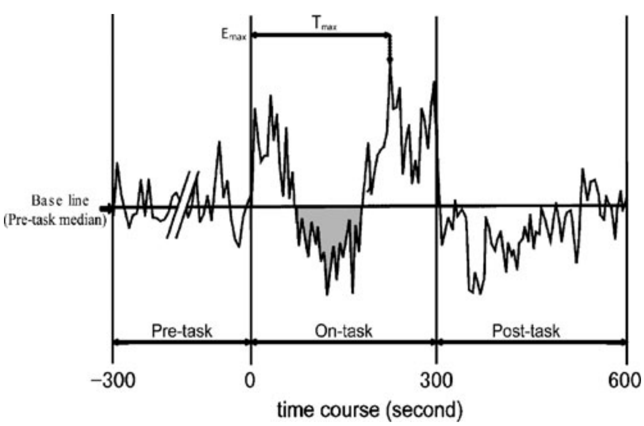

Fig. 1 Analysis of the area under the effect curve (AUEC), maximum value (E_{max}), and time to maximum value (T_{max}) in pre-task, on-task, and post-task periods. The area surrounding the wave of the experimental and baseline data (set by the median in the pre-task period) was calculated as AUEC in the on-task and post-task periods. In this figure, AUEC in the post-task period was calculated as the difference in area between data above and below the baseline

Discussion

TCD was introduced by Aaslid [10] in 1982, and employs low-frequency ultrasonography with low attenuation through the skull. Doppler ultrasonography, which uses the Doppler effect of ultrasound to measure blood flow velocity from outside the body, has now become a common method for the examination, diagnosis, and evaluation of treatment of intracranial vascular diseases [16, 17]. Among the cerebral blood vessels that can be measured using TCD, the MCA provides measurement values close to the true blood flow velocities, due to the small angle between the vessel and the ultrasound beam coming from the measurement site [18]. Using this TCD method, we succeeded in recording changes in cerebral blood flow continuously during clenching, gum chewing, and tapping, thus quantitatively elucidating changes in cerebral circulation [13]. TCD is also useful for studying the hemispheric dominance of changes in cerebral circulation during hand grip exercise [19] and chewing movement [13, 14].

By prescribing the side of gum chewing, a difference between right and left is likely to occur in muscle activity of the oromaxillofacial region, as well as the afferent information from sensory receptors of the periodontal membrane and muscle spindles [20, 21]. Part of such information is processed in the upper central nervous system, such as the cerebral cortex, and influences the actions of the pattern generator for chewing located in the

