Discharges of aortic and carotid sinus baroreceptors during spontaneous motor activity and pharmacologically evoked pressor interventions

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Received: 20 January 2014/Accepted: 18 April 2014/Published online: 11 May 2014
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Abstract Our laboratory has demonstrated that the cardiomotor component of aortic baroreflex is temporarily inhibited at the onset of spontaneous motor activity in decerebrate cats, without altering carotid sinus baroreflex. A reason for this dissociation may be attributed to a difference in the responses between aortic nerve activity (AoNA) and carotid sinus nerve activity (CsNA) during spontaneous motor activity. The stimulus–response curves of AoNA and CsNA against mean arterial blood pressure (MAP) were compared between the pressor interventions evoked by spontaneous motor activity and by intravenous administration of phenylephrine or norepinephrine, in which the responses in heart rate (HR) were opposite (i.e., tachycardia vs. baroreflex bradycardia), despite the identical increase in MAP of 34–40 mmHg. In parallel to the pressor response, mean AoNA and CsNA increased similarly by 78–81 and by 88 % of the baseline control, respectively, irrespective of whether the pressor response was evoked by spontaneous motor activity or by a pharmacological intervention. The slope of the stimulus–response curve of the mean AoNA became greater \((P < 0.05)\) during spontaneous motor activity as compared to the pharmacological intervention. On the other hand, the stimulus–response curve of the mean CsNA and its slope were equal \((P > 0.05)\) between the two pressor interventions. Furthermore, the slopes of the stimulus–response curves of both diastolic AoNA and CsNA (defined as the minimal value within a beat) exhibited a greater increase during spontaneous motor activity. All differences in the slopes of the stimulus–response curves were abolished by restraining HR at the intrinsic cardiac frequency. In conclusion, mean mass activities of both aortic and carotid sinus baroreceptors are able to encode the beat-by-beat changes in MAP not only at rest but also during spontaneous motor activity and spontaneous motor activity-related reduction of aortic baroreceptor activity is denied accordingly.

Keywords Arterial baroreceptors · Aortic baroreflex · Carotid sinus baroreflex · Central command · Exercise

Introduction

Aortic and carotid sinus baroreceptors are mechanically sensitive to transmural pressure of the aortic and carotid sinus regions, and convey information about the beat-by-beat blood pressures to the central nervous system. The arterial baroreceptors constitute arterial baroreflexes to help mean arterial blood pressure (MAP) remain constant. If MAP is raised by phenylephrine or norepinephrine, augmented discharges of the arterial baroreceptors cause bradycardia and vasodilation of systemic blood vessels. In contrast to the baroreflex bradycardia, heart rate (HR) increases during exercise, even though the same increase in MAP is observed. We have recently reported that the cardiomotor sensitivity of aortic baroreflex is temporarily inhibited at the onset of spontaneously-evoked motor activity in decerebrate cats, without changing the sensitivity of carotid sinus baroreflex \([1, 2]\). Thus, descending command from higher brain centers (termed central command) may suppress the cardiomotor sensitivity of aortic baroreflex at the onset of spontaneously-evoked motor activity.
activity. The next question is whether such inhibitory modulation of the aortic baroreflex by central command may occur in the periphery (i.e., via blunted afferent input from aortic baroreceptors) or on neurons along the central baroreflex pathways. The former hypothesis that central command might modify signal transduction of aortic baroreceptors is conceivable, because Kunze et al. [3] and Munch et al. [4] reported using in vitro aortic arch preparations that bath application of norepinephrine at high concentrations of $10^{-6}$ to $10^{-5}$ M sensitized signal transduction of aortic baroreceptors, independently of smooth muscle effects. The norepinephrine concentrations having a direct effect on aortic baroreceptors are higher than the norepinephrine concentrations of $10^{-8}$ to $10^{-7}$ M required to produce 50 % of the maximal $\alpha$-adrenergic response [5].

