Comparison of the exercise pressor reflex between forelimb and hindlimb muscles in cats

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Hayashi, Naoyuki, Shawn G. Hayes, and Marc P. Kaufman. Comparison of the exercise pressor reflex between forelimb and hindlimb muscles in cats. Am J Physiol Regulatory Integrative Comp Physiol 281: R1127–R1133, 2001.—In thirteen cats anesthetized with α-chloralose, we compared the cardiovascular and ventilatory responses to both static contraction and tendon stretch of a hindlimb muscle group, the triceps surae, with those to contraction and stretch of a forelimb muscle group, the triceps brachii. Static contraction and stretch of both muscle groups increased mean arterial pressure and heart rate, and the responses were directly proportional to the developed tension. The cardiovascular increases, however, were significantly greater (P < 0.05) when the triceps brachii muscles were contracted or stretched than when the triceps surae muscles were contracted or stretched, even when the tension developed by either maneuver was corrected for muscle weight. Likewise, the ventilatory increases were greater when the triceps brachii muscles were stretched than when the triceps surae muscles were stretched. Contraction of either muscle group did not increase ventilation. Our results suggest that in the anesthetized cat the cardiovascular responses to both static contraction and tendon stretch are greater when arising from forelimb muscles than from hindlimb muscles.

EXERCISE is well known to increase cardiovascular and ventilatory function (20, 24). These effects are widely believed to be caused by two neural mechanisms, central command (27) and the exercise pressor reflex (17, 21). In animals the latter mechanism is usually studied by contracting a hindlimb muscle group, such as the triceps surae. The reason for this is that the triceps surae muscles are relatively large and accessible. Moreover, they are innervated by the L₂ and S₁ dorsal and ventral roots, which are easily identified, long, and, therefore, readily manipulated.

Implicit in the use of the triceps surae muscles to study the exercise pressor reflex is the assumption that the autonomic responses evoked by contraction of this hindlimb muscle group are similar to the responses evoked by contraction of a forelimb muscle group. Support for this assumption in studies on humans is equivocal. For example, some studies have reported that exercising upper limb muscles evoked similar or greater responses than did exercising lower limb muscles, even though the latter used a larger muscle mass than did the former (4, 10, 23, 25). In contrast, other studies have reported that exercising upper limb muscles evoked smaller responses than did exercising lower limb muscles, a difference that was attributed to differences in muscle mass (11, 22). Human studies such as these have not been able to separate the effects of muscle mass from those of the limbs. Moreover, these studies do not allow one to determine how much of the cardiovascular response to exercise was caused by central command and how much of the response was caused by a reflex arising from contracting muscle.

This conflicting and uncertain literature prompted us to compare the reflex cardiovascular and ventilatory responses to forelimb muscular contraction with those to hindlimb muscular contraction in anesthetized cats. This preparation allowed us to evoke the exercise pressor reflex in the absence of central command. Moreover, it allowed us to make this comparison at points where the ratio between tension development and muscle weight (i.e., mass) were equal.

METHODS

General. Adult cats (2.8–4.1 kg) were anesthetized with a mixture of halothane (5%) and oxygen. The trachea, a jugular vein, and a common carotid artery were cannulated. Anesthesia was maintained with α-chloralose (60 mg/kg iv). The gaseous anesthetic was gradually reduced over a 30-min period as the α-chloralose took effect. Supplemental doses of α-chloralose (5 mg/kg iv) were given every 30 to 60 min; the total amount of α-chloralose given to each cat was ~100 mg/kg. The cats spontaneously breathed room air. A Fleisch (no. 00) heated pneumotachograph was placed in series with the trachea cannula. The pneumotachograph was attached to a Validyne differential pressure transducer (DP45–24) to measure airflow. The carotid catheter was attached to a Statham (P23XL) transducer to measure arterial blood pressure. Heart rate was calculated beat by beat with a Gould Biotach. Airflow was integrated breath by breath to yield tidal volume, which in turn was used to calculate minute volume of ventilation. Arterial blood gases and pH were measured at 1-h intervals on a Radiometer blood gas analyzer.

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Blood gases and pH were maintained within normal limits by infusing sodium bicarbonate solution intravenously (1 M) or by adding oxygen to the trachea cannula. Body temperature was measured and maintained between 37°C and 38°C. The nerves supplying the ipsilateral triceps brachii and triceps surae muscles were exposed. The skin flaps overlying the two muscle groups were attached to brass bars to form space for pools, which were then filled with warm (37°C) mineral oil. All visible nerves, except for those innervating the triceps brachii and triceps surae muscles, were cut. The calcaneal (Achilles) tendon and the tendon attaching the triceps brachii to the elbow were cut and attached to force transducers (Grass FT 10), which in turn were attached to rack and pinions. The origins of the two muscle groups were left intact. Clamps were placed on the ankle and knee of the hindlimb; likewise clamps were placed on the elbow and shoulder of the forelimb. These clamps prevented all visible movement of these limbs during contraction.

