Is the blood flow response to a single contraction determined by work performed?

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**Hamann, Jason J., John B. Buckwalter, Philip S. Clifford, and J. Kevin Shoemaker.** Is the blood flow response to a single contraction determined by work performed? *J Appl Physiol* 96: 2146–2152, 2004. First published February 6, 2004; 10.1152/japplphysiol.00779.2003.—Nine healthy volunteers performed a series of single handgrip isometric contractions to test the hypothesis that the blood flow response to a contraction is determined solely by the tension-time index (isometric analog of work). Contractions were performed in duplicate at 15, 30, and 60% of maximal voluntary contraction (MVC) at durations of 0.5, 1, and 2 s. Forearm blood flow (FBF) was measured beat by beat by using Doppler ultrasound. Peak FBF responded in a graded fashion to graded increases in peak tension with contraction time held constant (35, 56, and 90 ml/min for 15, 30, and 60% MVC for 1 s, respectively). When tension was kept constant, peak FBF responded in a graded fashion to graded increases in duration (77, 90, and 97 ml/min for 60% MVC for 0.5, 1, and 2 s). With a constant tension-time index, peak FBF responded in a graded fashion to graded increases in peak tension (48, 56, and 77 ml/min for 60% MVC for 0.5, 1, and 2 s). Similar trends were also observed for total postcontraction hyperemia. Blood flow increased regardless of whether the change in tension-time index was accomplished by an increase in tension or duration of contraction. However, with a constant tension-time index, the change in blood flow was related to the peak tension developed. Our results suggest that the blood flow response to a single muscle contraction is not determined solely by the work performed (tension-time index) but also by the number of muscle fibers recruited.

**METHODS**

**Subjects.** Nine healthy subjects (6 men, 3 women) participated in this study. The mean age of the subjects was 33 ± 9 (SD) yr, height was 177 ± 7 cm, and weight was 77 ± 14 kg. Subjects were informed of all testing procedures and any risks and discomforts associated with testing before giving their informed consent to participate. The University of Western Ontario Ethics Board for research on human subjects approved all procedures.

**Protocol.** Subjects were studied in the supine position, with the arm maintained at heart level. Static handgrip contractions were performed on a dynamometer instrumented with a force transducer. Two maximal voluntary contractions (MVCs) were performed, the largest of which was used to determine the relative intensity of all other contractions used during the protocol. During the test, subjects performed single handgrip contractions at 15, 30, and 60% of MVC with the target force displayed on an oscilloscope. Contractions were performed for durations of 0.5, 1, and 2 s and were followed by a 2-min recovery period. Subjects performed a minimum of two contractions at each exercise intensity.

Each subject performed three series of contraction protocols. In series 1, muscle tension was graded (15, 30, and 60% MVC) with contraction duration held constant at 1 s. During series 2, the muscle tension was graded (15, 30, and 60% MVC) while contraction duration (2, 1, and 0.5 s) was manipulated to maintain a constant TTI. For series 3, muscle tension was held constant at 60% MVC while the contraction duration was graded (0.5, 1, and 2 s). The order of the contraction series was varied across subjects, and the order of contractions within each series was randomly assigned.

**Measurements.** Mean arterial pressure (MAP) was measured continuously by finger-cuff plethysmography (Finapres, Ohmeda) on the middle finger of the nonexercising hand that was maintained at heart level. Heart rate was monitored continuously by an electrocardiogram. Muscle electromyogram (EMG) was obtained through the use of adhesive Ag-AgCl electrodes placed on the forearm. Raw EMG signal

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**DURING DYNAMIC EXERCISE, SKELETAL muscle blood flow is tightly coupled to the level of muscle activity. This coupling is evidenced by the direct relationship between the increase in muscle blood flow and increased contraction frequency (21), increased running speed (2, 17), and increased muscle oxygen consumption (3, 24). Despite evidence for a tight coupling of muscle blood flow with metabolic demand of the tissue during dynamic exercise, the factors controlling the blood flow response to a single muscle contraction have not been well elucidated.**

A protocol employing a single, brief contraction permits evaluation of the blood flow response unhindered by the potentially confounding effects of subsequent contractions or reflex effects on blood pressure. It is known that, after a single muscle contraction, there is an immediate and rapid increase in blood flow (27, 35, 37), the magnitude of which is related to the strength of the contraction (1, 4, 20). It has been postulated that the magnitude of blood flow response following contractions of different strengths is related to either the number of muscle fibers recruited (1) or the product of the tension and duration of contractions (20).