To test the hypothesis, we needed to identify and compare discharges of aortic and carotid sinus baroreceptors during exercise. To our knowledge, measurements of aortic nerve activity (AoNA) and carotid sinus nerve activity (CsNA) have never been attempted during exercise, although single and multifiber baroreceptor activity has been intensively analyzed using anesthetized animals [6–12]. This study was, therefore, undertaken to identify the effects of spontaneous motor activity on the stimulus–response relationships of AoNA and CsNA against blood pressure changes by comparing the baroreceptor responses between spontaneous motor activity and pharmacoologically evoked pressor interventions in decerebrate cats. Care was taken to unify the magnitude and rate of the blood pressure response between both pressor interventions. The doses of phenylephrine and norepinephrine intravenously administered to raise AP were assumed to be sufficiently low so that the drugs may not directly change aortic baroreceptor activity. If the hypothesis is denied based on the data acquired, the effect of central command on the central baroreflex pathways must be taken into account [1, 2, 13, 14]. Furthermore, since the HR responses are opposing between the two pressor interventions, the differential responses in pulse frequency may affect the dynamic characteristics of arterial baroreceptors. To examine this, the stimulus–response relationships of the AoNA and CsNA were compared between absence and presence of HR restraint at the lower intrinsic cardiac frequency.

**Methods**

The present study was conducted using 18 cats weighing $3.0 \pm 0.1$ kg in accordance with the “Guiding Principles for the Care and Use of Animals in the Fields of Physiological Sciences” approved by the Physiological Society of Japan and the Guidelines for Animal Experiments in Hiroshima University. The experimental protocols were approved by the Committee of Research Facilities for Laboratory Animal Science, Natural Science Center for Basic Research and Development, Hiroshima University.

**Preparations**

As soon as the cat was anesthetized with a gas mixture of halothane (4 %), $O_2$ (1.0 L/min), and $N_2O$ (0.5 L/min) in a small box, an endotracheal tube was inserted into the airway. Surgical anesthesia was maintained with a gas mixture of halothane (0.5–1.0 %), $O_2$, and $N_2O$ through the endotracheal tube to implant catheters, perform decerebration surgery, and isolate the aortic and carotid sinus nerves. The animal breathed spontaneously, or the lungs were artificially ventilated by an artificial ventilator (SN-480-5, Shimano, Tokyo, Japan), if necessary. An electrocardiogram (ECG), HR, and thoracic respiratory movement were monitored throughout the experiments. To maintain a surgical level of anesthesia, the concentration of halothane was increased to 1.5–2.5 % if HR and/or respiration spontaneously increased and/or if limb withdrawal occurred in response to a noxious pinch of the paw. One polyvinyl catheter was inserted into the right cephalic vein for administering drugs. Another one was inserted into the right brachial artery for measuring AP and further progressed toward the heart by 8–10 cm. The catheter tip was placed approximately in the middle of the aortic–carotid artery route, and blood pressure of the brachiocephalic artery was measured in this study. The arterial catheter was connected to a pressure transducer (DPT-6100, Kawasumi Laboratories, Tokyo, Japan). HR was derived from the R wave of ECG with a tachometer (model 1321, GE Marquette Medical Systems, Tokyo, Japan). Body temperature was measured rectally and maintained at 37–38 °C with a heating pad and a lamp. The head of the cat was then mounted on a stereotaxic frame (SN-2N, Narishige, Tokyo, Japan). Decerebration was performed by electrocoagulation at the precollicular–premammillary level as previously described [1, 2, 15–17]. To do this, a stainless steel electrode with insulation removed 5 mm from the tip was inserted into the hypothalamus rostral to the mammillary bodies (coordinates from the midpoint of interaural line: anterior 13 mm, horizontal 6 mm, lateral 1–11 mm with an angle of 14° from perpendicular line; from stereotaxic atlases [18, 19]). A negative DC current (1 mA) was passed through the electrode for 30 s. The electrode was withdrawn 4 mm and the current was passed again. This procedure was bilaterally repeated for a total of 42 tracks at 0.5 mm intervals. At the end of each experiment, the animal was killed with an overdose of pentobarbital sodium and the transected area of the brain was examined histologically. We confirmed that the cerebral cortex, the thalamus, and a rostral part of the hypothalamus (the anterior
hypothalamic area, the supraoptic nucleus, and the rostral part of the lateral hypothalamic area) were disconnected from the brain stem as previously reported [16, 17].