Protocols. Our goal was to compare the pressor, cardioaccelerator, and ventilatory responses to contraction and stretch of a hindlimb muscle group, the triceps surae, with those to contraction and stretch of a forelimb muscle group, the triceps brachii. Contraction was induced by electrical stimulation of the nerves supplying the muscles (30–40 Hz; 0.025 ms; 3 times motor threshold). Although it was possible to stimulate the ventral roots innervating the triceps surae muscles, it was not possible to stimulate the ventral roots innervating the triceps brachii muscles. The ventral roots innervating the latter muscle group are in the cervical region and are too short to place on stimulating electrodes after they have been sectioned. We believed that our comparison was best served if we used the same technique to contract both muscle groups.

Three different intensities (i.e., developed tension) of contraction were evoked for each muscle group. Different intensities of contraction were obtained by varying either the frequency of pulses or the current applied to the nerves. An increase in current recruited additional motor units, whereas an increase in frequency caused the same number of motor units to contract more forcefully. Both methods were needed to match tension-to-weight ratios from the two muscle groups (see below). The site of stimulation was at or near the junction of the nerve (i.e., either tibial or brachial) with the muscle. To show that the responses to contraction were reflex in origin, we paralyzed the cat (vecuronium bromide; 0.1 mg/kg iv) and stimulated the nerves with the same frequency, pulse duration, and current intensity as when the cats were not paralyzed. In some instances, we also cut the nerves and stimulated the peripheral end with the same parameters as when the nerves were intact; this maneuver...

Fig. 1. Responses to static contraction of the triceps brachii muscles (●) and triceps surae muscles (○) plotted against the ratio of developed tension and muscle weight. *Increase in mean arterial pressure (MAP) or heart rate (HR) evoked by contraction of the triceps brachii muscles was significantly greater (P < 0.05) than corresponding increase evoked by contraction of triceps surae muscles. VE, minute volume of ventilation.

Fig. 2. Static contraction of the triceps surae muscles (hindlimb; left) evoked a smaller reflex response than did static contraction of the triceps brachii muscles (forelimb; right). Records are from the same cat. The pressor response to triceps brachii contraction was larger than that to triceps surae contraction even though the former developed less tension than did the latter. AP, arterial pressure; VT, tidal volume.
Effects of tendon stretch and static contraction after cutting the nerve supply to the hindlimb muscles.

Table 1. Baseline and peak values for pressor, cardioaccelerator, and ventilatory responses to static contraction and tendon stretch

<table>
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<tr>
<th>Limb</th>
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Values are means ± SE; n = no. of cats. MAP, mean arterial pressure; HR, heart rate; VE, minute volume of ventilation. Tensions are in g of tension development/g of muscle weight. HL, hindlimb (triceps surae muscles); FL, forelimb (triceps brachii muscles). * Peak value is significantly greater than corresponding baseline value (P < 0.05).

contracted the muscles but interrupted the connection between sensory innervation and the spinal cord.

Finally, we determined in three cats the maximal amount of tension that could be generated by the contracting muscles. We accomplished this by electrically stimulating the tibial and brachial nerves at levels that recruited supramaximally motor axons (i.e., 40 Hz; 0.5 ms; 10 times motor threshold). These stimulation parameters also activated the axons of group III afferents, and therefore the cardiovascular and ventilatory responses to this maneuver could not be attributed to static muscular contraction. Consequently, the cardiovascular and ventilatory responses from these three cats were discarded.

Tendon stretch was induced by turning a rack and pinion. We attempted to match the tension developed by stretch with that developed by contraction. Consequently, three different levels of stretch were initiated. To show that the responses to tendon stretch were reflex in origin, we cut the nerves supplying the muscles and repeated the maneuver. All tendon stretches and static contractions lasted for 60 s. At the end of each experiment, both the triceps surae and triceps brachii muscles were excised from the cat and weighed.

Data analysis. We plotted the change in each dependent variable (i.e., mean arterial pressure, heart rate, and minute volume of ventilation) against the ratio of the developed tension and the muscle weight. When this ratio is equal for two muscle groups, then equal muscle masses can be considered to be developing the same tensions. All values are expressed as the mean ± SE. Statistical significance was determined by a two-way, repeated-measures analysis of variance. Comparisons between individual means were done with Tukey’s post hoc tests. The criteria for significance was P < 0.05.

