Differential sympathetic outflow and vasoconstriction responses at kidney and skeletal muscles during fictive locomotion

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Koba, Satoshi, Takayoshi Yoshida, and Naoyuki Hayashi. Differential sympathetic outflow and vasoconstriction responses at kidney and skeletal muscles during fictive locomotion. Am J Physiol Heart Circ Physiol 290: H861–H868, 2006—We compared sympathetic and circulatory responses between kidney and skeletal muscles during fictive locomotion evoked by electrical stimulation of the mesencephalic locomotor region (MLR) in decerebrate and paralyzed rats (n = 8). Stimulation of the MLR for 30 s at 40-μA current intensity significantly increased arterial pressure (+38 ± 6 mmHg), triceps surae muscle blood flow (+17 ± 3%), and both renal and lumbar sympathetic nerve activities (RSNA +113 ± 16%, LSNA +31 ± 7%). The stimulation also significantly decreased renal cortical blood flow (−18 ± 6%) and both renal cortical and triceps surae muscle vascular conductances (RCVC −38 ± 5%, TSMVC −17 ± 3%). The sympathetic and vascular conductance changes were significantly dependent on current intensity for stimulation at 20, 30, and 40 μA. The changes in LSNA and TSMVC were significantly less than those in RSNA and RCVC, respectively, at all current intensities. At the early stage of stimulation (0–10 s), decreases in RCVC and TSMVC were significantly correlated with increases in RSNA and LSNA, respectively. These data demonstrate that fictive locomotion induces less vasoconstriction in skeletal muscles than in kidney because of less sympathetic activation. This suggests that a neural mechanism mediated by central command contributes to blood flow distribution by evoking differential sympathetic outflow during exercise.

Central command; mesencephalic locomotor region; sympathetic nerve system; renal blood flow; muscle blood flow

Central command is a neural drive that originates from the brain stem and regulates both locomotor and cardiorespiratory systems during exercise (47). This neural activation evokes cardiovascular responses, such as increase in blood pressure, through sympathetic outflow (47).

During static exercise in cats (7) and dynamic exercise in rats (34), baboons (18), and humans (21), the distribution of the cardiac output includes a decrease in blood flow to internal organs such as the kidney and an increase in blood flow to skeletal muscles. These responses are essential to maintain adequate blood pressure and to match an increased metabolic demand in the muscles. It is well known that sympathetic outflow elicits renal vasoconstriction and consequently decreases renal blood flow during exercise (33) and central command (22). On the other hand, although sympathetic outflow constricts skeletal muscle vessels (2, 3, 12, 34), muscle vasodilation and an increase in muscle blood flow abruptly occur at the onset of exercise (3) and are maintained during exercise (2, 3). Muscle contraction triggers the release of local vasodilator substances from muscle cells (8, 11, 41), red blood cells (9), and endothelial cells (11, 38). The vasodilation caused by the nonneural mechanisms counters the sympathetic vasoconstriction in the muscles [termed “functional sympatholysis” by Remensnyder et al. (36)]. Therefore, the local vasodilator mechanisms independent of a neural pathway are important contributors to blood flow distribution during exercise.

In addition to the nonneural vasodilator mechanisms, the neural mechanism can also be important in contributing to the blood flow distribution during exercise. It is hypothesized that if the sympathetic outflow to contracting muscles is less than that to internal organs during exercise the magnitude of sympathetic vasoconstriction would be less in the muscles than in the internal organs. Dean and Coote (5) reported that stimulation of the hypothalamus or the midbrain defense area shows different discharge patterns between renal and lumbar (which regulates hindlimb circulation) sympathetic nerve activities (RSNA and LSNA, respectively). However, they investigated neither the difference in sympathetic responses between RSNA and LSNA nor the magnitude of sympathetic vasoconstriction in the kidney and the skeletal muscles. Thus it was uncertain whether the hypothetical neural mechanism plays a role in blood flow distribution.

The present study was designed to test the presence of this hypothetical mechanism. We compared sympathetic and circulatory responses between kidney and hindlimb skeletal muscles during fictive locomotion (central command stimulation) in rats. Fictive locomotion was evoked by electrical stimulation of the mesencephalic locomotor region (MLR) of the precollinear decerebrate and paralyzed rat (1, 47). This preparation allowed us to rule out the effect of the vasodilator mechanisms exerted by muscle contraction and enabled us to focus on the neural role played by central command in regulating the cardiovascular system. We hypothesized that less sympathetic activation induces less vasoconstriction in the skeletal muscles than in the kidney during fictive locomotion.