Recording of aortic and carotid sinus baroreceptor activity

After the decerebration was completed, the cat was removed from the stereotaxic frame and placed in a lateral posture. The left aortic nerve was identified between the cervical vagal and sympathetic nerves and remained intact. Multifiber AoNA was measured with a pair of Teflon-coated silver wire electrodes (bare diameter 0.076 mm) and amplified by a differential preamplifier (S-0476, Nihon Kohden, Tokyo, Japan) with a band-pass filter of 50–5,000 Hz in 15 decerebrate cats. The amplified output of AoNA was sampled at a frequency of 10 kHz and the spike peaks in the AoNA were converted to standard pulse trains using a digital technique that detected the peaks of the original signal [20]. The pulse trains were integrated by a resistance–capacitance integrator with a time constant of 20 ms. The right carotid sinus nerve was identified in the carotid sinus region and remained intact. Multifiber CsNA was measured and analyzed in 12 decerebrate cats as similarly as AoNA; both AoNA and CsNA were recorded in nine decerebrate cats.

The left tibial nerve innervating the triceps surae muscle was dissected at the popliteal fossa in all cats. For measurement of tibial motor nerve activity, the tibial nerve bundle was placed on a pair of Teflon-coated, silver-wire electrodes (bare diameter 0.076 mm), and then the peripheral portion of the nerve bundle was ligated. The original tibial motor nerve activity was amplified by a differential preamplifier (S-0476, Nihon Kohden, Tokyo, Japan) with a band-pass filter of 50 and 3,000 Hz. The amplified output was rectified and integrated by a resistance–capacitance integrator having a time constant of 20 ms.

Protocols

After all surgical and preparatory procedures were completed, inhalation anesthesia was stopped. A neuromuscular blocker (pancuronium bromide 2 mg) was intravenously administered and the lungs were artificially ventilated at a tidal volume of 14–16 mL/kg body weight and a frequency of 20 rotations/min. The experiments were started 2–3 h after the cessation of halothane anesthesia. Spontaneous, fictive motor activity could be evoked without any kind of artificial stimulation and was identified by occurrence of tibial motor nerve activity.

To identify the stimulus–response relationship between AP and AoNA or CsNA, two types of pressor interventions (spontaneous motor activity and pharmacological challenges with phenylephrine or norepinephrine) were conducted under the absence or presence of HR restraint at the intrinsic frequency. The beat-by-beat changes in AoNA, CsNA, AP, and HR were recorded during the interventions. Spontaneous motor activity lasted for a duration of 16 ± 0.8 s (n = 230 trials in 17 cats). Phenylephrine (9 ± 0.6 μg/kg) and norepinephrine (1 ± 0.1 μg/kg) were intravenously administered to raise AP pharmacologically (n = 109 trials in 17 cats). Care was taken to unify the magnitude and rate of the blood pressure response between both pressor interventions. Following the HR restraint at the intrinsic frequency with combined intravenous administration of atropine methyl nitrate (0.1–0.2 mg/kg) and atenolol (1 mg/kg), the same types of pressor interventions were repeated.

Data treatment and statistical analysis

Original and integrated AoNA and CsNA, HR, AP, ECG, and rectified tibial motor nerve activity were continuously recorded on an eight-channel pen-writing recorder (Recti-8 K, GE Marquette Medical Systems, Tokyo, Japan). The data were stored in a computer with an analog-to-digital converter (MP150, BIOPACK Systems, Santa Barbara, CA, USA) at a sampling frequency of 2 kHz. The beat-to-beat values of the cardiovascular variables were recalculated with the R wave of the ECG using a software program (AcqKnowledge 3.9.1, BIOPACK Systems, Santa Barbara, CA, USA). The integrated AoNA and CsNA, HR, AP, and rectified tibial motor nerve activity were displayed on a computer screen. The start and end of spontaneous motor nerve activity were visually determined using the tibial motor nerve activity. The start of the pressor response during pharmacological challenges was visually determined.