RESULTS

Using three levels of tendon development, we compared the exercise pressor reflex arising from the hind-

Table 2. Effect of electrical stimulation of the tibial nerve (3 times motor threshold) during paralysis and effects of tendon stretch and static contraction after cutting the nerve supply to the hindlimb muscles or the forelimb muscles on MAP, HR, and VE

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<tr>
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<td>5.4 ± 0.8</td>
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<td>201 ± 12</td>
<td>201 ± 12</td>
<td>230 ± 16</td>
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All values represent means ± SE; n = no. of cats. Contraction was induced by electrical stimulation (3 times motor threshold) of the cut peripheral ends of the tibial and brachial nerves, respectively. HL, triceps surae; FL, triceps brachii. None of the peak values were significantly different from their corresponding baseline values (P > 0.05).
limb (triceps surae muscles) with that arising from the forelimb (triceps brachii muscles). Likewise, using three levels of tendon stretch, we compared the muscle mechanoreceptor reflex arising from the hindlimb with that arising from the forelimb. Peak developed tension, regardless of whether the muscles were being contracted or stretched, did not exceed 7.4 kg. On average, the triceps surae muscles weighed 33.8 ± 3.1 g (n = 13), whereas the triceps brachii muscles weighed 19.7 ± 3.7 g (n = 13). Just before the start of the experiments arterial Po2, PCO2, and pH averaged 92.5 ± 3.2 mmHg, 39.0 ± 1.8 mmHg, and 7.36 ± 0.01, respectively (n = 13). In three cats, the maximal developed tension generated by the triceps surae muscles averaged 8.3 ± 0.2 kg; likewise, the maximal tension generated by the triceps brachii muscles averaged 3.1 ± 0.7 kg.

**Static contraction.** We found that static contraction of the forelimb muscles (triceps brachii) evoked larger pressor and cardioaccelerator responses than did static contraction of the hindlimb muscles (triceps surae). This was the case for each of the three levels of contraction tested (Figs. 1 and 2; Table 1). In contrast, both static contraction of the triceps brachii and static contraction of the triceps surae muscles had only trivial effects on minute volume of ventilation (Fig. 2; Table 1).

The triceps brachii muscles did not appear to fatigue more rapidly during the 60-s contraction period than did the triceps surae muscles. For example, at the highest level of contraction used in our experiments, the triceps surae developed 5.3 ± 0.5 kg of tension, a peak level that decreased to 3.5 ± 0.5 kg of tension 50 s into the contraction period. Percentage-wise, this decline averaged 66 ± 6% of the peak tension. In contrast, the triceps brachii developed 2.1 ± 0.2 kg of peak tension at the maximal level used and decreased to 1.3 ± 0.6 kg tension after 50 s of contraction. Percentage-wise, this decline averaged 61 ± 8% of the peak tension developed (P > 0.05).

In three cats paralyzed with vecuronium bromide (0.1 mg/kg iv), we stimulated the nerves supplying the triceps surae and triceps brachii muscles. The stimulus parameters before paralysis were the same as those during paralysis. Stimulation of the nerves during paralysis neither contracted the muscles nor evoked increases in arterial pressure, heart rate, and ventilation (Table 2). Likewise, in five nonparalyzed cats, we stimulated the peripheral cut ends of the nerves supplying the triceps surae and triceps brachii muscles. Stimulation of the nerves with the same parameters as when the nerves were intact had no effect on arterial pressure, heart rate, or ventilation, even though the muscles contracted statically (Table 2).

**Tendon stretch.** Stretching the tendon attached to the triceps brachii muscles evoked significantly larger pressor, cardioaccelerator, and ventilatory responses than did stretching the tendon attached to the triceps surae muscles (P < 0.05; Figs. 3 and 4; Table 1). This was the case for each of the three levels of tendon stretch tested (Fig. 3). Section of the nerves supplying both the triceps surae muscles and the triceps brachii muscles abolished the pressor, cardioaccelerator, and ventilatory responses to tendon stretch (Table 2).

**DISCUSSION**

We have shown that both static contraction and stretch of a forelimb muscle group, the triceps brachii, evoked larger reflex cardioaccelerator and pressor responses than did contraction and stretch of a hindlimb muscle group, the triceps surae. We also showed that
stretching the triceps brachii muscles evoked larger reflex ventilatory increases than did stretching the triceps surae muscles. In contrast, static contraction of either forelimb or hindlimb muscles in our experiments did not significantly increase ventilation, and consequently no comparison between the two muscle groups could be made.

An essential component of our comparisons was examining the responses to contraction and stretch when the ratio between tension development by the muscles and weight of the muscles was equal. Attempts to make such a comparison in humans would be difficult because one cannot precisely control the number of muscles being contracted. In addition, this type of study in humans would need to separate the contribution of the exercise pressor reflex from that of central command, a distinction that is also difficult to achieve.

