Pressor responses to isometric biting are evoked by somatosensory receptors in periodontal tissue in humans

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Okada Y, Kamijo Y, Okazaki K, Masuki S, Goto M, Nose H. Pressor responses to isometric biting are evoked by somatosensory receptors in periodontal tissue in humans. J Appl Physiol 107: 531–539, 2009. First published May 28, 2009; doi:10.1152/japplphysiol.91199.2008.—Jaw muscle contraction, such as mastication and biting (BT), is known to evoke pressor responses. We examined whether the responses were evoked by somatosensory receptors in periodontal tissue and, moreover, whether they were accompanied by altered arterial baroreflex sensitivity. In the first experiment, we measured mean arterial pressure, heart rate, and muscle sympathetic nerve activity from the peroneal nerve during 2-min isometric BT at 50% maximal voluntary contraction before [control (CNT)] and after pharmacological alveolar nerve block (BLK) in eight young men, while monitoring finger cutaneous vascular conductance, gingival vascular conductance (GVC), surface electromyogram of masseter muscle, and BT force. In the second experiment, cardiac and sympathetic baroreflex sensitivities were successfully determined in eight and five of the subjects, respectively, by the modified Oxford method during 5-min BT at 30% maximal voluntary contraction and also during resting without BT in CNT and BLK, respectively. In the first experiment, although BT in CNT and BLK significantly increased mean arterial pressure, heart rate, and total muscle sympathetic nerve activity (burst amplitude × burst incidence), and decreased finger cutaneous vascular conductance and GVC (P < 0.05), all changes except GVC were markedly attenuated in BLK (P < 0.05). There were no significant differences in integrated electromyogram and BT force among any trials. In the second experiment, although BT in CNT significantly decreased cardiac and sympathetic baroreflex sensitivities (both, P < 0.05), these changes disappeared in BLK. These results suggest that somatosensory receptors in periodontal tissue were involved in pressor responses to isometric BT, which was accompanied by decreased arterial baroreflex sensitivity.

sympathetic nerve activity; baroreflex; periodontal receptor

MECHANICAL STIMULATION of teeth by biting (BT) has been known to evoke pressor responses, increasing heart rate (HR) and arterial blood pressure (BP), in proportion to BT force (11). These responses have been suggested to be involved in the maintenance of cardiovascular homeostasis and the disturbance of BT behavior and conditions; bruxism and tooth loss, might be associated with the development of cardiovascular diseases (16, 20, 26, 40). However, the detailed mechanism and the location of receptors causing pressor responses remain unknown.

Since there have been many studies suggesting that afferent signals from somatosensory receptors in the contracting skeletal muscles to the cardiovascular center cause the responses (29, 37, 39), the receptors in the masseter muscle likely contribute to BT-induced pressor responses. On the other hand, Brodin et al. (4) reported in humans that mechanical stimulation of teeth evoked inhibitory or excitatory feedback effects on BT force so as not to damage the teeth while masticating foods of various hardness. However, more importantly for the present study, it was found that these effects were abolished when afferent signals from periodontal tissue were blocked with local anesthetic, suggesting that receptors of the reflex were present in periodontal tissue, but not in the masseter muscle. Moreover, Ikeda et al. (19) found in anesthetized rats that the increase in adrenal sympathetic nerve activity by biting a stick was abolished when sensory afferent signals from periodontal tissue were blocked by surgically cutting maxillary and inferior alveolar nerves. These results suggest that periodontal receptors were involved in pressor responses, as well as in the feedback control of BT force (4, 46). Based on these findings, we hypothesized that somatosensory receptors in periodontal tissue significantly contributed to the BT-induced pressor responses, accompanied by altered arterial baroreflex sensitivity, as suggested by somatosensory receptors in the skeletal muscles (37).

To examine these hypotheses, we compared the responses to BT with and without pharmacological block of the afferent nerves from the periodontal tissue, while keeping those from the masseter muscle intact. In addition, we determined cardiac and sympathetic baroreflex sensitivities in each condition.