AoNA and CsNA had pulse-synchronous discharges in association with pulsatile blood pressure changes. The maximal value of AoNA or CsNA in a given beat was defined as systolic AoNA or CsNA; the minimal value as diastolic AoNA or CsNA. The baseline levels of the baroreceptor activities and cardiovascular variables were defined as the mean values for more than 30 beats preceding the pressor interventions. The absolute values of the baroreceptor activities and cardiovascular variables, and their changes from the baseline levels in a given trial were aligned at the onset of each pressor intervention and further averaged among trials. The time-course data of the responses were statistically analyzed by a one-way ANOVA. If either the normality or equal variance test failed, a Kruskal–Wallis one-way ANOVA on ranks was performed. When a significant F value in the main effect of time was present, a Dunn’s post hoc test was performed to
detect a significant difference from the control. The peak changes in the cardiovascular and baroreceptor variables from the baseline control were compared during spontaneous motor activity and during the pharmacologically induced pressor response by an unpaired $t$ test. If either the normality or equal variance test failed, a Mann–Whitney rank sum test was performed. Using the time-course data over all bouts, the average responses of the baroreceptor activities were plotted against the increases in systolic AP (SAP), MAP, and diastolic AP (DAP), to construct the stimulus–response curves of AoNA or CsNA during each pressor intervention with or without HR restraint. Moreover, the slopes of the stimulus–response curves at the raising phase of blood pressure, calculated with a linear regression method in individual cats, were compared between the two pressor interventions with a paired $t$ test and between the absence and presence of the HR restraint with an unpaired $t$ test. The level of statistical significance was defined as $P < 0.05$ in all cases. The data are expressed as mean ± SE.

**Results**

The baseline HR of $211 ± 8$ beats/min was significantly ($P < 0.05$) decreased to the lower intrinsic HR of $154 ± 6$ beats/min following combined administration of atropine methyl nitrate and atenolol. On the other hand, the baseline blood pressures were not different ($P > 0.05$) between the absence and presence of the HR restraint; SAP, $157 ± 4$ versus $158 ± 7$ mmHg, respectively; MAP, $137 ± 3$ versus $135 ± 6$ mmHg; DAP, $115 ± 3$ versus $111 ± 6$ mmHg. Similarly, the baseline systolic, mean, and diastolic values of AoNA and CsNA were the same between the absence and presence of the HR restraint. The systolic and mean values of AoNA were much greater ($P < 0.05$) to 231–262 % of those of CsNA; the systolic AoNA and CsNA were $1,175 ± 110$ and $509 ± 50$ impulses/s, respectively; the mean AoNA and CsNA were $335 ± 38$ and $128 ± 15$ impulses/s, respectively.

Aortic baroreceptor discharges during spontaneous motor activity and pharmacologically evoked pressor interventions

Typical responses in AoNA, HR, AP, and integrated tibial nerve activity during spontaneous motor activity are shown in Fig. 1. When AP and HR simultaneously increased during spontaneous motor activity, AoNA increased in parallel with the pressor response (Fig. 1A). On the other hand, when AP was increased to the same extent by phenylephrine, baroreflex bradycardia was evoked instead of exercise tachycardia. Despite the identical level of MAP, the increase in diastolic AoNA became smaller during the phenylephrine-evoked pressor response as compared to spontaneous motor activity (Fig. 1B).