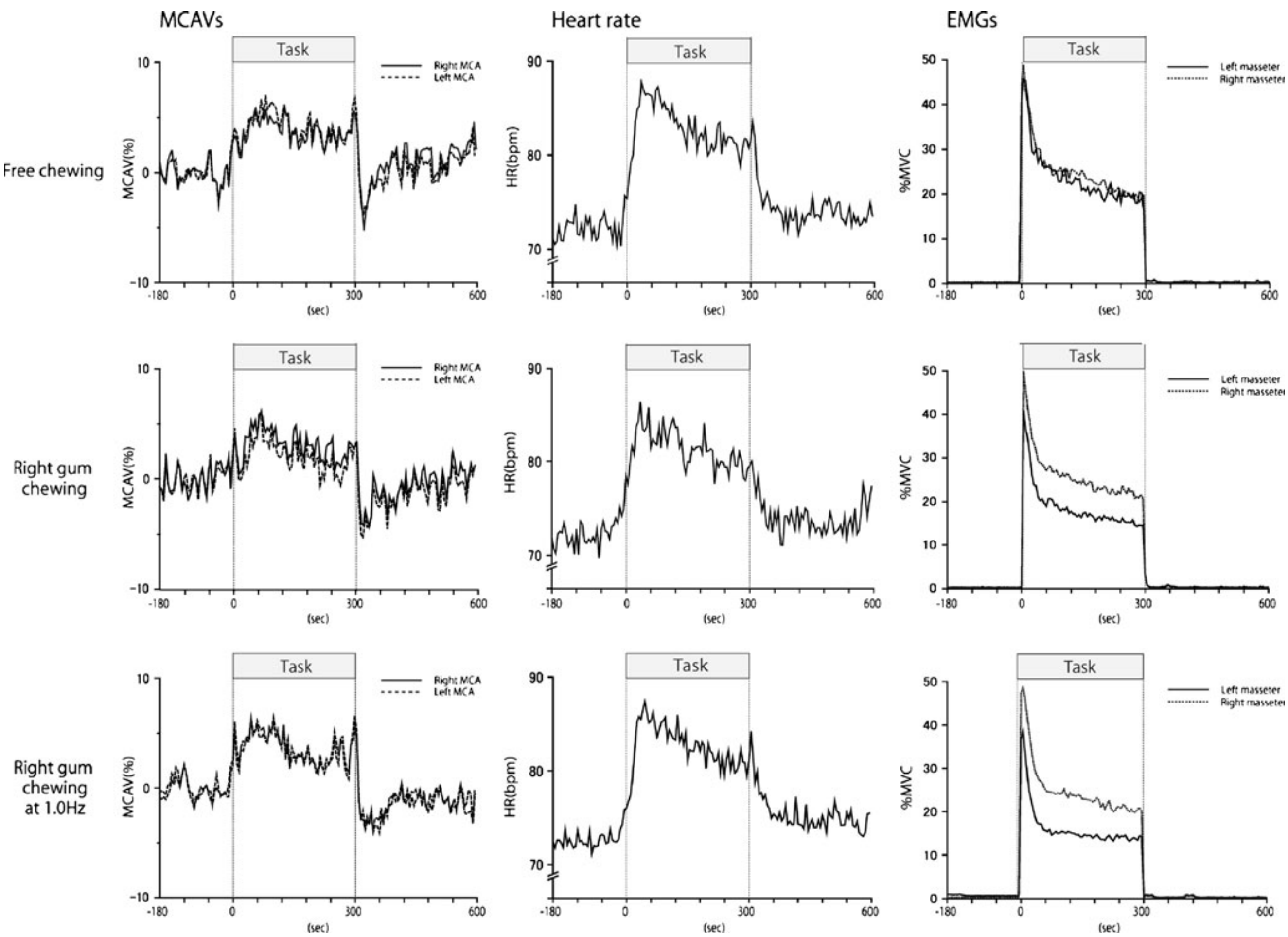

Fig. 2 Mean data of all subjects for middle cerebral artery blood flow velocity (MCAV) bilaterally, heart rate, and electromyographic activities of bilateral masseter muscles (EMG). Data represent the mean of all measurements (n=25)

Table 1 Maximum value (Emax) and time to Emax (Tmax) for middle cerebral arteries blood flow velocity (MCAV) bilaterally, heart rate (HR) and EMG activities of bilateral masseter musles (EMGs) during each chewing task

		T_{max}	E_{max}
MCAV(%)			
Free gum chewing	*I*-MCA	128.2±9.6	18.0±0.8
	r-MCA	132.3±9.9	18.2±1.4
Right gum chewing	*I*-MCA	128.6±11.0	16.5±0.8
	r-MCA	114.1±10.4	15.0±1.4
Right gum chewing at 1.0 Hz	*I*-MCA	147.6±10.6	16.5±0.9
	r-MCA	142.8±11.0 (s)	16.0±1.2 (%)
HR (bpm)			
Free gum chewing		117.2±10.9	116.0±2.7
Right gum chewing		105.0±9.4	108.5±1.3
Right gum chewing at 1.0 Hz		119.5±10.0 (s)	110.3±2.1 (bpm)
EMGs(%MVC)			
Free gum chewing	*I*-Masseter	13.4±2.0	58.6±6.2
	r-Masseter	15.5±4.1	59.7±5.0
Right gum chewing	*I*-Masseter	14.0±3.0	47.2±2.8
	r-Masseter	13.1±2.6	63.9±5.2
Right gum chewing at 1.0 Hz	*I*-Masseter	7.4±1.4	44.0±2.3
	r-Masseter	9.7±1.7 (s)	59.8±5.0 (%MVC)

Table 2 Analysis of an area under the effect curve (AUEC) for bilateral middle cerebral arteries blood flow velocity (MCAV) during on-task and post-task periods of each chewing task

	l-MCAV (%)	*r*-MCAV (%)	L–R difference
On-task			
Free gum chewing	3.6±0.8[a]	3.7±0.7[a]	NS (*P*=0.75)
Right gum chewing	3.3±0.9[a]	2.4±0.7[a]	NS (*P*=0.18)
Right gum chewing at 1.0 Hz	3.2±0.8[a]	3.2±0.8[a]	NS (*P*=0.91)
Task-difference	NS	NS	
Post-task			
Free gum chewing	3.8±0.8[a]	0.4±0.6[a]	NS (*P*=0.45)
Right gum chewing	−0.5±0.9[a]	−0.9±0.7[a]	NS (*P*=0.48)
Right gum chewing at 1.0 Hz	−1.3±0.5[b]	−0.7±0.6[a]	NS (*P*=0.28)
Task-difference	Free >right at 1.0 Hz *P*=0.013	NS	

Mean ± SE

[a] MCAV is higher than that in pre-task period or post-task period

[b] MCAV is lower than that in pre-task period

lower brainstem, thus contributing to the control of chewing movements [15]. Therefore, some influence on cerebral blood circulation seems likely. Furthermore, chewing on one side requires conscious rotation of the tongue [22], and such voluntary movement of the tongue reportedly influences local blood circulation in the brain [23].