METHODS

Subjects

This study was performed according to the Declaration of Helsinki and approved by the Institutional Review Board on Human Experiments, Shinshu University School of Medicine. Eight healthy young men gave written informed consent before participating in these studies. Their physical characteristics (means ± SD) were 23 ± 5 yr old, 178 ± 6 cm tall, and 66.2 ± 5.8 kg body wt. Regarding their dental condition, subjects had normal occlusion with Angle’s class I, normal overlap in full dentition [overbite; 2.3 ± 1.2 mm, overjet; 2.2 ± 1.2 mm (means ± SD)], and did not suffer from acute tooth ailments, temporo-mandibular joint disease, or muscle pain in the head or neck regions. Moreover, they were nonsmokers and had no overt history of cardiovascular, respiratory, or any other chronic diseases. None were currently taking any medications to potentially impact cardiovascular function.

Protocol

Preparation before the first experiment. Several days before the first experiment, subjects visited the laboratory. First, they were asked...
to bite 10 times at their maximal force to determine their individual maximal voluntary contraction (MVC) force of the masseter muscle using an occlusal force meter (GM10; Nagano Keiki, Tokyo, Japan) with $510 \pm 108$ N (SD) as an average of 10 repetitions in all subjects. Then, a splint fitting the teeth in both jaws on the voluntary chewing side was made with dental resin for each subject. The splint was used in the experiment to fix a load cell to measure BT force, a round disk of 6.0 mm in diameter and 2.0 mm in thickness (PA-70KA M260; KYOWA, Tokyo), on the upper second premolar region, such that the surface of the cell touched the surface of another metal disk, 9.0 mm in diameter and 1.0 mm in thickness, fixed over the lower second premolar region at the same position and with the same angle in each BT trial.

When they visited the laboratory again, the conformity of the splint was checked to avoid stimulating oral mechanoreceptors other than in periodontal tissue and was improved if necessary. Moreover, subjects mastered isometric BT for 2 min at 30% of MVC by adjusting the output voltage from the load cell to the targeted level displayed on the screen of an oscilloscope in a feedback manner and were informed that they would undergo the same protocol in the following experiments. Before leaving the laboratory, subjects were instructed to refrain from strenuous physical activity for at least 24 h and also alcoholic and caffeinated beverages for at least 12 h before the experiment.

The first experiment. We measured pressor responses to BT in eight subjects. Subjects reported to the laboratory at 8:00 AM on the experimental day. First, the splint was placed in the mouth with the load cell and the metal disk on the upper and lower experimental teeth, respectively. Subjects then entered an environmental chamber at 29°C (28–30°C) [mean (range)] of ambient temperature and ~30% relative humidity. Thereafter, three-lead electrocardiogram (ECG) and electromyogram (EMG) electrodes (Vitoorode; Nihon Koden, Tokyo) were placed on the skin surface of the chest and the masseter muscle, respectively. A cuff for finger photoplethysmography (Finometer; Finapres Medical Systems, Amsterdam, The Netherlands) was placed around the right middle finger, and another cuff for automated sphygmomanometry (STBP model 780B; Colin, Komaki, Japan) was placed around the left upper arm to measure BP. The precision of sphygmomanometry (STBP model 780B; Colin, Komaki, Japan) was checked to avoid stimulating oral mechanoreceptors other than in periodontal tissue and was improved if necessary. Moreover, subjects mastered isometric BT for 2 min at 30% of MVC by adjusting the output voltage from the load cell to the targeted level displayed on the screen of an oscilloscope in a feedback manner and were informed that they would undergo the same protocol in the following experiments. Before leaving the laboratory, subjects were instructed to refrain from strenuous physical activity for at least 24 h and also alcoholic and caffeinated beverages for at least 12 h before the experiment.