Moreover, it was necessary to examine the sympathetic role to determine skeletal muscle vasomotor tone during stimulation of the MLR. Although various studies suggested that there is sympathetic vasoconstriction in skeletal muscles during exercise (2, 3, 12, 34), other studies reported that there are vasodilator neural components in the skeletal muscle sympathetic fibers (4, 10, 24–26) that can contribute to muscle...
vasodilation. Therefore, to determine whether sympathetic outflow induces muscle vasoconstriction during fictive locomotion, the effect of lumbar sympathectomy (LS), which removed the hindlimb sympathetic outflow, on hindlimb muscle circulatory responses to stimulation of the MLR was also examined in a subset of rats.

MATERIALS AND METHODS

General procedures. All experimental procedures of the present study were approved by the Research Ethic Committee of the School of Health and Sport Sciences, Osaka University, and were conducted in accordance with the “Guiding Principles in the Care and Use of Animals in the Fields of Physiological Sciences” published by the Physiological Society of Japan. Sixteen Sprague-Dawley rats (male, 8–9 wk, wt 280–360 g) were used in the present study. The rat was anesthetized with a mixture of halothane (<4%) and oxygen, and the trachea was cannulated, and then the lungs were artificially ventilated with a respirator (SN-480–7, Shinnano) (tidal volume 2 ml and frequency 65–70 min–1). The left jugular vein and common carotid artery were cannulated to administer drugs and to record arterial pressure (AP), respectively. The arterial catheter was attached to a pressure transducer (P23 XL-1, Ohmeda). Arterial pH was measured at 30-min intervals with a pH meter (B-212, Horiba). If necessary, metabolic acidosis was corrected with intravenous infusion of sodium bicarbonate solution or with change of the ventilation volume. Needle electrodes were set on the back to record ECG, and the ECG signal was amplified with a differential amplifier (AB-621G, Nihon Kohden). Heart rate (HR) was calculated beat to beat with detection of the time between successive R waves in the ECG. Body temperature was maintained adequately with a heating lamp. The Achilles tendon was isolated by cutting the calcaneous bone, and the left triceps surae muscles were carefully isolated. The rat was held in a stereotaxic apparatus (ST-7, Narishige). The left hindlimb was secured in space with a patellar precision clamp, and the common triceps surae muscles were lightly stretched and positioned at heart level.

Recording sympathetic nerve activities and blood flow. In the control group of rats (n = 8), RSNA, LSNA, renal cortical blood flow (RCBF), and triceps surae muscle blood flow (TSMBF) on the left side were recorded. RSNA and LSNA were recorded by a method described in previous studies (28, 29, 50). To record RSNA, the left kidney was exposed retroperitoneally through a left flank incision. A bundle of renal nerve fibers was carefully dissected from other connective tissues. A piece of laboratory film was placed on the isolated bundle, and two tips of a bipolar electrode to record RSNA were placed between the bundle and the film. These were embedded in a silicon gel. Once the gel was hardened, the silicon rubber was fixed to the surrounding tissue with a glue containing α-cyanoacrylate. To record LSNA, a midline abdominal incision was made, and the abdominal aorta and vena cava were pulled aside to expose the left lumbar sympathetic trunk. The lumbar sympathetic trunk at the L1–L4 or L4–L5 segment was carefully dissected from other connective tissues. LSNA at the L3–L4 or L4–L5 segment reflects the component regulating hindlimb muscle circulation (29). In a similar way to the RSNA recording, a piece of laboratory film was placed under the trunk at the L3–L4 or L4–L5 segment, the tips of a bipolar electrode were set between the film and the isolated trunk, and they were embedded in the silicon gel. RSNA and LSNA signals were amplified with a differential amplifier (MEG2100, Nihon Kohden) with a band-pass filter of 150 Hz in low-cut frequency and of 1 kHz in high-cut frequency and made audible.

The left RCBF was recorded by laser-Doppler flowmetry with a needle-type probe (ALF21, Advance). The probe was inserted in the left triceps surae muscles to a depth of ~3 mm from the fascia and stabilized. The TSMBF was measured within a 1-mm radius from the tip of the probe.

Lumbar sympathectomy. In a subset of rats (n = 8), unilateral LS at the L3–L4 segment was carried out. A midline abdominal incision was made, and the abdominal aorta and vena cava were pulled aside to expose the left lumbar sympathetic trunk. The trunk at the L3–L5 segment was stripped and removed. In this group, AP, ECG, HR, and TSMBF were recorded.