Meanwhile, stimulus of sound reportedly activates localized areas of the brain [24], and changing the rhythm of chewing using a metronome influences brain activity [25]. Processing of information in the cerebral cortex to control the rhythm of chewing activity through auditory stimulus may thus exert some influence on cerebral blood circulation. These considerations lead to the assumption that changes in blood circulation in localized areas of the brain induced by free chewing without any prescribed conditions regarding the side and rhythm of chewing may be smaller than those induced by right gum chewing or right rhythmic gum chewing, and that this may influence cerebral circulation during chewing.

However, the present results showed significant increases in bilateral MCAV in all three chewing tasks, with no difference in rate of increase among tasks. This suggests that cerebral circulation is activated on both sides during gum chewing, irrespective of voluntary control of the masticatory side and rhythm, and that no difference is seen in the degree of activation. The only explanation we can think of at present is that the systemic circulation responds to the cerebral circulation during chewing movements. In the present study, the elevated heart rate was maintained although masseter muscle activity decreased during chewing movement. Obviously, the elevated heart rate supports long-lasting increases in brain circulation. As

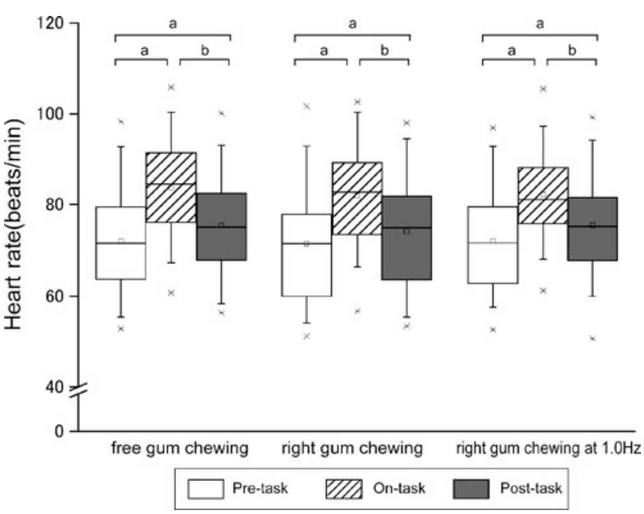

Fig. 3 AUEC of heart rate during pre-task, on-task, and post-task periods of each chewing task. Mean (*box symbol*), median (*horizontal line*), 25th and 75th percentiles (*box*), 5th and 95th percentiles (*whisker*) and 1st and 99th percentiles (*multiplication symbol*). *a* There are significant difference between pre-task and on-task, pre-task and post-task ($p<0.05$). *b* There are significant difference between on-task and post-task ($p<0.05$)

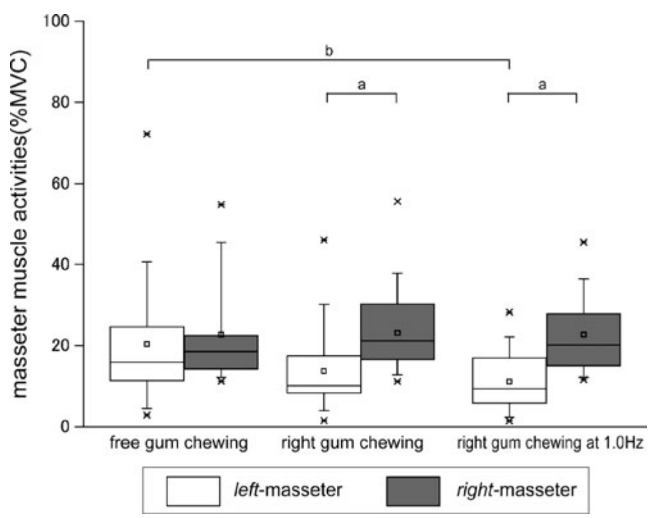

Fig. 4 AUEC of bilateral masseter muscle activity during on-task periods of each chewing task. Mean (*box symbol*), median (*horizontal line*), 25th and 75th percentiles (*box*), 5th and 95th percentiles (*whisker*) and 1st and 99th percentiles (*multiplication symbol*). *a* Right masseter muscle activity is higher than left masseter muscle activity. *b* There are significant differences in muscle activity between two tasks ($p<0.05$)

chewing movements are created through continuous contraction and dilation of muscles of the head and neck, blood circulation in this area is always in an activated state, and blood supply in activated areas of the brain may exceed the energy required for nerve activity [19]. This means that even if the voluntary control during gum chewing as specified in the present study creates some differences in neuron activity for localized areas, such differences would be obscured by the influence of systemic circulation and would not be visible as changes in MCAV. Chewing function should be considered not only in view of nutrient uptake and better quality of life, but also from the point of view of maintenance of brain function.

Conclusions

The results of the present study suggest that daily gum chewing, even without any voluntary control, increases cerebral circulation. We regard that this gives new significance to dental medicine for elderly people aiming at recovery and maintenance of chewing function.

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