Effect on arterial pressure of rhythmically contracting the hindlimb muscles of cats

MARC P KAUFMAN, KENNETH J. RYBICKI, TONY G. WALDROP,
AND JERE H. MITCHELL

Departments of Physiology and Internal Medicine, and Harry S. Moss Heart Center,
The University of Texas Health Science Center, Dallas, Texas 75235

KAUFMAN, Marc P., KENNETH J. RYBICKI, TONY G. WALDROP, AND JERE H. MITCHELL. Effect on arterial pressure of rhythmically contracting the hindlimb muscles of cats. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 56(5): 1265-1271, 1984. Although static contraction of the hindlimb muscles of anesthetized cats is known to reflexly increase arterial pressure and heart rate, the cardiovascular effects of rhythmic contractions of these muscles is unclear. To help clarify this issue, we determined, in chloralose-anesthetized cats, the effects on arterial pressure and heart rate of rhythmically contracting the hindlimb muscles at a frequency of 5 Hz. In addition, we determined the effect of rhythmic contractions on the impulse activity of group III and IV muscle afferents whose activation is known to increase cardiovascular function. We found that rhythmic contractions increased arterial pressure (from 108 ± 8 to 134 ± 9 mmHg; P < 0.05) and heart rate (from 192 ± 13 to 208 ± 10 beats/min; P < 0.05) in 10 cats and decreased arterial pressure (from 107 ± 8 to 93 ± 9 mmHg; P < 0.05) but did not change heart rate in 9 other cats. The increases were reflex, because they were prevented by cutting the spinal roots innervating the contracting hindlimb. The decreases, however, were not reflex, because they persisted after spinal root section. The differences in the arterial pressure responses to rhythmic contractions may have been partly due to individual differences in the level of anesthesia, because in three cats the pressor responses to this maneuver were converted to depressor responses after giving the cats additional chloralose. Rhythmic contractions of the triceps surae muscles stimulated 8 of 10 group III afferents and 9 of 16 group IV afferents. We conclude that rhythmic contraction is capable of reflexly increasing cardiovascular function in cats provided that the effect is not depressed by anesthesia.

Perez-Gonzalez (19), using the same preparation as that used by Coote et al. (5) and Mitchell et al. (15), also found that static contraction of the hindlimb muscles reflexly increased arterial pressure. In the same cats, however, Perez-Gonzalez (19) found that rhythmic twitch contractions of the hindlimb muscles decreased arterial pressure. Moreover, the depressor response to rhythmic contractions was not reflex in origin, because it persisted after cutting the spinal roots innervating the contracting hindlimb.

We were surprised by the lack of a reflex cardiovascular response to rhythmic twitch contractions of the hindlimb muscles, because in preliminary experiments in cats we found that this maneuver stimulated group III and IV afferents with endings in the triceps surae muscles. We have therefore reexamined the effects of rhythmic twitch contractions on arterial pressure and heart rate in this species. In addition, we have reported the effect of rhythmic twitch contractions on the impulse activity of group III and IV muscle afferents.

METHODS

Reflex studies examining effects of muscular contraction on arterial pressure and heart rate. Cats were anesthetized either with α-chloralose (60-100 mg/kg ip) or with a combination of α-chloralose (40-50 mg/kg ip) and urathan (200-300 mg/kg ip). The cervical trachea, right external jugular vein, and right common carotid artery were cannulated. The lungs were ventilated mechanically (Harvard Apparatus) with a mixture of room air and O₂. Arterial PO₂, PCO₂, and pH were measured periodically (Radiometer ARL-3) and kept within normal limits (i.e., PO₂ = 90-120 Torr, PCO₂ = 30-40 Torr, pH = 7.35-7.45). Blood pressure in the aortic arch was measured through the carotid arterial cannula, which was connected to a Statham P23ID transducer. Heart rate was derived from the arterial pressure pulse using a Gould Biotach. Tension, generated by the right triceps surae muscles, was measured by connecting the calcaneal tendon to a force-displacement transducer (Grass FT-10). The tension measurement was used as an index of the strength of overall hindlimb muscular contraction.

The L₄-S₂ spinal roots were exposed, after which the cat was placed in a Kopf spinal unit. The skin overlying the exposed spinal roots was tied to curved stainless steel bars to form a pool, which was filled with warm (37°C)
mineral oil. The dura was then incised. The right L₇-S₁ ventral roots were identified and cut; each of the cut peripheral ends of the ventral roots was placed on a separate shielded and grounded stimulating electrode. The right hindlimb was clamped to prevent its movement.