Decerebration procedure. Decerebration at the precollucellar level was carried out with a method described in a previous study (28). Dexamethasone (0.2 mg) was given intravenously to minimize brain edema. Immediately before the decerebration, the right carotid artery was occluded to reduce brain bleeding. The upper skull and dura mater were removed, and then cortical tissue was removed with aspiration. The brain was then sectioned vertically with a blade at the precollucellar level. All neural tissue rostral to the section as well as the cortical tissues covering the cerebellum were aspirated. Small pieces of cotton gauze were set in the cranial vault to arrest bleeding, and then halothane anesthesia was withdrawn. The cranial vault was filled with mineral oil. To replace the blood loss during decerebration (approximately <1 ml), saline was given intravenously in an amount sufficient to maintain basal AP. A recovery period of 90 min was allowed before the experimental protocols to abolish the effects of anesthesia and to stabilize the preparation.

Experimental design. After the recovery period, the junction of the superior and inferior colliculus was searched to find the site of the MLR with electrical stimulation at 30- to 40-μA current intensity (60 Hz, 1-ms duration) with a glass-cored tungsten microelectrode connected to an electronic stimulator via an isolator (SS 202J, Nihon Kohden) [see method described by Bedford et al. (1)]. The electrode was designated as the cathode, and the anode was placed in exposed skin tissue in the head wound. The site of the MLR was at the border of the inferior and superior colliculus (1), 0.5–0.7 mm anterior, 1.8–2.0 mm lateral, and 4.0–4.5 mm deep from the surface junction of the colliculi. The determination of the site of the MLR was affirmed from the physiological criteria as follows: 1) threshold of locomotion with reciprocal limb movement <30 μA, 2) stimulus-bound locomotion, and 3) graded activity of locomotion and gait changes with increased stimulation current (1). After determination of the site of the MLR, we paralyzed the rat with an intravenous infusion of vecuronium bromide (1 mg/kg). After 30 s of baseline data collection, we electrically stimulated the MLR for 30 s at 20-, 30-, and 40-μA current intensity. The order of the current intensities was random. A period (≥5 min) between each recording was allowed. At the conclusion of the experiments, the rat was killed humanely with an overdose of anesthesia (pentobarbital sodium), and the background noise signal of RSNA and LSNA and the artifacts of RCBF and TSMBF were recorded.

Data acquisition and statistical analysis. All measured variables were displayed continuously on a computer monitor and stored on a hard disk through analog-digital conversion (Powerlab/8s, AD Instruments) at a 1-kHz sampling rate. Recorded RCBF and TSMBF artifacts, which were <5% of the basal RCBF and TSMBF, were subtracted. Mean AP (MAP), HR, RCBF, and TSMBF were calculated beat by beat and then averaged over every 5 s. Signals of the sympathetic nerve activities were transformed into absolute value, integrated over every 1 s, subtracted by the 1-s integrated background noise, and averaged over every 5 s. The absolute values of the sympathetic activities and blood flows varied among rats. To quantify the sympathetic and blood flow responses to stimulation of the MLR, baseline values were obtained by taking mean values for 30 s immediately before stimulation and evaluating the mean as 100%, and then relative changes from baseline during and after stimulation were evaluated. Renal cortical vascular conductance (RCVC) and triceps surae muscle vascular conductance (TSMVC) were obtained by di-
Table 1. Basal MAP and HR in control and LS groups

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<th>MAP, mmHg</th>
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<tr>
<td>Control rats (n = 8)</td>
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<tr>
<td>20 μA</td>
<td>116±9</td>
<td>339±7</td>
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<td>30 μA</td>
<td>114±9</td>
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<tr>
<td>40 μA</td>
<td>119±7</td>
<td>338±7</td>
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<td>LS rats (n = 8)</td>
<td></td>
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<tr>
<td>20 μA</td>
<td>108±9</td>
<td>360±8</td>
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<tr>
<td>30 μA</td>
<td>104±7</td>
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<tr>
<td>40 μA</td>
<td>105±8</td>
<td>359±11</td>
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Values are means ± SE. MAP, mean arterial pressure; HR, heart rate; LS, lumbar sympathectomy. There were no significant differences between trials in each group or between the groups.

Results

Responses in sympathetic and circulatory responses at kidney and skeletal muscles to stimulation of MLR. Basal MAP and HR of the control group (n = 8) are presented in Table 1. There were no significant differences between trials.