Figure 2 compares the time courses and magnitudes of the average responses in AoNA, the pressor responses, and HR between spontaneous motor activity and the pharmacological pressor intervention. Without the HR restraint (Fig. 2A), HR increased by $14 ± 1$ beats/min during spontaneous motor activity from the baseline control, whereas HR decreased by $42 ± 5$ beats/min during the pharmacologically evoked pressor response. Although SAP and MAP increased similarly in either condition, the peak DAP of $151 ± 2$ mmHg during spontaneous motor activity was greater ($P < 0.05$) than that of $142 ± 2$ mmHg during the pharmacological intervention. Accordingly, the peak pulse pressure of $57 ± 2$ mmHg during spontaneous motor activity was smaller ($P < 0.05$) than the peak pulse pressure of $64 ± 2$ mmHg during the pharmacological intervention. Even though AoNA increased in association with the pressor responses during spontaneous motor activity and the pharmacological intervention, the dynamic characteristics of AoNA were different between the two pressor interventions (Fig. 2A). The peak increase in diastolic AoNA of $324 ± 35$ impulses/s during spontaneous motor activity was much greater ($P < 0.05$) than that of $150 ± 42$ impulses/s during the pharmacologically evoked pressor response. On the contrary, the peak increase of $180 ± 24$ impulses/s in systolic AoNA during spontaneous motor activity was smaller ($P < 0.05$) than that of $272 ± 29$ impulses/s during the pharmacological pressor response, probably due to the smaller increase in pulse pressure. Since the changes in diastolic and systolic AoNA were counterbalanced, the response in mean AoNA was not significantly different ($P > 0.05$) between the two pressor interventions.

When HR was restraint at the lower intrinsic frequency (Fig. 2B), there were no significant differences ($P > 0.05$) in the time courses and magnitudes of blood pressures and AoNA between the spontaneous motor activity and pharmacologically evoked pressor interventions.

Carotid sinus baroreceptor discharges during spontaneous motor activity and pharmacologically evoked pressor interventions

Typical responses in CsNA, AP, and HR during spontaneous motor activity and the phenylephrine-evoked pressor intervention are shown in Fig. 3. The time courses and magnitudes of the average responses in CsNA, the pressor responses, and HR are compared between the two pressor interventions in Fig. 4. The differences in the average cardiovascular responses between the two pressor
interventions were recognized as similar to those in the case of AoNA (Fig. 4). Although the peak increases in systolic and mean CsNA were not different ($P > 0.05$) between the two pressor interventions, the peak increase of $33 \pm 4$ impulses/s in diastolic CsNA during spontaneous motor activity was greater ($P < 0.05$) than that of $16 \pm 5$ impulses/s during the pharmacologically evoked pressor response (Fig. 4A). Under the HR restraint condition at the lower intrinsic frequency, there were no significant differences in the CsNA and the cardiovascular variables between the two pressor interventions (Fig. 4B).

The stimulus–response curves of AoNA and CsNA

Figure 5 illustrates the stimulus–response curves of the average changes in AoNA and CsNA reconstructed from
Fig. 2 The average responses in AP (systolic, mean, and diastolic), pulse pressure, HR, and AoNA (systolic, mean, and diastolic) are compared between spontaneous motor activity and pharmacologically evoked pressor interventions without (A) and with (B) the restraint HR at the lower intrinsic frequency.
the time course data in Figs. 2 and 4. The response curves of the changes in systolic, mean, and diastolic AoNA and CsNA in relation to the respective changes in SAP, MAP, and DAP are compared between spontaneous motor activity and pharmacologically evoked pressor interventions. One striking finding was that the stimulus–response curves of both AoNA and CsNA (e.g., ΔMAP–Δmean AoNA and ΔMAP–Δmean CsNA) showed a clockwise hysteresis loop, irrespective of whether the pressor response was induced by either spontaneous motor activity or pharmacologically evoked pressor intervention. It was of interest that the hysteresis loops of the stimulus–response curves were seen even under the restraint HR condition. Another striking finding was that, as compared to the pharmacologically evoked pressor intervention, the augmented diastolic AoNA and CsNA during spontaneous