In the reflex experiments, we used the following protocol. With the dorsal roots intact, we electrically stimulated the peripheral cut ends of the L₇-S₁ ventral roots for 45–60 s. We used two frequencies of stimulation, 5 and 40 Hz (pulse duration = 0.1 ms). The former frequency caused rhythmical “twitch contractions” of the right hindlimb, whereas the latter frequency caused tetanic “static contraction” of this limb. After measuring the arterial pressure and heart rate responses to hindlimb muscular contraction, we then cut the dorsal and ventral roots (L₅-S₂) and repeated the contractions in an attempt to determine how much of the observed responses were reflex in origin.

Electrophysiological studies examining effects of rhythmic contractions on activity of group III and IV muscle afferents. For experiments designed to determine the effect of rhythmic twitch contractions on the impulse activity of group III and IV muscle afferents, we anesthetized cats with pentobarbital sodium (35 mg/kg ip). The primary site of action of general anesthetics is believed to be on synapses in the central nervous system and in sympathetic ganglia (17). Therefore, the type of anesthetic used should have little effect on the responses of muscle afferents to rhythmic contractions. The cats were prepared in the same way as that described in the preceding section (see above), except that in these experiments the right obturator and femoral nerves were cut. In addition, all visible branches of the right sciatic nerve were cut, except for those innervating the triceps surae. In these and in the reflex experiments, resting tension of the triceps surae was set with a rack and pinion at 0.5–1.0 kg. The triceps surae was rhythmically contracted by electrically stimulating the L₇-S₁ ventral roots at a frequency of 5 Hz. The lungs were ventilated mechanically with a mixture of room air and O₂. Arterial blood gases were measured periodically and were maintained within normal limits.

We recorded afferent impulses from the right L₇ or S₁ dorsal roots and identified afferents having endings in the right triceps surae muscles by probing their receptive fields either with a glass probe or with a blunted forceps. The method we used to locate the receptive fields of endings in the triceps surae was very similar to that previously used by Coleridge et al. (4) to locate the receptive fields of cardiac vagal C-fibers, most of whose endings were not mechanoreceptors inasmuch as they were not stimulated by increases in cardiac volume or pressure. We discarded all afferents whose receptive fields we could not locate in the triceps surae. The right lateral or medial gastrocnemius nerves were electrically stimulated, and the conduction time from stimulating to recording electrodes was measured. Conduction velocities were calculated by dividing the conduction distance by the conduction time. Triceps surae afferents were classified as group III if their conduction velocities ranged between 2.6 and 30 m/s. Afferents were classified as group IV if their conduction velocities were 2.5 m/s or less (14, 16). We did not examine the effect of rhythmic twitch contractions on the impulse activity of group I and II afferents, because they do not reflexly evoke cardiovascular effects (12, 14, 20, 21, 24).

**RESULTS**

Effects of rhythmic twitch contractions of hindlimb muscles on arterial pressure and heart rate. We examined the effects of rhythmic contractions on arterial pressure and heart rate in 19 cats. Rhythmic contractions evoked two patterns of cardiovascular response (Figs. 1A and 2A), neither of which appeared to depend on whether the cats were anesthetized with chloralose (60–100 mg/kg) or with chloralose (40–50 mg/kg) and urethan (200–300 mg/kg). The first pattern of response to rhythmic contractions, observed in 10 of the 19 cats studied, consisted of increases in both mean arterial pressure and heart rate (Figs. 1A and 4B). Tension, generated by the contracting triceps surae muscles, averaged 1.5 ± 0.2 kg. Mean arte-

![FIG. 1. Pressor response to rhythmic contractions is a reflex. A: rhythmically contracting right hindlimb muscles increased arterial pressure and heart rate. In this cat, spinal roots were intact except for right L₇-S₁ ventral roots whose peripheral ends were placed on electrodes and stimulated at a frequency of 5 Hz. B: statically contracting right hindlimb muscles increased arterial pressure and heart rate. C: right L₇-S₁ dorsal and ventral roots were cut, after which hindlimb was rhythmically contracted. Note that increases in arterial pressure and heart rate evoked previously by this maneuver (see A) were abolished by cutting the spinal roots. D: statically contracting right hindlimb muscles after cutting spinal roots greatly attenuated increases in arterial pressure and heart rate evoked previously by this maneuver (see B).](image-url)
A: rhythmically contracting hindlimb muscles decreased arterial pressure but had no effect on heart rate in a cat whose spinal roots were intact except for right L₅-S₁ ventral roots (see legend of Fig. 1). B: statically contracting hindlimb muscles, induced by stimulating L₅-S₁ ventral roots at a frequency of 40 Hz, increased arterial pressure and heart rate. C: right L₅-S₁ dorsal and ventral roots were cut, and right hindlimb was rhythmically contracted by stimulating right L₅-S₁ ventral roots at a frequency of 5 Hz. Note that arterial pressure still decreased in response to rhythmic contractions. D: statically contracting right hindlimb muscles after cutting L₅-S₁ dorsal and ventral roots greatly attenuated increases in arterial pressure and heart rate evoked previously by this maneuver (see B). A-D were from the same cat and were separated by 30-min intervals.