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The second experiment. Several days after the first experiment, the second experiment was performed to determine arterial baroreflex sensitivity in four trials on the same subjects as in the first experiment: No-BT and BT at 30% of MVC with CNT and those with BLK. The reason for adopting the lower BT force than in the first experiment was that it was difficult for subjects to maintain 50% of MVC for 5 min with no change in the respiration rate. Subjects reported to the laboratory at 8:00 AM. After making the same preparation as in the first experiment, an 18-gauge Teflon catheter (SR-FS1832; TERUMO, Tokyo) was placed in the antecubital vein for bolus injections of sodium nitroprusside (SNP, 100 μg) and phenylephrine HCl (PE, 150 μg) to determine cardiac and sympathetic baroreflex sensitivities by the modified Oxford method, as reported previously (9, 13, 38). After resting for an additional 10 min, subjects underwent arterial baroreflex measurement in four sequential trials of 5 min each, separated by 20-min recovery (Fig. 1B). To determine the baroreflex sensitivities, we measured ECG and MSNA in response to BP, altered by intravenous bolus injections of SNP and PE. SNP was injected after 2-min baseline measurement, the responses were measured for the following 1 min, and then PE was injected, and the response was measured for the following 2 min. The SNP injection evoked a maximal reduction of ~20 mmHg in mean

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Fig. 1. Time lines for the first (A) and second experiments (B). Each protocol was performed with (BLK) and without alveolar nerve block [control (CNT)]. In the second experiment, sodium nitroprusside (SNP) was injected at 2 min, phenylephrine (PE) at 3 min, after the start of resting without biting (No-BT) and biting (BT), respectively, to determine baroreflex sensitivities.
arterial pressure (MAP), and the PE injection evoked a maximal increase of \(\sim 14\) mmHg from the baseline.

Alveolar Nerve BLK

The anesthetic solution was prepared by filling a standard 1.8-ml local anesthetic cartridge with 3% mepivacaine hydrochloride without a vasoconstrictor (Scandonest 3%; Septodont, Saint-Maur des Fossés, France). We used this solution because it was known to have no effect on either HR or BP (35, 41). The solution was then injected into an area close to the mandibular foramen on the medial side of the ascending ramus of the mandible, where the inferior alveolar nerves run far from the afferent nerves of the masseter muscle (33). Moreover, we infiltrated the solution locally into the buccal, palatal, and lingual sides of the root apexes of upper and lower premolars (6, 7, 22). Since the procedure is known to localize anesthetic solution in the area close to the tooth of interest and the inferior alveolar nerve, it has been broadly used to anesthetize the nerves from intraoral somatosensory receptors without blocking those from the masseter muscle in previous studies (1, 3, 4, 15, 46). Loss of sensation by anesthesia was confirmed by stroking the surface of the gingiva with a cotton ball, pricking it with a pin, or by asking subjects to bite down hard. If the depth of anesthesia was found to be insufficient, additional cartridges of anesthetic solution were injected, but not beyond 300 mg or 4.4 mg/kg mepivacaine, when the subject’s weight was \(\sim 69\) kg (22). In addition, we injected an additional anesthetic solution during BLK trials when we judged it was needed. In CNT, 1.8 ml of saline solution were injected into each area close to the superior and inferior alveolar afferent nerves and the mucosa in the same way as in BLK.

Measurements

MSNA. MSNA was measured by microneurography (44, 47). Multunit postganglionic MSNA was recorded from the peroneal nerve just posterior to the fibular head with a tungsten microelectrode (200-\(\mu\)m shaft diameter, \(<1-\mu\)m tip, and impedance of 4 M\(\Omega\) at 1 kHz) inserted percutaneously and positioned in the muscle nerve fascicle. An Ag-AgCl electrode was placed on the skin surface \(\sim 5\) cm apart from the active electrode as a reference. The recorded signal was amplified 100,000-fold and passed through a band-pass filter of 0.7–2 kHz. The signal was then rectified and integrated by a capacitance-integrated circuit with a time constant of 0.1 s to obtain a mean voltage neurogram. To confirm the successful measurement of the neurogram during the experiments, the filtered neurogram was routed to an oscilloscope and loudspeaker. The criteria for identifying an MSNA burst were spontaneous discharges synchronized with the heartbeat and enhanced by the Valsalva maneuver or apnea, but showing no change in response to cutaneous touch or arousal stimuli (21, 47).

EMG. EMG was recorded with bipolar Ag-AgCl surface electrodes through a band-pass filter of 10–5,000 Hz (MEG-2100; Colin, Komaki), and the wave was rectified, integrated, and presented as relative change from the resting value of 100\% in each subject.