In the present study, we sought to examine the blood flow response to single contractions when tension and contraction time were independently manipulated. These manipulations were intended to help clarify the separate influences of fiber recruitment and work performed on the blood flow response to contraction. We hypothesized that the peak blood flow response and total postcontraction hyperemia after a brief contraction of the human forearm would be determined by the tension-time index (TTI; isometric analog of work). If this were the case, then the blood flow response should be independent of the number of muscle fibers recruited.

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was rectified, filtered (0.2–7.0 kHz), and averaged. Brachial artery mean blood velocity (MBV) was measured beat by beat with Doppler ultrasound (GE/Vingmed System Five, 5 MHz). All analog signals were recorded in real time at 100 Hz (PowerLab, ADInstruments) and stored on a computer for subsequent analysis. Brachial artery diameter was measured by using B-mode echo imaging (GE/Vingmed System Five, 10 MHz) with measures made in triplicate at rest before commencement of the protocol. It was presumed that no change in diameter would occur after a single contraction because previous studies (34, 38) showed no changes within the first 30 s of repeated moderate- or high-intensity contractions.

Calculations. The beat-by-beat MBV and MAP data for each contraction were averaged for each subject to obtain a representative response for each exercise intensity. Beat-by-beat forearm blood flow was calculated as the product of MBV and the vessel cross-sectional area (πr²), where r is the vessel radius. The blood flow data were analyzed in two ways. The peak blood flow response was determined as the peak blood flow after contraction minus the baseline blood flow. Total postcontraction hyperemia was calculated by integrating the blood flow response for 30 s after the release of the contraction minus the baseline blood flow.

Data analysis. Differences in responses across contraction intensities for all variables measured (peak blood flow, total postcontraction hyperemia, MAP, EMG, and TTI) were determined by a repeated-measures one-way ANOVA. An α level of ≤0.05 was used to determine statistical significance in all cases. Data are presented as means ± SE.

RESULTS

Data for TTI with each series are presented in Table 1. As planned, stepwise increases in muscle tension with contractions of similar duration resulted in stepwise increases in the TTI as shown under series 1. When muscle tension was increased in a graded fashion with a concomitant decrease in contraction duration to maintain a constant TTI the 60% MVC/0.5-s contraction resulted in a reduced TTI compared with the other contractions within series 2 (P ≤ 0.05). In series 3, contractions of similar muscle tension (60% MVC) with graded increases in contraction duration produced graded increases in TTI.

Table 1 also presents the mean EMG data for each series. Within series 1, mean EMG activity was not different between contractions of low muscle tension but was augmented with contractions of high muscle tension. During contractions of similar TTI (series 2), graded increases in muscle tension produced mean EMGs that were different only between the lowest and highest muscle tensions. Mean EMG activities were not different among contractions of similar muscle tension (series 3).

Figure 1 is composed of original tracings of the blood flow and tension response to static handgrip contractions obtained during series 1 for one subject. It can be seen from this figure that after a brief contraction blood flow rapidly increased to a peak and then gradually declined back to the resting level within ~30 s. This figure also reflects the intensity-dependent nature of the blood flow response to static handgrip contractions.

Figures 2A, 3A, and 4A summarize the change in peak blood flow for each contraction in series 1, 2, and 3, respectively. As expected (4, 20, 27), in series 1 (Fig. 2A), the change in peak blood flow increased in a graded fashion with contractions of graded muscle tension and TTI (35 ± 8, 56 ± 8, 90 ± 14 ml/min). When muscle tension was graded from 15 to 60% MVC and contraction duration was manipulated to maintain a constant TTI (series 2), the change in peak blood flow (Fig. 3A) was not different between contractions of low muscle tension (48 ± 7 and 56 ± 8 ml/min). However, even under conditions

Table 1. Arterial pressure and contraction indexes for muscle contraction in series 1, 2, and 3

<table>
<thead>
<tr>
<th></th>
<th>15% MVC/1 s</th>
<th>30% MVC/1 s</th>
<th>60% MVC/1 s</th>
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<tbody>
<tr>
<td>Arterial pressure, mmHg</td>
<td>97.2 ± 3.2</td>
<td>99.8 ± 3.6</td>
<td>98.7 ± 3.6</td>
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<tr>
<td>Tension-time index, %MVC's</td>
<td>11.6 ± 0.5</td>
<td>24.0 ± 0.8</td>
<td>48.3 ± 3.7</td>
</tr>
<tr>
<td>Mean EMG, %maximum</td>
<td>18.7 ± 6.1</td>
<td>26.5 ± 2.9</td>
<td>60.0 ± 16.7</td>
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</tbody>
</table>

*Significantly different from lowest intensity in series, P < 0.05. †Significantly different from middle intensity in series, P < 0.05.