In 7 of the 10 cats showing pressor responses to rhythmic contraction, we cut the spinal roots innervating the working hindlimb. In each of the seven, the increases in arterial pressure and heart rate evoked by rhythmic contractions were abolished (Figs. 1C and 4D). In six of the seven, arterial pressure now decreased in response to rhythmic contractions; in one, this variable did not change (Fig. 1C). Before cutting the spinal roots in the remaining three cats, we gave more chloralose anesthesia (15–60 mg/kg iv) and converted the pressor responses to rhythmic contractions to depressor responses, effects which persisted after cutting the spinal roots (Fig. 3, A and C). When the roots were intact in these three cats, the additional anesthesia also prevented the heart rate increase evoked by rhythmic contractions.

The second pattern of cardiovascular responses to rhythmic contractions, observed in 9 of the 19 cats studied, consisted of a decrease in mean arterial pressure and no change in heart rate (Figs. 2A and 4A). The depressor response to rhythmic contractions started 9.2 ± 2.0 s after the onset of this maneuver. Tension, generated by the contracting triceps surae, averaged 1.8 ± 0.2 kg. The depressor response to rhythmic contractions remained in each of the nine cats after section of the L₄-S₂ spinal roots innervating the contracting hindlimb (Figs. 2C and 4C). Moreover, the depressor response to rhythmic contraction remained in each of four cats when the right hindlimb was further denervated by cutting both the L₄ spinal root and the cauda equina.

Static contraction of the hindlimb muscles in the nine cats showing depressor responses to rhythmic contractions increased mean arterial pressure (from 112 ± 8 to 135 ± 8 mmHg; P < 0.05) and heart rate (from 166 ± 17 to 174 ± 17 beats/min; P < 0.05) (Fig. 2B). Tension, generated by the right triceps surae, averaged 5.9 ± 0.7 kg. Section of the spinal roots innervating the right hindlimb prevented most of these increases (Fig. 2D).

Static contraction of the hindlimb muscles in the 10 cats showing pressor responses to rhythmic contractions increased mean arterial pressure (from 108 ± 8 to 154 ± 7 mmHg; P < 0.05) and heart rate (from 190 ± 10 to 208 ± 10 beats/min; P < 0.05); both effects were either
abolished or greatly attenuated by cutting the spinal roots (Fig. 1D). Tension, generated by the right triceps surae, averaged 5.8 ± 6.0 kg. Static contraction evoked significantly greater increases in both mean arterial pressure and heart rate in the 10 cats showing pressor responses to rhythmic contractions than in the 9 cats showing depressor responses to this maneuver. Hence, mean arterial pressure and heart rate increased by 47 ± 9 mmHg and 18 ± 4 beats/min, respectively, in the former group, whereas these variables increased by 23 ± 5 mmHg and 7 ± 2 beats/min, respectively, in the latter group (both P < 0.05).

Effects of rhythmic twitch contractions on impulse activity of group III and IV afferents. We examined the effect of rhythmic twitch contractions on the impulse activity of 10 group III afferents (conduction velocity 10.5 ± 1.6 m/s; range 5.0–20.4 m/s) and 16 group IV afferents (conduction velocity 1.2 ± 0.1 m/s; range 0.6–2.5 m/s). The endings of each of the 26 group III and IV afferents were in the triceps surae. Rhythmically contracting this muscle group at a frequency of 5 Hz stimulated 8 of the 10 group III afferents and 9 of the 16 group IV afferents. Tension, generated by the contracting triceps surae, averaged 1.2 ± 0.1 kg for the 26 afferents tested.

All eight group III afferents stimulated by rhythmic contractions discharged in response to the first muscle twitch evoked by stimulating the ventral roots. Five group III afferents fired continuously throughout the 45 s of contraction (Fig. 5). The remaining three group III afferents fired at the onset of contraction and then stopped firing after the first 10–25 s of this maneuver. A most impressive feature of the discharge patterns of seven of the eight group III afferents stimulated by rhythmic contractions was that their firing, when it occurred, appeared synchronized with the muscle twitch (Fig. 5). The remaining group III afferent stimulated by rhythmic contraction discharged irregularly.