Data Analyses

HR, MAP, and vascular conductances. HR was calculated from the R-R wave interval measured by ECG. Systolic (SBP) and diastolic BP (DBP) were obtained from the arterial-pressure waveform by a finometer, and MAP was calculated as MAP = DBP + (SBP – DBP)/3. Finger cutaneous vascular conductance (FCVC) and gingival vascular conductance (GVC) were calculated by dividing FSBF and GFB by MAP, respectively.

MSNA. Peaks and leading or trailing edges of each MSNA burst were identified from the trace of the mean voltage neurogram, according to the previous method (13, 38), after our modification. Burst amplitude was obtained by subtracting either a leading or trailing edge value, which was lower than the other, from the peak value:

\[
\text{amplitude} = \text{peak value} - \text{lower edge value}
\]

If the amplitude did not exceed the level threefold higher than the baseline fluctuation of more than 5-s silent period with no bursts, they were excluded from the following analyses. For the purpose of quantification, MSNA was expressed as follows:

\[
\begin{align*}
\text{burst frequency} &= \frac{\text{burst number}}{\text{minutes}} \\
\text{burst incidence} &= \frac{\text{burst number}}{100 \text{ heartbeats}} \\
\text{mean burst amplitude} &= \frac{\sum_{k=1}^{\text{burst number}} \text{amplitude}(k)}{\text{burst number}} \\
\text{amplitude (max)/burst number} &= \frac{\sum_{k=1}^{\text{burst number}} \text{amplitude}(k)/\text{amplitude (max)/heartbeats} \times 1,000}{\text{units/burst}}
\end{align*}
\]

where amplitude (max) is the highest amplitude of burst during the baseline, assigned a value of 1,000 to normalize amplitudes of other bursts, so that they could be compared between subjects.

Cardiac baroreflex sensitivity. Cardiac baroreflex sensitivity was determined from HR response to SNP and PE, as reported previously (9, 38). To do this, HR corresponding to the beat-by-beat SNP was determined from the interval between the R wave of ECG immediately after a given SNP and the next R wave. SNP and the corresponding HR were then grouped into bins of a 2-mmHg increment covering the lowest to highest SNP. To determine a pair of representative SNP and HR values for each bin, we adopted the averaged values of SNP and HR belonging to the bin. Since the sensitivity determined from the pair of representative HR and SNP in response to SNP injection (9, 38) was not significantly different from that in response to PE injection (0.745 ± 0.045 vs. 0.795 ± 0.077 beats·min\(^{-1}\)·mmHg\(^{-1}\), \(P = 0.618\)), sensitivity was determined from the pooled representative values (14) after confirming that they were significantly correlated at \(R^2 > 0.49\), as in previous studies (38, 42). The averaged SNP and HR for a 30-s period before SNP injection were adopted as the baseline in each trial.

Sympathetic baroreflex sensitivity. Sympathetic baroreflex sensitivity was determined from the MSNA response to DBP, altered by SNP and PE injections (13, 38, 44). To do this, we adopted the MSNA burst appearing \(\sim 1.3\) s after a given R wave of ECG and a beat-by-beat DBP wave just after the R wave. Then they were grouped into bins of a 3-mmHg increment covering the lowest to highest DBP. To determine a pair of representative DBP and total MSNA values for each bin, we adopted the averaged values of DBP and total MSNA belonging to the bin after excluding bins with no MSNA burst. This procedure was suggested to decrease the statistical impact of the inherent or aberrant beat-by-beat variability in MSNA due to nonbaroreflex causes, such as respiration (9). The baroreflex sensitivity was determined in each subject similarly to the cardiac baroreflex sensitivity after confirming that \(R^2\) was >0.25, as in previous studies (5, 38). The averaged DBP and MSNA for a 30-s period before SNP were adopted as the baseline in each trial.

Statistical Analysis

Values are expressed as the means ± SE, except when noted. The differences in MAP, HR, FCVC, GVC, total MSNA, EMG, and BT force between trials (CNT, BLK) during BT were tested by two-way ANOVA for repeated measures (see Fig. 3). The effects of BT stimuli on baroreflex sensitivities were tested by a 2 (CNT, BLK) × 2 (No-BT, BT) ANOVA for repeated measures (see Figs. 4C and 5C),
which was also used to test differences in the averaged values of the measurements between trials (see Tables 1 and 2). Subsequent post hoc tests to determine significant differences in various pairwise comparisons were performed by Fisher’s least significant difference test. The null hypothesis was rejected at the level of $P < 0.05$.