Fig. 3 A An example of carotid sinus nerve activity (CsNA), AP, HR, and integrated tibial motor nerve activity during spontaneous motor activity and during a pressor response by intravenous administration of phenylephrine in a decerebrate cat. B The beat-by-beat changes in CsNA, AP, and HR taken from the data in A (denoted a, b, and c) are shown at a higher chart speed. Open column the duration of spontaneous motor activity
Fig. 4  The average responses in AP (systolic, mean, and diastolic), pulse pressure, HR, and CsNA (systolic, mean, and diastolic) are compared between spontaneous motor activity and pharmacologically evoked pressor interventions without (A) and with (B) the restraint
HR at the lower intrinsic frequency.
Fig. 5 The stimulus–response curves of the average changes in systolic, mean, or diastolic AoNA (ΔAoNA) in responses to the respective blood pressure changes during spontaneous motor activity and pharmacologically evoked pressor interventions without (A) and with (B) the restraint HR at the lower intrinsic frequency. The stimulus–response curves of the average changes in systolic, mean, or diastolic CsNA (ΔCsNA) in response to the respective blood pressure changes during spontaneous motor activity and pharmacologically evoked pressor interventions without (C) and with (D) the restraint HR at the lower intrinsic frequency. Using the time course data over all bouts taken in Figs. 2 and 4, the average responses of the baroreceptor activities were plotted against the increases in SAP, MAP, and DAP to construct the stimulus–response curves of ΔAoNA or ΔCsNA during each pressor intervention with or without HR restraint.
motor activity were not simply due to the greater rise in DAP (Fig. 5).

In fact, the slopes of the stimulus–response curves of the changes in AoNA and CsNA (ΔAoNA and ΔCsNA) at the raising phase of blood pressure are compared between the spontaneous motor activity and pharmacologically evoked pressor interventions in Fig. 6. With respect to the AoNA (Fig. 6A), the slopes of the ΔDAP–Δdiastolic AoNA and ΔMAP–Δmean AoNA curves were greater ($P < 0.05$) during spontaneous motor activity than during the pharmacologically evoked pressor response; however, the slope of the ΔSAP–Δsystolic AoNA was similar between the two...
pressor interventions. With respect to the CsNA (Fig. 6B), the slope of the ΔDAP–Δdiastolic CsNA curve was greater 
\( P < 0.05 \) during spontaneous motor activity than during the pharmacologically evoked pressor response, whereas
\[ \text{the slopes of } \Delta MAP–\Delta \text{mean AoNA and } \Delta SAP–\Delta \text{asystolic AoNA curves were not significantly different } \] 
\( P > 0.05 \) between the two pressor interventions. The differences in
\[ \text{the sensitivity of the stimulus–response curves of the } \]
AoNA and CsNA between the two pressor interventions were abolished by restraining HR at the lower intrinsic
\[ \text{cardiac frequency (Figs. 5, 6). Furthermore, the slopes of } \]
the stimulus–response curves of ΛAoNA and ΔCsNA during spontaneous motor activity tended to be blunted by the
\[ \text{HR restraint, although the decreases were not statistically significant except for the case of the } \]
Δdiastolic CsNA.

**Discussion**

We have examined for the first time the discharge characteristics of aortic and carotid sinus baroreceptors during spontaneous motor activity and pharmacologically evoked pressor interventions in premammillary–precollicular decerebrate cats. The pressor response during spontaneous motor activity occurred simultaneously with tachycardia, whereas the pressor response during a pharmacological pressor intervention elicited baroreflex bradycardia. The new findings of this study are that (1) both AoNA and CsNA did not decrease, but increased in parallel to the pressor response during spontaneous motor activity; (2) the increases in MAP and mean AoNA and CsNA were similar between the spontaneous motor activity and pharmacologically evoked pressor interventions; (3) the slopes of the stimulus–response curves of Δasystolic AoNA and Δasystolic and mean CsNA matched between the two pressor interventions, whereas the slopes of the stimulus–response curves of Δdiastolic AoNA and Δmean and diastolic CsNA were augmented during spontaneous motor activity, as compared to the pharmacologically evoked pressor intervention; (4) the differences in the slopes of the baroreceptor stimulus–response curves between the two pressor interventions were abolished by restraining HR at the lower intrinsic frequency, suggesting the significant effect of pulse frequency. Taken together, mean aortic and carotid sinus baroreceptors are able to convey information about the beat-by-beat MAP to the central nervous system not only at rest but also during spontaneous motor activity in decerebrate cats. In other words, it is unlikely that the signal transduction of the arterial baroreceptors is modified in association with spontaneous motor activity, in particular by descending central command signal.