Of the nine group IV afferents stimulated by rhythmic contractions, three fired in response to the first muscle twitch (Fig. 6), five started to fire after 1–3 s of the onset of contraction, and one started to fire 18 s after the onset of this maneuver. Once firing started, six group IV afferents maintained their increased discharge throughout the rhythmic contraction, whereas three group IV afferents stopped firing 4–14 s after the onset of contraction. The discharge patterns of the group IV afferents stimulated by rhythmic contractions were very different from those of the group III afferents stimulated by this maneuver. For example, although three group IV afferents fired in synchrony with the muscle twitches during the first few seconds of contraction, their discharge soon became irregular and sporadic, though still above baseline levels. In addition, the remaining six group IV afferents stimulated by rhythmic contractions never fired synchronously with the muscle twitches; their discharge was always irregular and sporadic.

DISCUSSION

Rhythmically contracting the hindlimb muscles of chloralose-anesthetized cats increased arterial pressure and heart rate in 10 of the 19 cats that we studied. These increases were found to be reflex in origin, because they were prevented by cutting the spinal roots innervating the contracting hindlimb. Rhythmically contracting the hindlimb muscles in the remaining nine cats decreased arterial pressure, an effect which was not a reflex inasmuch as it persisted after cutting the spinal roots. The most likely explanation for the depressor response to rhythmic contractions is that it was caused by a metabolically induced vasodilation in the contracting muscles of cats whose reflex mechanisms were depressed by anesthesia (16, 19).

Two lines of evidence support the notion that individual differences in the level of anesthesia was likely to be one factor in determining whether rhythmic hindlimb contractions increased or decreased arterial pressure in
RHYTHMIC CONTRACTION INCREASES ARTERIAL PRESSURE

FIG. 5. Stimulation of a group III afferent (conduction velocity = 20.4 m/s) by rhythmically contracting the triceps surae at a frequency of 5 Hz. A: note both group III afferent that responded to first muscle twitch and stimulus artifact that preceded this twitch. In addition note that afferent was stimulated by a small increase in tension, (i.e., only 0.5 kg). B: 25 s after end of A, group III afferent is still discharging vigorously to rhythmical contractions.

FIG. 6. Stimulation of a group IV afferent (conduction velocity = 2.0 m/s) by rhythmically contracting the triceps surae at a frequency of 5 Hz. A: note maintained discharge of group IV afferent in response to 60 s of rhythmic contractions, which is represented by bar. B: recording of impulse activity and tension shown in A. Note that discharge of group IV afferent was synchronized to muscle twitch.

In our experiments, First, static hindlimb contraction evoked significantly smaller reflex increases in mean arterial pressure and heart rate in cats showing depressor responses to rhythmic contractions than in cats showing pressor responses to rhythmic contractions. Second, the pressor responses to rhythmic contractions in three cats were converted to depressor responses by injecting additional chloralose anesthesia.

Although we can only speculate as to the site of action of the additional chloralose anesthesia that abolished the reflex pressor response to rhythmic twitch contractions, supraspinal structures appear to be the most likely candidates. The lateral reticular nucleus, for example, has been shown to be an essential pathway in the reflex arc that increases arterial pressure and heart rate in response to static hindlimb contraction in barbiturate anesthetized cats (8). Moreover, the fastigial nucleus has been shown to be essential for the full expression of cardiovascular increases evoked by dynamic exercise in conscious dogs (6).

The reflex effect on arterial pressure evoked by rhythmic twitch contractions of the hindlimb has been found to differ across species. For example, in both dogs and rabbits rhythmic twitch contractions have been reported to reflexly decrease arterial pressure (2, 3, 22), whereas in cats our results show that this maneuver is capable of reflexly increasing arterial pressure. Tibes (23) has also reported that rhythmic contractions of the dog’s hindlimb reflexly increased arterial pressure; however, it must be pointed out that this investigator used intermittent tetanic contractions, whereas Clement (2, 3), Tallarida et al. (22), and ourselves used rhythmical twitch contractions.