Values are means ± SE. MVC, maximal voluntary contraction; EMG, electromyogram.
of constant TTI, the change in peak blood flow was significantly augmented with the highest muscle tension (77 ± 10 ml/min). In series 3, when muscle tension was held constant at 60% MVC and contraction duration was extended from 0.5 to 2 s, the longer contraction durations resulted in significantly greater changes in blood flow (77 ± 10 vs. 90 ± 14, 97 ± 13 ml/min, Fig. 4A). Analysis of the time course for the blood flow response revealed that blood flow increased within 1 s after the release of contraction under all conditions. The mean times to peak blood flow ranged from 2.8 ± 0.3 to 4.1 ± 0.3 s (Table 2).

The mean total postcontraction hyperemia values for each contraction for series 1, 2, and 3 are depicted in Figs. 2B, 3B, and 4B, respectively. As demonstrated in Fig. 2A for change in peak blood flow, total postcontraction hyperemia (Fig. 2B) was also intensity dependent with contractions of increasing tension and TTI (5.4 ± 1.4, 8.7 ± 1.7, and 14.8 ± 2.5 ml). When the total postcontraction hyperemia is compared across contractions of similar TTI (series 2, Fig. 3B), the 60% MVC/0.5-s contraction had a significantly enhanced total postcontraction hyperemia over the contractions of lower muscle tension (7.5 ± 1.5 and 8.7 ± 1.7, vs. 11.5 ± 2.0 ml). After contractions of similar tension (series 3), the total postcontraction hyperemia (Fig. 4B) showed a trend for greater total postcontraction hyperemia with greater contraction duration (11.5 ± 2.0, 14.8 ± 2.5, and 20.3 ± 3.1 ml) with significantly greater total postcontraction hyperemia at 60% MVC/2 s compared with the shorter durations.
DISCUSSION

The purpose of this study was to determine the separate influences of fiber recruitment and TTI (isometric analog of work) on the blood flow response to brief contractions. This study provides new evidence showing that the blood flow response to a single muscle contraction is not determined solely by the work performed. When TTI was held constant, there were increments in blood flow related to the degree of muscle fiber recruitment as determined by EMG. Thus the number of muscle fibers recruited contributes independently to changes in blood flow.

It is well known that there is a linear relationship between oxygen consumption and workload during dynamic exercise. In addition, there is a tight coupling of muscle blood flow to this level of muscle activity (2, 3, 17, 21, 24) that is thought to subserve the increased metabolic demand for oxygen. Al-though these relationships exist for dynamic exercise, there is scant evidence describing the relationship of muscle work to the blood flow response to a single muscle contraction. We questioned whether muscle work was the sole determinant of the hyperemic response to a single contraction.

Using strain gauge plethysmography, Corcondilas et al. (4) investigated the blood flow response of the human forearm to short-duration (0.3 s) contractions of varying tension. Under conditions of similar contraction duration, the increase in blood flow was linearly related to the tension produced. Similar results have been presented for contractions evoked by electrical stimulation of the dog hindlimb (27). Stimulation of the motor nerve for 1 s at graded intensities elicited graded increases in blood flow that were related to the intensity of the contraction. Data from series 1 of the present investigation replicate the findings of the above-mentioned experiments and bolster the idea that blood flow responds in a stepwise fashion to increases in developed tension. However, because both muscle tension and work increased under the conditions of these studies, it cannot be determined whether the blood flow response is determined by the tension developed (fiber recruitment) or the work performed.

There is evidence to support fiber recruitment as a determinant of the blood flow response to contraction. Anrep and von Saalfeld (1) measured the blood flow response to brief tetanic contractions of the gastrocnemius muscle of the dog. Electrical stimulation of the whole motor nerve produced a blood flow response of greater magnitude and lasted for a longer period of time with increasing stimulation strength (Fig. 4b of Ref. 1). These data led them to conclude that the hyperemic response after muscle contraction is related to the strength of the stimulus, and they postulated that the vasodilation that follows a contraction is dependent on the number of muscle fibers involved. Motor unit recruitment has also been implicated in facilitating the vasodilatory response observed during rhythmic contractions of the hamster retractor muscle (39).