Similar and dissimilar baroreceptor responses between spontaneous motor activity and pharmacologically evoked pressor interventions

The average activities of multifiber aortic and carotid baroreceptor afferents responded approximately in the same manner to both spontaneous motor activity and pharmacologically evoked pressor interventions. Mean AoNA and CsNA per beat increased similarly in parallel to the MAP increase, irrespective of whether the pressor response was evoked by either spontaneous motor activity or the pharmacological intervention. The slope of the stimulus–response curve of the mean CsNA was also identical between the two pressor interventions, although the slope of the stimulus–response curves of the mean AoNA was slightly augmented during spontaneous motor activity. Furthermore, when HR was restrained constantly at the cardiac intrinsic frequency, the slopes of the stimulus–response curves of the mean AoNA and CsNA were not at all different between the two pressor interventions. Based on these present findings, it is likely that, as compared to a pharmacological pressor intervention, activities of aortic and carotid sinus baroreceptors increase similarly or somewhat vigorously in response to a given increase in MAP during spontaneous motor activity.

As a dissimilar point between the two pressor interventions, the pressor response during spontaneous motor activity accompanied tachycardia, whereas the pressor response during a pharmacological intervention produced baroreflex bradycardia. It was considered that the difference in pulse frequency may influence the dynamic characteristics of the AoNA and CsNA. Previous studies have examined this issue by changing the pulse frequency according to cardiac pacing or vagal nerve stimulation using in vivo preparations [6, 21], or by changing the frequency of artificially controlled sinusoidal blood pressure using in vitro preparations [22–24]. Unfortunately, the previous findings are controversial. A unitary activity of aortic baroreceptors per unit time decreased [22] or was unchanged [6, 23, 24] as the pulse frequency was elevated. On the other hand, a unitary activity of carotid sinus baroreceptors per unit time increased [21] or was unchanged [6] as the pulse frequency was increased. The present study examined whether the dynamic characteristics of multifiber AoNA and CsNA had clear dependence upon the pulse frequency. As shown in Figs. 5 and 6, the slopes of the stimulus–response curves of the diastolic AoNA and CsNA were greater during spontaneous motor activity than during a pharmacological pressor intervention with baroreflex bradycardia. The differences are either due to a change in pulse frequency or due to an enhanced sensitivity of aortic and carotid sinus baroreceptors against the DAP. Since the differences in the
dynamic characteristics of diastolic and systolic AoNA and CsNA were abolished by fixing HR at the intrinsic frequency, the significant effect of the pulse frequency in in vivo natural conditions is strongly suggested. Unlike cardiac pacing and increasing the frequency of artificially controlled sinusoidal blood pressure, spontaneous motor activity is expected to cause simultaneous increases in ventricular filling, stroke volume, and cardiac output as well as cardiac frequency, which may elevate DAP and facilitate diastolic baroreceptor activity. Furthermore, as the diastolic phase of AP was shortened with tachycardia, the discharges of AoNA and CsNA were more sustained at that phase (Figs. 1, 3). Thus, exercise tachycardia may play a crucial role in increasing arterial baroreceptor input in the diastolic phase to the central nervous system and causing central facilitation of arterial baroreflexes.