An example of cardiovascular changes before, during, and after 30-s stimulation of the MLR at 30 μA in a control rat is presented in Fig. 1. Stimulation of the MLR increased AP, HR, RSNA, LSNA, and TSMBF; on the other hand, it decreased RCBF. It decreased both RCVF and TSMVC. The changes in LSNA and TSMVC were less than those in RSNA and RCVF, respectively.

Changes in MAP and HR from baseline during 30-s stimulation of the MLR at 20, 30, and 40 μA are presented in Fig. 2. Stimulation of the MLR increased MAP (P < 0.05), whereas it did not significantly change HR at all current intensities (Fig. 2). Changes in sympathetic nerve activities, blood flow, and vascular conductance from baseline during 30-s stimulation of the MLR at 20, 30, and 40 μA are presented in Fig. 3. Stimulation of the MLR decreased RCBF at 40 μA (P < 0.05) and increased TSMBF at all current intensities (P < 0.05) (Fig. 3). Significant differences between the changes in RCBF and TSMBF (P < 0.05) were observed during stimulation at all current intensities (Fig. 3). Stimulation of the MLR increased RSNA and LSNA (P < 0.05). It decreased RCVF at all current intensities (P < 0.05) and decreased TSMVC at 30 and 40 μA (P < 0.05) (Fig. 3). During stimulation at all current intensities, the changes in sympathetic nerve activity and vascular conductance were significantly less at the skeletal muscles than at the kidney (P < 0.05; Fig. 3).
The effect of current intensity on the peak sympathetic and circulatory responses was examined as presented in Fig. 4. The increases in RSNA and LSNA and the decreases in RCVC and TSMVC were significantly correlated with current intensity ($P < 0.05$; Fig. 4). Changes in RCBF and TSMBF were not correlated with current intensity (Fig. 4). The increases in MAP were also significantly correlated with current intensity ($r = 0.42$, $P < 0.05$).

The effect of sympathetic activation on the vasoconstrictor response to stimulation of the MLR on the kidney and the skeletal muscles was examined at the early (0–10 s) and late (20–30 s) stages of stimulation (Fig. 5). Decreases in RCVC were significantly correlated with increases in RSNA at both early and late stages of stimulation ($P < 0.05$; Fig. 5). Decreases in TSMVC also significantly correlated with increases in LSNA at the early stage ($P < 0.05$) but not at the late stage of stimulation (Fig. 5). There was no significant difference in the slope of the regression line between RSNA-RCVC (slope $-0.17$) and LSNA-TSMVC (slope $-0.17$) at the early stage (Fig. 5).

Effects of LS on triceps surae muscle circulatory responses to stimulation of MLR. Basal MAP and HR in the LS group ($n = 8$) are presented in Table 1. There were no significant differences between trials and between the control and the LS rats. In this group, stimulation of the MLR increased MAP and TSMBF at all current intensities ($P < 0.05$; Fig. 6), and the greatest values were correlated with, and therefore dependent on, current intensity ($P < 0.05$). It did not change TSMVC from baseline at all current intensities (Fig. 6).

DISCUSSION

In agreement with a previous report (48), we found that fictive locomotion decreased RCBF and increased TSMBF. The new findings of the present study were that fictive locomotion induced $J$ less of an increase in LSNA than in RSNA.
and 2) less of a decrease in TSMVC than in RCVC and that 3) the decreases in RCVC and TSMVC were significantly correlated with the increases in RSNA and LSNA, respectively, at the early stage of fictive locomotion. Moreover, as shown in our previous (22) and present studies, sympathectomy abolished the decreases in vascular conductance at both kidney and triceps surae muscles during fictive locomotion. The decreases in vascular conductance suggest that the vessels were constricted. Thus the vasoconstriction in the muscles was less than that in the kidney. Vasoconstriction being dependent on sympathetic activation is also supported by the significant correlations between the increases in sympathetic nerve activity and the decreases in vascular conductance at kidney and skeletal muscles. These data confirmed our hypothesis that fictive locomotion induces less sympathetic activation in the skeletal muscles than in the kidney, which leads to less vasoconstriction in the skeletal muscles. The decreases in vascular conductance suggest that the vessels were constricted. Thus the vasoconstriction in the muscles was less than that in the kidney. Vasoconstriction being dependent on sympathetic activation is also supported by the significant correlations between the increases in sympathetic nerve activity and the decreases in vascular conductance at kidney and skeletal muscles. These data confirmed our hypothesis that fictive locomotion induces less sympathetic activation in the skeletal muscles than in the kidney, which leads to less vasoconstriction in the skeletal muscles. The present study provided evidence supporting the idea that the blood flow distribution during exercise is due to not only the action of a nonneural vasodilator mechanism in skeletal muscles exerted by contraction (8, 9, 11, 38, 41) but also differential sympathetic outflow to internal organs and skeletal muscles evoked by central command.