Alternatively, muscle work may be the primary determinant of the hyperemic response to a single muscle contraction. Besides corroborating the findings of Corcondilas et al. (4) that blood flow increases linearly with muscle tension, Lind and Williams (20) demonstrated that blood flow also increases linearly with the duration of the contraction when muscle tension is held constant. More importantly, when muscle tension was produced in a square-wave, ramp-up or ramp-down fashion for a given duration, the blood flow response was not determined by the peak tension produced. In fact, for any given peak tension, the blood flow after the ramp contractions was

Table 2. Delay from release of contraction to peak blood flow

<table>
<thead>
<tr>
<th>Workload</th>
<th>Time to Peak/s</th>
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<tbody>
<tr>
<td>15% MVC/1 s</td>
<td>2.8±0.3*</td>
</tr>
<tr>
<td>15% MVC/2 s</td>
<td>2.9±0.2*</td>
</tr>
<tr>
<td>30% MVC/1 s</td>
<td>3.2±0.2</td>
</tr>
<tr>
<td>60% MVC/0.5 s</td>
<td>3.0±0.2*</td>
</tr>
<tr>
<td>60% MVC/1 s</td>
<td>3.4±0.2</td>
</tr>
<tr>
<td>60% MVC/2 s</td>
<td>4.1±0.3</td>
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Values are means ± SE. *Significantly different from 60% MVC/2 s, P < 0.01.
similar to square-wave contractions of one-half that tension. This finding points to the amount of work performed and not the peak tension developed as the factor influencing the blood flow response. These data support the conjecture that muscle work is the primary determinant of the blood flow response to a single contraction.

In the present investigation, blood flow increased in a graded fashion with contractions of graded muscle fiber recruitment and work (TTI, series 1). However, when the work was held constant, there were increments in blood flow related to the degree of muscle fiber recruitment (series 2), suggesting that work alone does not determine the magnitude of the hyperemia. In addition, under conditions of similar fiber recruitment, there was only a modest (27%) change in blood flow with a fourfold increase in work in series 3, whereas a fourfold increase in work in series 1 elicited a 153% increase in blood flow. In series 1, both work and fiber recruitment were allowed to change. Thus this difference in the magnitude of the blood flow increase reflects the influence of fiber recruitment on the blood flow response and demonstrates that the fiber recruitment contributes to the magnitude of the blood flow response to contraction. The present data support previous findings showing that fiber recruitment in and of itself can promote vasodilation (39).

Although the specific mechanism was not investigated in the present study, it is appropriate to consider how fiber recruitment might influence muscle blood flow. A traditional view with which to explain the enhanced blood flow response with greater fiber recruitment centers on the metabolic theory of blood flow control. The metabolic theory of blood flow control postulates that skeletal muscle fibers govern their own blood flow through the release of vasoactive metabolites released in accordance with the metabolic demand of the tissue. However, one would estimate that the time required for metabolite production, accumulation, and diffusion makes metabolic vasodilation too slow to account for the initial contraction-induced hyperemia. Although the metabolic theory has focused on the vasoactive properties of metabolites, it is possible that the substance(s) responsible for initiating the blood flow response to contraction is related to contraction, but it is not a metabolically produced substance. For example, muscle fibers release potassium ions during activation (9, 12, 25), and an increased number of recruited muscle fibers would be expected to release more potassium ions. Another possible mechanism to explain the influence of fiber recruitment on blood flow is that with greater fiber recruitment a larger portion of the vascular bed undergoes mechanical compression. Deformation of the vascular wall has been shown to result in release of vasoactive substances that cause vasodilation (13, 15, 28).

In the preceding paragraph, we postulated that substances released from the muscle or endothelium can elicit dilation of terminal arterioles. It should be recognized that the full expression of exercise hyperemia requires dilation of more than just terminal arterioles (32). Feed arteries must dilate, yet they are located outside of the muscle parenchyma and thus out of the direct influence of substances released from contracting muscle. One mechanism by which vasomotor responses can be coordinated within a vascular network is conducted vasodilation (31), whereby dilation initiated at one point in the vasculature can ascend along the vessel wall. This mechanism may be important for blood flow control during exercise (30). Another potential mechanism for transmitting vasodilation throughout the vasculature is flow-mediated dilation. As a consequence of downstream dilation, there is increased flow through proximal segments that evokes dilation via an endothelial-mediated response to increased shear stress (14, 29). Regardless of the initiating stimulus, conducted vasodilation and/or flow-mediated vasodilation are likely to be essential for coordinating the response of the skeletal muscle vascular bed to contraction, although the involvement of these mechanisms in the blood flow responses to brief contractions in this study cannot be ascertained.