We can only speculate about the factors causing forelimb skeletal muscles to generate larger reflex cardiovascular and ventilatory responses than hindlimb skeletal muscles. One important factor might be differences in the fiber type composition of the two muscle groups, both of which serve an extensor function. This composition, however, appears to be similar (1, 5, 6). Specifically, both muscle groups contain about the same percentages of fast-twitch glycolytic fibers (i.e., 15–20%). Not surprisingly, the two muscle groups displayed similar fatigue properties in our experiments. In addition, the triceps surae muscle group contains a pure slow-twitch muscle, the soleus (1), the analog of which in the triceps brachii is the medial head (6). Static contraction of the soleus muscle in cats and rabbits reflexly increases arterial pressure and heart rate (12, 28), whereas the reflex cardiovascular effect of contraction of the medial head of the triceps brachii muscles is not known.

Two other factors that might have caused this difference are the number of thin-fiber afferents supplying the two muscle groups and their central connections. The information concerning the number of group III and IV afferents in the triceps brachii and triceps surae muscles is sparse, therefore making any comparison between their sensory innervations difficult. Likewise, little information is available about the spinal connections of thin-fiber afferents innervating the triceps brachii muscles. In contrast, there is some information available about the spinal and supraspinal connections of thin-fiber afferents innervating the triceps surae muscles of cats (8, 9, 18, 19). However, without information about the spinal connections of triceps brachii afferents, a comparison is not possible.

Nevertheless, speculation as to how contraction of forelimb muscles evoked a larger exercise pressor reflex than did contraction of hindlimb muscles is possible. Specifically, anatomic studies have shown that cervical dorsal horn neurons display a much heavier projection to the ventrolateral medulla (i.e., lateral reticular nucleus) than do lumbar dorsal horn neurons (7, 26). This area of the brain stem is well known to be part of the circuitry comprising the exercise pressor reflex arc (2, 3, 13–15).

Our study has two important limitations, namely, the level of tension development during static contraction and tendon stretch, as well as the use of α-chloralose anesthesia. The tension developed by both muscle groups during contraction probably did not exceed 75% of their maximum. Consequently, our conclusion that contraction of the triceps brachii muscles evoked larger reflex effects than did contraction of the triceps surae muscles is limited to the levels of tension developed in our experiments. The use of α-chloralose anesthesia probably explains the relatively low levels of minute ventilation reported in our experiments. Nevertheless, these levels were able to maintain arterial blood gases at normal values. Furthermore, our use of α-chloralose anesthesia in combination with moderate to low levels of tension development during contraction and tendon stretch was probably the cause of the modest responses to these stimuli.

Assessing the cardiovascular and ventilatory responses to contraction of the two muscle groups in terms of percentage of maximal tension development

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**Fig. 4.** Stretching the triceps surae muscles (hindlimb; left) evoked less of a reflex response than did stretching the triceps brachii muscles (forelimb; right). Tension developed by stretching the triceps brachii muscles was less than that developed by stretching the triceps surae muscles.
might be viewed as a useful method of interpreting our data. Indeed, rough calculations based on the maximal tension development cited in RESULTS suggest that converting our data to percentage of maximal tension development cannot explain our finding that contraction of the triceps brachii muscles evoked greater responses than did contraction of the triceps surae muscles. Nevertheless, this method of data interpretation should be viewed with caution because it is based on maximal tension levels obtained from one group of cats, and the cardiovascular and ventilatory responses to contraction were obtained from another group of cats. We have often observed marked differences in the maximal tension evoked by nerve stimulation from the same muscle group in different cats.

In conclusion, previous studies in humans that have examined the cardiovascular responses to exercise have had difficulty distinguishing the effect of muscle mass from that of the particular limb muscles being contracted. In addition, these studies have had difficulty distinguishing the effect of central command from that of the exercise pressor reflex (4, 10, 11, 22, 23, 25). Using an anesthetized cat preparation, we have provided evidence that forelimb muscles generate larger reflex responses to static contraction than do hindlimb muscles when the amount of muscle mass is controlled.

Perspectives

Our findings have challenged the assumption that static contraction of muscles of equal masses and to equal tensions generates similar, if not identical, pressor reflex responses. We speculate that the difference between the pressor reflexes arising from contraction of the two muscle groups was caused by differences in the central neural circuitries of the two reflex arcs. The physiological significance of evoking a larger pressor reflex from static contraction of forelimb muscles than from static contraction of hindlimb muscles is unclear. Nevertheless, our findings highlight the point that the central neural integration of the exercise pressor reflex is complex, with thin-fiber inputs from various muscles being summed in a nonalgebraic manner. The most likely sites for such nonalgebraic summation are the dorsal horn of the spinal cord (9) and the ventrolateral medulla (14, 16).

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