RESULTS

The First Experiment

Figure 2 shows typical examples of BP, HR, integrated MSNA, and EMG in response to BT in a subject for CNT (A) and BLK (B). Although BP, HR, and integrated MSNA in both trials increased gradually after the onset of BT, the increases were markedly attenuated in BLK, while there were no differences in EMG between the trials.

Figure 3 summarizes MAP, HR, FCVC, GVC, and total MSNA in response to BT for 2 min in eight subjects for CNT and BLK trials as their changes from the values before BT. MAP, HR, and total MSNA increased gradually after the onset of BT, but these increases were significantly lower in BLK than in CNT ($P < 0.001$, all) ~1 min after the start of BT. Also, the reduction in FCVC was significantly less in BLK than in CNT ($P < 0.001$). On the other hand, the reduction in GVC was not significantly different between the trials ($P = 0.414$), and the reduction disappeared after 80 s. EMG during BT increased by $568 \pm 34\%$ in CNT and $573 \pm 32\%$ in BLK from the baseline, with no significant differences between them ($P = 0.944$). Similarly, BT force was $248 \pm 6$ N in CNT and $239 \pm 8$ N in BLK, with no significant differences between the trials ($P = 0.664$). After the cessation of BT, MAP, FCVC, HR, and total MSNA rapidly returned to the baseline with, overall, no significant differences between the trials during recovery.

Table 1 summarizes the variables at the baseline and the last 10 s of BT. There were no significant differences in any variables at the baseline between CNT and BLK. Although SBP, DBP, MAP, HR, burst frequency, burst amplitude, and total MSNA all increased significantly during BT in CNT, none of them, except for burst frequency, increased in BLK. All variables, except for burst frequency, burst incidence, and HR during BT, were significantly lower in BLK than in CNT.

The Second Experiment

Figure 4A shows a typical example of the relationship between SBP and HR; cardiac baroreflex sensitivity, for a subject during No-BT and BT in CNT and BLK, respectively, and the results in eight subjects are summarized in Fig. 4, B and C. After confirming that HR was significantly correlated with SBP at $R^2 = 0.55–0.97$ (all, $P < 0.05$), we determined the slope of HR/SBP as cardiac baroreflex sensitivity in all subjects. In CNT, the sensitivity decreased (i.e., a less negative slope) in all subjects during BT compared with No-BT: $-0.53 \pm 0.04$ vs. $-0.74 \pm 0.05$ beats·min$^{-1}$·mmHg$^{-1}$ ($P = 0.004$). In contrast, we found that the significant decrease during BT in CNT disappeared in BLK with significantly lower sensitivity in CNT than in BLK ($P = 0.034$).

Similarly, Fig. 5A shows a typical example of the relationship between DBP and total MSNA; sympathetic baroreflex sensitivity, for a subject during No-BT and BT in CNT and BLK, respectively, and the results of five subjects whose MSNA was successfully measured in all trials are summarized in Fig. 5, B and C. After confirming that MSNA was significantly correlated with DBP at $R^2 = 0.55–0.96$ (all, $P < 0.05$), we determined the slopes of total MSNA/DBP as sympathetic baroreflex sensitivity. In CNT, the sensitivity decreased in all subjects during BT compared with No-BT: $-11.2 \pm 1.6$ vs. $-16.8 \pm 1.4$ units·beat$^{-1}$·mmHg$^{-1}$ ($P = 0.0003$). In contrast, we found that the significant decrease during BT in CNT disappeared in BLK with significantly lower sensitivity in CNT than in BLK ($P = 0.0004$).
Table 2 shows the baseline of SBP, DBP, HR, and total MSNA. In No-BT, HR was significantly higher in BLK than CNT \((P < 0.001)\), while there were no significant differences in SBP, DBP, and total MSNA between BLK and CNT (all, \(P > 0.05\)). In CNT, HR and total MSNA were significantly higher in BT than in No-BT \((P = 0.014\) and \(P = 0.027\), respectively); however, these significances disappeared in BLK.