Modulation of arterial baroreflex function during spontaneous motor activity

It is known that signal transduction of aortic and carotid sinus baroreceptors against AP-evoked distension of the arterial vessels is influenced by sympathetic efferent nerve activity and catecholamines [3, 4, 25–27]. Since central command increases renal and cardiac sympathetic nerve activities at the start of spontaneous motor activity in decerebrate cats [15, 16], it is conceivable that central command may change sympathetic nerve activity innervating smooth muscles in the vascular walls of the aortic and carotid sinus regions, and thereby may modify discharges of aortic and carotid sinus baroafferents. Recently we have found that the cardiomotor sensitivity of aortic baroreflex is temporarily inhibited at the onset of spontaneous motor activity in decerebrate cats, without altering the sensitivity of carotid sinus baroreflex [1, 2]. As mentioned before, it was hypothesized that the modulation of arterial baroreflex function is attributed to spontaneous motor activity-related changes in the dynamic characteristics of AoNA, which may be different from those of CsNA.

Under the restrained condition of HR for avoiding the effect of pulse frequency, the stimulus–response curves of the AoNA and CsNA and their sensitivity were not different between spontaneous motor activity and pharmacologically induced pressor responses (Figs. 5, 6). Recently, we conducted a study using brief occlusion of the abdominal aorta given before and during spontaneous motor activity, to produce a mechanically evoked increase in MAP and to examine the stimulus–response relationships of AoNA and CsNA [28]. Although the sensitivity of the MAP–HR baroreflex curve is markedly blunted during spontaneous motor activity, the stimulus–response relationships of AoNA and CsNA were not influenced by spontaneous motor activity, irrespective of the absence or presence of the HR restraint [28]. Thus, it is unlikely that central command modifies signal transduction of aortic and carotid sinus baroreceptors during spontaneous motor activity in decerebrate cats. The inhibition of the cardiac baroreflex by central command [1, 2] must occur on neurons along the medullary baroreflex pathways rather than in the periphery. This concept is supported by the following evidence. Stimulation of the hypothalamic and mesencephalic defense areas causes suppression of the cardiac component of the aortic baroreflex [29–31], while stimulation of the mesencephalic locomotor region causes resetting of the cardiac and vasomotor components of the carotid sinus baroreflex [32]. When constant aortic baroreceptor input is transmitted to the cardiovascular centers, the resultant baroreflex bradycardia is blunted immediately before or at the start of voluntary static exercise in conscious cats [13] and spontaneous motor activity in decerebrate cats [1, 2, 14].

Limitations

Several substantial limitations are involved in this study. First, although the doses of phenylephrine and norepinephrine intravenously administered were too low to cause the direct effects on aortic baroreceptor activity, plasma concentrations of phenylephrine and norepinephrine were not measured in this study. To avoid such pharmacological effect on arterial baroreceptor activity, AP should be raised with mechanical intervention. Indeed, when the changes of AoNA and CsNA against the pressor response were examined with brief occlusion of the abdominal aorta [28], spontaneously evoked motor activity did not influence the changes of AoNA and CsNA, in good agreement with the present findings. Second, since blood pressure of the brachiocephalic artery was measured in this study, it cannot be denied that the recorded blood pressure waveform may not be always similar to the pressure waveform of the aorta or the carotid sinus artery. In addition, although a more direct stimulus for arterial baroreceptors is a mechanical transformation of the vascular wall rather than the blood pressures themselves, we did not measure any changes in the vessel diameter. Third, the responses of aortic and carotid sinus baroreceptors to any depressor challenges were not examined. Thus, the threshold pressures of arterial baroreceptors were not known, and the stimulus–response curves of the baroreceptors did not cover the entire range of blood pressure but were confined only over a higher pressor range from the operating point. Finally, since single fiber activity of aortic and carotid sinus baroafferents was not recorded in this study, any differences in the responses between medullated and non-medullated baroreceptor afferents could not be discriminated.

In conclusion, the present finding that the stimulus–response curves of the mean AoNA and CsNA against the
changes in MAP almost matched between spontaneous motor activity and pharmacologically evoked pressor intervention suggests that the mean activities of aortic and carotid sinus baroreceptors are able to code the beat-by-beat changes in MAP not only at rest but also during spontaneous motor activity.

Acknowledgments This study was supported by Grants-in-Aid for Scientific Research (B) and for Exploratory Research from the Japan Society for the Promotion of Science.

Conflict of interest The authors declare that they have no conflict of interest.

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