In our experiments, both group III and IV muscle afferents were stimulated by rhythmic twitch contractions of the triceps surae muscles to tension levels similar to those which evoked an “exercise pressor reflex.” This reflex has been defined by Mitchell et al. (14) to consist of all the cardiovascular changes that serve to increase arterial pressure during muscular contraction. Although rhythmic twitch contractions do not precisely mimic any natural contraction that these muscles may perform, this maneuver may provide us with clues that allow speculation about the discharge properties of group III and IV muscle afferents. For example, the endings of the group III afferents that fired in synchrony with the rhythmic twitch contractions were likely to have been mechanoreceptors. On the other hand, the endings of the six group IV afferents that did not fire in synchrony with the rhythmic twitch contractions were unlikely to have been mechanoreceptors; instead, these group IV afferents may have been stimulated by the metabolic products of contraction. Last, the endings of the three group IV afferents that fired synchronously with each twitch for the first few seconds of contraction, but then fired irregularly during the rest of this maneuver, may have been sensitive to both mechanical and metabolic stimuli occurring in the working triceps surae.

Although several other groups of investigators have examined the responses of group III and IV muscle afferents to single twitch contractions of the triceps surae (7, 11, 18), we are, to our knowledge, the only investiga-
tors to have examined the responses of these afferents to a stimulus proved to reflexly increase arterial pressure and heart rate. Thus, when examining the effects of rhythmic contractions on the impulse activity of group III and IV afferents, we made sure that the triceps surae contracted to tension levels similar to those found to evoke reflex increases in arterial pressure and heart rate. Likewise, we made sure that this muscle group contracted with the same frequency and for the same time period as those found to evoke these reflex increases. These factors may explain why a greater proportion of group III and IV afferents were stimulated by muscular contractions in our experiments than were stimulated by this maneuver in the experiments of Ellaway et al. (7), Kniffki et al. (11), and Paintal (18).

Another explanation for the difference in proportion of muscle afferents stimulated by contraction may be due to the methods by which the afferents were selected. In this and previous reports (9, 10), we studied only those fibers whose endings could be located by probing their receptive fields in the triceps surae. Although this method of selection unequivocally identifies an afferent as having its ending in the triceps surae, it may exclude afferents whose endings are totally unresponsive to mechanical stimuli. On the other hand, Ellaway et al. (7), Kniffki et al. (11) and Paintal (18) seem to have accepted as triceps surae afferents all fibers that were discharged by electrically stimulating the gastrocnemius nerves. We chose not to use this latter method of selection because of our concern that the high current intensities needed to discharge group III and IV afferents would result in the spread of current from the gastrocnemius nerves to the tibial nerve, an effect which may result in the misidentification of tibial fibers as triceps surae afferents. It would not be surprising, therefore, that these wrongly identified tibial fibers, most of which were severed from their endings, were unresponsive to muscular contraction.

In our experiments, static contraction always evoked greater increases in both arterial pressure and heart rate than did rhythmic contractions. Three factors were likely to account for these effects. First, static contraction of the hindlimb muscles always generated more tension than did rhythmic contractions of these muscles. The discharge rates of group III afferents, whose stimulation reflexly increases cardiovascular function (21), has been shown to increase as the tension generated by muscular contraction increases (10). Second, the metabolic products of contraction were likely to accumulate to higher levels in statically working muscles than in rhythmically working muscles, because arterial blood flow to the former is decreased from resting levels, whereas flow to the latter is increased from resting levels (19). The accumulation of these metabolites within the statically contracting muscle is widely believed to stimulate the group III and IV muscle afferents evoking the exercise pressor reflex (14, 16). Third, static contraction was likely to have increased total peripheral resistance, whereas rhythmic contractions were likely to have decreased this variable. These changes in vascular resistance, induced by contraction, were likely to be caused by a mechanical hindrance to blood flow in the statically working muscles (1, 19) and by a metabolic vasodilation in the rhythmically working muscles (19).

In summary, we have shown that rhythmic twitch contractions of the hindlimb muscles is capable of reflexly increasing arterial pressure and heart rate. We have also shown that group III and IV afferents, whose activation reflexly increases cardiovascular function (13, 21) were stimulated by rhythmic contractions of the triceps surae muscles. These findings raise the possibility that the mechanical effect of muscular contraction is capable of discharging some group III and IV afferents to levels that reflexly increase cardiovascular function.

We thank James Jones for his expert surgical assistance and Jan Wright and Julee Waldrop for typing the manuscript.

This study was supported by National Heart, Lung, and Blood Institute Program Project Grant HL-06296, the American Heart Association, Texas Affiliate, and the Lawson and Rogers Lacy Research Fund in Cardiovascular Diseases. K. J. Rybicki and T. G. Waldrop were supported by National Heart, Lung, and Blood Institute Training Grant HL-07960.

Received 19 August 1983; accepted in final form 21 December 1983.

REFERENCES