**DISCUSSION**

The major findings of the present study were as follows: 1) isometric BT evoked pressor responses; 2) cardiac and sympathetic baroreflex sensitivities significantly decreased during BT; and 3) these decreases were abolished by alveolar nerve BLK. Thus we found that novel somatosensory receptors in periodontal tissue were involved in pressor responses during BT.

**Periodontal Receptors**

As previously reported (1, 3, 4, 15, 46), to block afferent nerves from periodontal tissue while keeping those from the masseter muscle intact, we carefully injected an anesthetic into a site far distal from the infratemporal fossa, where the nerves from the masseter muscle and periodontal tissue merge with the mandibular nerve (22, 33) and around the teeth (6, 7). Moreover, in the present study, we prepared the splint fitted for individuals so that BT did not stimulate other receptors than those in periodontal tissue of experimental teeth. Based on these established experimental conditions, we were certain that all differences in the pressor responses between CNT and BLK were caused by the lack of only somatosensory afferent inputs from the periodontal tissue to the cardiovascular center, not from the masseter muscle. Moreover, we confirmed that the stimuli of periodontal tissue during BT were the same among the trials, since there were no significant differences in BT force.

**Mechano- or Chemoreceptors**

To our knowledge, few studies have investigated which factor the receptors in periodontal tissue sense to cause pressor responses, mechanical or chemical factors; however, as in Fig. 3, significantly higher pressor responses to BT in CNT than in BLK appeared \(~1\) min after the start of BT despite the same BT force among trials. In contrast, Stebbins et al. (43) and Cui et al. (8) examined the reflex effects of skeletal muscle mechano-receptor stimulation by passive stretch on the cardiovascular system in cats and humans, respectively, and suggested that the significant increases in BP, HR, and MSNA occurred \(~10\) s after the onset of stimulation. The delayed increases in total MSNA, HR, and MAP with a reduction in FCVC in the present study suggest that pressor responses were not caused by mechano-receptors (4, 19, 46), but by other receptors, such as chemoreceptors (25, 39).

This idea might be supported by the results in Table 1 that the increase in burst amplitude by BT in CNT was attenuated in BLK while the increase in burst frequency remained unchanged. Malpas and Ninomiya (23, 24) examined the effects of chemoreceptor stimulation by asphyxia, hypoxia, and hypercapnia on renal sympathetic nerve activity in anesthetized cats and suggested that the burst frequency was controlled by a central oscillator and/or baroreflexes, while the burst ampli-
Cardiovascular Responses by Periodontal Receptors

Table 1. Cardiovascular and MSNA responses to isometric biting

<table>
<thead>
<tr>
<th>No-BT</th>
<th>CNT</th>
<th>BLK</th>
<th>BT</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP, mmHg</td>
<td>119±2</td>
<td>133±4†</td>
<td>121±3</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>71±3</td>
<td>84±4†</td>
<td>71±5</td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>87±2</td>
<td>100±4†</td>
<td>87±4</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>56±3</td>
<td>66±4†</td>
<td>60±2</td>
</tr>
<tr>
<td>Burst frequency, bursts/min</td>
<td>32±1</td>
<td>41±4†</td>
<td>39±3</td>
</tr>
<tr>
<td>Burst incidence, bursts/100 beats</td>
<td>56±2</td>
<td>65±9</td>
<td>63±6</td>
</tr>
<tr>
<td>Mean burst amplitude, units/burst</td>
<td>425±19</td>
<td>666±25†</td>
<td>372±18</td>
</tr>
<tr>
<td>Total MSNA, units/beat</td>
<td>237±11</td>
<td>433±62†</td>
<td>231±24</td>
</tr>
</tbody>
</table>

Values are means ± SE for 8 subjects for 5-min baseline [no biting (No-BT)] and last 10 s of the biting period (BT) under the conditions of normal control (CNT) or anesthetized alveolar nerve sensation [block (BLK)], respectively. SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; HR, heart rate; MSNA, muscle sympathetic nerve activity. *Significant differences from CNT, P < 0.05. †Significant differences from No-BT, P < 0.05.