The significant correlation between LSNA and TSMVC at the early stage (0–10 s) of stimulation of the MLR disappeared at the late stage (20–30 s). This should be due to an additional effect of a local vasodilator mechanism, that is, the endothelial response to the increases in blood pressure and/or flow in the muscles. Mechanical stimuli on the muscle microvessels exerted by the increase in blood pressure and/or flow, not by muscular activity, produce nitric oxide from endothelial cells, which induces smooth muscle hyperpolarization and then muscle vasodilation (10, 23, 39). It was reported that the endothelial vasodilator response to the mechanical stimuli became greater with stimulation duration increase in rats (23, 39). These findings suggest that the duration-dependent vasodilator capacity of endothelial response to the increase in blood pressure and/or flow impaired sympathetic vasoconstriction in the muscles and consequently abolished the correlation between LSNA and TSMVC at the late stage.

The present study indicates that sympathetic outflow during fictive locomotion induces muscle vasoconstriction. Stimulation of the MLR increased LSNA and decreased TSMVC in the control rats; on the other hand, it did not change TSMVC in the LS rats. Likewise, many studies have provided evidence that sympathetic outflow constricts vessels in the skeletal muscles during exercise (2, 3, 12, 34). In contrast, other studies have reported that there are vasodilator neural components in skeletal muscle sympathetic fibers (4, 10, 24–26). If the effect of vasodilator components had countered that of vasoconstrictor components during stimulation of the MLR, muscle vasodilation could have occurred through sympathetic outflow in the present study. It is unclear whether stimulation of the MLR...
activated muscle sympathetic vasodilator fibers. However, because the slopes of the regression lines between sympathetic nerve activity and vascular conductance responses were the same between kidney and skeletal muscles at the early stage (0–10 s) of stimulation of the MLR, the sensitivity of vasoconstrictor response to sympathetic outflow in the muscles was suggested to be equal to that in the kidney. The contribution made by muscle sympathetic vasodilator components during stimulation of the MLR might be negligible.

Central command evoked by stimulation of the MLR increased RSNA, as previously reported in cats (15) and rats (22). Moreover, the present study showed that stimulation of the MLR also increases LSNA, reflecting hindlimb muscle sympathetic nerve activity (29). A series of studies by Hill and colleagues (16, 17), on the other hand, showed that stimulation of the MLR of the decerebrate cat did not increase sympathetic nerve activity of triceps surae muscles (16) but increased hindlimb skin sympathetic nerve activity (17). Their studies imply that the increases in LSNA during stimulation of the MLR in our experiments were mainly due to sympathetic activation of hindlimb skin, but not muscles, because LSNA includes both hindlimb skin and muscle sympathetic nerve activities. However, there are several pieces of evidence that disaffirm this implication. First, LS abolished the decreases in TSMVC in the lumbar sympathectomized group (Fig. 3). Second, the skin is not a predominant organ in the exercise at 75% MVC, also increased the nerve activity more than five times from muscle relaxation level and intermittent handgrip exercise after partial neuromuscular blockade, in which subjects attempted to continue to perform the exercise at 75% MVC, also increased the nerve activity more than three times. On the basis of these observations, light to moderate activation of central command should have a minor role in increasing muscle sympathetic nerve activity whereas intense activation of central command should increase the nerve activity, as Victor et al. (45) suggested. Thus activation of central command in the present study would be above a threshold that could increase muscle sympathetic nerve activity, whereas the lesser activation of central command in the study by Hill et al. (16) would not. Nevertheless, the increases in LSNA during stimulation of the MLR, whose
maximal value was <35% on average, were relatively low compared with data observed in human studies.