We observed an increased blood flow within 1 s after the release of contraction. Can this represent an immediate and rapid vasodilation? There is conflicting evidence regarding the latency to vasodilation in directly observed arterioles after muscle contraction. Marshall and Tandon (23) observed vasodilation of terminal arterioles within 2 s of contraction. However, Gorczynski et al. (7) and Jacobs and Segal (10) report a delay of 5–20 s depending on vessel size. A delay in arteriolar vasodilation has also been inferred from the finding that capillary red blood cell velocity increased within 1–2 s with only a modest change in red blood cell flux (11). Wunsch et al. (40) recently examined the time course of vasodilation of cannulated first-order arterioles to four different vasodilators: adenosine, acetylcholine, potassium, and nitroprusside. All the dilators displayed a minimum 4-s delay to vasodilation, which led them to conclude that none of these substances produced vasodilation rapid enough to contribute to the initial increase in blood flow after muscle contraction. There are two points worthy of note. First, the latency observed by Wunsch et al. is a much slower response than observed after intra-arterial injection of the same vasodilators in vivo (J. J. Hamann, unpublished results). Second, it is possible that the vasodilators that are responsible for the immediate and rapid contraction-induced vasodilation were not utilized in their investigation.

The time course of vasodilation after muscle contraction in situ studies has been used to support the idea that the skeletal muscle pump initiates the increase in blood flow after muscle contraction. The muscle pump is believed to aid muscle perfusion by emptying the venous circulation within the muscle during contraction, which results in a lowered venous pressure during relaxation (16, 33). Whether venous pressures drop to the magnitude required to produce the degree of blood flow attained after muscle contraction is not known. The strongest evidence in support of the muscle pump comes from investigations in which resting venous pressures were manipulated by positioning of the exercising limb. Leg blood flows were higher in human subjects exercising in a head-up compared with a supine posture (6, 19). Similarly, forearm blood flow was higher during contraction when the arm was positioned below the heart (35, 37). However, other investigations have failed to support the ability of the muscle pump to increase blood flow (5, 18, 22, 26). In addition, recent data from our laboratory (8) demonstrated that the putative contraction-induced decrements in venous pressure were incapable of enhancing blood flow through the muscle. Despite controversy over the muscle pump concept, it is interesting to speculate.
how fiber recruitment might affect the muscle pump. In the present investigation, we observed increments in blood flow related to the degree of muscle fiber recruitment. It is possible the greater fiber recruitment in this investigation augmented the mechanical compression of the intramuscular veins and venules and enhanced the effectiveness of the skeletal muscle pump.

There are several advantages to our experimental approach. First, blood flow to the human forearm was assessed continuously with Doppler ultrasound. This noninvasive approach enabled us to follow the time course of changes in response to contraction. Second, the blood flow response to contraction was observed immediately after a brief single contraction in which there was no confounding effect of a follow-up contraction on the blood flow response. Third, a single contraction of the human forearm does not elicit alterations in arterial blood pressure and consequent reflex effects. Fourth, EMG activity was measured to determine the proportion of muscle fibers recruited during each contraction (36).

It must be acknowledged that the goal of series 2 of the present investigation was to maintain a constant TTI across the three contractions, and this goal was not fully realized. As shown in Table 1 for series 2, the TTI in the 60% MVC/0.5-s contraction was significantly lower than the other two contractions in this series. If the blood flow response to contraction is determined solely by the TTI, then the blood flow should have been attenuated with the reduced TTI. However, as shown in Fig. 3, the blood flow response was significantly greater after the 60% MVC/0.5-s contraction despite the reduced TTI. If the TTI would have been similar across contractions of series 2, it would be expected that the blood flow response to the 60% MVC/0.5-s contraction would have been enhanced. This would have accentuated the finding that fiber recruitment plays a role in determining the blood flow response to a single contraction.

In conclusion, this investigation provides new evidence showing that the blood flow response to a single muscle contraction is not determined solely by the work performed (TTI). Our results suggest that muscle fiber recruitment contributes independently to changes in blood flow.

GRANTS

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REFERENCES