Cardiovascular responses to isometric biting were controlled by chemoreceptors. Moreover, as in Fig. 3, GVC in CNT and BLK decreased significantly from the baseline until 70 s after the onset of BT. Thereafter, it gradually increased, and the significance disappeared after 80 s, while a decrease in FCVC was shown even after 80 s. These results suggest that the accumulation of metabolites due to compression of blood vessels in periodontal tissue by BT worked as local vasodilators to increase GVC (36). The similar trend changes observed in the two trials suggest that stimulation by the metabolites was not different between the trials. Despite this, pressor responses concomitantly occurring with the increase in GVC in CNT were attenuated when the afferent nerves were blocked in BLK. Thus chemoreceptors in periodontal tissue significantly contributed to pressor responses by BT with altering burst pattern of MSNA (25, 39).

Baroreflex Sensitivities During BT

As in Fig. 4, cardiac baroreflex sensitivity decreased during BT in CNT, which was abolished when alveolar nerve was blocked. To our knowledge, this is the first study suggesting that BT stimulation of periodontal receptors decreased cardiac baroreflex sensitivity in humans and there have been few previous studies available to explain the mechanisms.

Fig. 4. A: typical example of the relationship between systolic blood pressure (SBP) and HR in No-BT and BT for CNT and BLK, respectively, in a subject. B: cardiac baroreflex sensitivity determined from the slope of SBP vs. HR for 8 subjects in CNT and BLK, respectively, for the second experiment. C: the means and SE of the sensitivity for 8 subjects in CNT and BLK. *Significant difference from CNT, and †significant difference from No-BT at the level of P < 0.05.
Although it is uncertain whether the same mechanism works in the present study, central command and/or somatosensory afferent nervous inputs from chemoreceptors in the contracting skeletal muscles are suggested to decrease cardiac baroreflex sensitivity (32, 34, 37). Regarding central command, Raven et al. (34) suggested, using the cardiac baroreflex model, that although the threshold, where no further increase in HR occurs despite further reduction in SBP, and the central point, where highest sensitivity is observed, both similarly moved toward the upper-right by activated central command during exercise, SBP does not increase up to the central point, so that HR response to altered SBP occurs near the threshold, where the slope of HR/SBP is lower than near the central point. Thus reduced cardiac baroreflex sensitivity might be caused by upper-right shift of the cardiac baroreflex curve, with less increase of SBP by activated central command.

On the other hand, Iellamo et al. (18) examined the muscle metaboreflex contribution to HR during voluntary static exercise and during arrested leg occlusion after exercise and found that cardiac baroreflex sensitivity decreased during static leg extension but recovered during arrested leg occlusion, while BP was sustained higher than before exercise, suggesting that cardiac baroreflex sensitivity was reduced by the muscle metaboreflex only in the presence of central command. In the present study, we found that the reduced cardiac baroreflex sensitivity during BT was attenuated in BLK, suggesting that periodontal receptors decreased cardiac baroreflex sensitivity, at least in the presence of central command.

As in Fig. 5, we also found that sympathetic baroreflex sensitivity decreased during BT, although the sensitivity reportedly remained unchanged by activated central command and muscle metaboreflexes (17, 31). The details are unclear; however, Gugic et al. (12) compared sympathetic baroreflex sensitivity during posthandgrip ischemia in normoxia and hypoxia and suggested that sympathetic baroreflex sensitivity was reduced in hypoxia, while not in normoxia. These results suggest that periodontal receptors are more sensitive to changes in oxygen and/or other chemical concentrations than those in skeletal muscles.
In Fig. 4B, cardiac baroreflex sensitivity was reduced in three of eight subjects by BT even in BLK, although the reduction was attenuated in two of the three subjects, whereas, as in Fig. 5B, sympathetic baroreflex sensitivity was not reduced in any of five subjects by BT in BLK. These results suggest that the reduction in sympathetic baroreflex sensitivity during BT was caused mainly by the stimulation of periodontal receptors, while that in cardiac baroreflex sensitivity was caused also by other mechanisms: vagal withdrawal by activated central command (30, 37).

Thus we found that afferent nervous inputs from periodontal receptors suppressed both cardiac and sympathetic baroreflex sensitivities, different from previous studies on chemoreceptors in the contracting muscles (17, 31, 34, 37).