In rats, renal sympathetic preganglionic neurons are located from T6 to L1 and are concentrated at T11 and T12 (19). On the other hand, lumbar sympathetic preganglionic neurons that regulate hindlimb muscle circulation have been suggested to be located at the L3–L5 segment (29). Thus it is reasonable to consider that sympathetic outflows to kidney and hindlimb skeletal muscles were differentially regulated at the preganglionic level. The involvement of the supraspinal neural circuits that provide excitatory and inhibitory input to preganglionic neurons in the differential sympathetic outflow can also be pointed out. Neural drive from the MLR stimulates the medulla, an important region that regulates the sympathetic nervous system (6, 20). Several sites in the medulla, for example, the rostral ventrolateral medulla, rostral ventromedial medulla, and raphe, have been identified as having direct neural projections to the intermediolateral cell column in the spinal cord and as regulating sympathetic outflow differentially to various organs (40). It was demonstrated that stimulating or inhibiting one of these sites results in differential sympathetic responses at various organs (14, 27, 31, 35, 49). Although anatomic and/or functional interaction between these sites including the MLR has not been concluded, it is possible that the neural circuits containing them produced differential sympathetic outflow during stimulation of the MLR.

Morrison (30) has reviewed differential sympathetic outflow responses to several physiological stimuli, for example, heat stress, baroreceptor reflex, and pharmacological stimulation of a site in the central nervous system. Other studies have reported that central command contributes to differential sympathetic outflow between skin and skeletal muscles in cats (16, 17) and humans (46). The present study provides new insight into the effect of fictive locomotion (central command stimulation) on differential sympathetic outflow contributing to blood flow distribution. However, the effect of actual locomotion or exercise on the physiological phenomenon is unclear. Recently, Miki and colleagues (28, 29, 50) investigated the differential sympathetic outflow and its role in regulating circulation in daily life, with direct records of neural activities of the conscious rat. They reported that, at the transition from non-rapid eye movement (NREM) sleep to rapid eye movement (REM) sleep, RSNA decreased (28, 50) and renal blood flow increased (29) whereas LSNA increased and hindlimb blood flow decreased (29). Moreover, the changes in renal vascular conductance were dependent on the changes in RSNA through NREM sleep, REM sleep, and moving and grooming states (50). Their studies lead us to anticipate that differential sympathetic outflow also results in the blood flow distribution in actual exercise. Future studies are needed for better understanding the neural contribution to the blood flow distribution during exercise.

Limitations. Three limitations must be kept in mind when interpreting the present data. First, electrical stimulation might activate not only cell bodies but also fibers of the neural pathway in the MLR. Chemical stimulation, on the other hand, can stimulate only cell bodies. For example, picrotoxin, a GABA antagonist, was used in a previous study to stimulate the MLR (32). Nevertheless, cardiovascular responses to electrical stimulation of the MLR in the present study might be mainly due to cell body activation because a previous study (1) showed that injection of GABA into the MLR reduced pressor response to electrical stimulation of the MLR >70%.

Second, the correlation between the increases in LSNA and the decreases in TSMVC at the early stage of stimulation of the MLR was relatively weak, although it was statistically significant. This might be because LSNA includes both hindlimb skin and muscle sympathetic nerve activities, although LSNA should be a valid index of sympathetic nerve activity of triceps surae muscles in the present study. The components that were not related to regulation of triceps surae muscle circulation might weaken the correlation between LSNA and TSMVC.

Third, although it is well recognized that central command is a powerful neural drive to increase HR during exercise (42), stimulation of the MLR did not increase it in the present study. In this regard, previous studies have shown inconsistent results, increase (1, 15–17, 32) and no change (22, 32) in HR during electrical or chemical stimulation of the MLR in cats and rats. We can only speculate that the neural drive originating in the MLR affects vasomotor tone greatly, compared with HR regulation.

In summary, we tested the hypothesis that less sympathetic activation to skeletal muscles than to internal organs induces different vasoconstriction between them during exercise. Stimulation of the MLR increased both RSNA and LSNA and decreased both RCVC and TSMVC. The changes in sympathetic and vascular conductance were less at the skeletal muscles than at the kidney and were significantly dependent on current intensity for stimulation. At the early stage of stimulation of the MLR (0–10 s), the decreases in vascular conductance were significantly correlated with the increases in sympathetic nerve activity at both kidney and skeletal muscles and the slopes of the regression lines were the same between them. The present data indicate that differential sympathetic outflow induced the corresponding vasoconstriction at kidney and skeletal muscles during fictive locomotion. This suggests that a neural mechanism mediated by central command contributes to the blood flow distribution by evoking differential sympathetic outflow during exercise. We conclude that the blood flow distribution during exercise is due to not only the action of nonneural vasodilator mechanisms in contracting skeletal muscles but also differential sympathetic outflow to internal organs and muscles.

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REFERENCES

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