The Relation of Periodontal Receptors, Pressor Responses, and Baroreflex Sensitivities

As shown in Table 1 and Fig. 3, pressor responses during BT in CNT were abolished in BLK, with blunted reduction in cardiac and sympathetic baroreflex sensitivities, suggesting that the stimulation of periodontal receptors was deeply involved in these responses.

Although the precise mechanisms are unclear, it is suggested that pressor responses during exercise were abolished when carotid and/or aortic baroreceptors were denervated (27), suggesting that the cardiovascular center needs afferent inputs of current SBP to evoke pressor responses and probably alter baroreflex sensitivities during exercise. Indeed, O’Leary (32) suggested that pressor responses occurred in the presence of a concomitant reduction in cardiac baroreflex sensitivity at the onset of exercise, but thereafter sensitivity returned to the baseline when SBP increased up to the target level reset by central command and/or metaboreflexes (37). They suggested that enhanced pressor response and blunted cardiac baroreflex sensitivity were driven by error signals between the current and target BP levels at the onset of exercise.

When the same concept is applied to the findings in the present study, the cardiovascular center might directly or indirectly monitor oxygen and/or other chemical concentrations in periodontal tissue and, based on the afferent inputs, it might drive pressor responses with reduced baroreflex sensitivities to restore the concentrations in periodontal tissue by increasing GBF and washing the chemicals out of periodontal tissues. This might be evoked by error signals between the current and target SBP levels, although it is uncertain which target level of SBP is equivalent to current chemical concentrations in periodontal tissue.

Limitation

In the present study, we determined baroreflex sensitivity in each condition by only one modified Oxford trial. On the other hand, Minson et al. (28) measured baroreflex sensitivity by two trials of this method and reported an averaged value. However, they also suggested that the baroreflex sensitivity was almost identical to that determined after 20-min interval in the same condition (14, 28, 38). Since we determined baroreflex sensitivity in each condition after a 20-min interval, we are certain that the significant difference in the sensitivity between No-BT and BT or between CNT and BLK were caused by each different condition.

Moreover, since we used the anesthetic in No-BT and BT for BLK, if we did baroreflex test twice in each condition, we should have conducted four times of the local anesthesia, which was beyond the limit clinically permitted in human subjects (22). Furthermore, if we performed a total of eight sets of the trials, we should have requested subjects to keep the same position for over 240 min, which too long for them. For these reasons, we determined baroreflex sensitivity by only one modified Oxford trial, which was also done in the previous studies (13) for similar purposes as in the present study.

As in Tables 1 and 2, an increase in SBP in the second experiment during BT was lower than in the first experiment due to lower BT force, and also baroreflex sensitivities were determined ~2 min after the start of BT in the second experiment. Therefore, it might be difficult to be sure that the increase in SBP during BT in the first experiment had any involvement in the altered arterial baroreflex sensitivities. However, since we found that HR and total MSNA increased during BT in the second experiment as in the first experiment, we were certain that the altered baroreflex sensitivities in the second experiment also occurred in the first experiment.

Perspectives

Recently, Joshipura et al. (20) and Hung et al. (16) examined the effects of partial tooth loss on more than 40,000 male subjects in a longitudinal study for more than 12 yr and suggested that subjects who had lost at least one tooth more than 2 yr previously had a significantly higher morbidity rate of chronic cardiovascular diseases than those who had lost teeth less than 2 yr beforehand. Takeuchi and Yamamoto (45) found that BT force per unit area of teeth was significantly correlated with the number of lost teeth and attachment loss of periodontal tissue in 198 patients, suggesting that this was caused by incomplete feedback control of BT force (4). Martihol et al. (26) and Sjoholm et al. (40) suggested that increased BT force, such as by bruxism during sleep, enhanced sympathetic activity and sometimes caused cardiovascular diseases. These results suggest that the maintenance of somatosensory afferent inputs from periodontal tissue by keeping teeth intact significantly contributed to the maintenance of cardiovascular homeostasis.

In conclusion, somatosensory receptors in periodontal tissue were involved in pressor responses to isometric BT through enhanced MSNA, which was accompanied by reduced arterial baroreflex sensitivity.

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