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Effects of epinephrine and lactate on the increase in oxygen consumption of nonexercising skeletal muscle after aerobic exercise

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Abstract. The purpose of this study was to measure O_2 consumption of nonexercising skeletal muscles ($\dot{V}O_{2nonex}$) at rest and after aerobic exercise and to investigate the stimulant factors of O_2 consumption. In experiment 1, we measured the resting metabolic rate of the finger flexor muscles in seven healthy males by ^{31}P-magnetic resonance spectroscopy during a 15 min arterial occlusion. In experiment 2, the $\dot{V}O_{2nonex}$ of the finger flexor muscles was measured using near infrared continuous wave spectroscopy at rest, immediate postexercise, and 3, 5, 10, 15, and 20 min following a cycling exercise at a workload corresponding to 50% of peak pulmonary O_2 uptake for 20 min. We also monitored deep tissue temperature in the $\dot{V}O_{2nonex}$ measurement area and determined catecholamines and lactate concentrations in the blood at rest and immediate postexercise. $\dot{V}O_{2nonex}$ at rest was 1.1 ± 0.1 μM O_2/s (mean $\pm$ standard error) and $\dot{V}O_{2nonex}$ after exercise increased $59.6 \pm 7.2\%$ ($p < 0.001$) from the resting values. There were significant correlations between the increase in $\dot{V}O_{2nonex}$ and the increase in epinephrine concentration ($p < 0.01$), and between the increase in $\dot{V}O_{2nonex}$ and the increase in lactate concentration ($p < 0.05$). These results suggest that epinephrine and lactate concentrations are important $\dot{V}O_{2nonex}$ stimulant factors. [S1083-3668(00)00304-X]

Keywords: near infrared spectroscopy, muscle O_2 consumption, catecholamines, lactate, muscle temperature.

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1 Introduction

Nonexercising muscles play various important roles during exercise, such as the regulation of blood flow, and glucose and lactate metabolism.[1–3] Furthermore, considering the large size of the inactive muscle mass, we cannot disregard the potential metabolic changes in the case of exercises such as walking and cycling.

In recent studies,[4,5] it has been reported that near infrared continuous wave spectroscopy (NIR_{cws}) is very useful for the evaluation of muscle metabolism. Muscle oxygenation level monitored by NIR_{cws} represents a dynamic balance between O_2 supply and O_2 consumption. NIR_{cws}, therefore, has been used to measure muscle O_2 consumption as the initial rate of decline of the muscle oxygenation level during arterial occlusion reflects the muscle O_2 consumption.[5]

Recently, moderate aerobic exercise (~50% of aerobic capacity) has been recommended in exercise therapy for health promotion and to treat different kinds of disease.[6] Although research has been conducted on the effect of aerobic exercise from many angles, until now there have been few studies on the changes in nonexercising muscle metabolism during aerobic exercise. The purpose of the present study, therefore, was to noninvasively measure oxygen consumption of nonexercising skeletal muscle ($\dot{V}O_{2nonex}$) by NIR_{cws} at rest and after aerobic exercise and to investigate the stimulant factors on oxygen consumption.

2 Methods

We tested the left finger flexor muscles of seven healthy males (age, 28.6 ± 0.8; peak pulmonary O_2 uptake, 44.8 ± 1.5 ml/kg/min). We chose the upper extremities as our measurement site because they could be kept at a resting state during a cycling exercise. We measured the resting muscle metabolic rate in experiment 1 and the changes in O_2 consumption of nonexercising muscle in experiment 2.

In experiment 1, we measured the resting metabolic rate of the finger flexor muscles using ^{31}P-magnetic resonance spectroscopy (^{31}P-MRS; Otsuka Electronics Inc., 2.0 T superconducting 26 cm bore magnet, 3-cm-diam circular two-turn surface coil).[5] The metabolic rate was calculated from the phosphocreatine (PCr) breakdown rate after complete oxygen depletion during a 15 min arterial occlusion.[5,7] Because the

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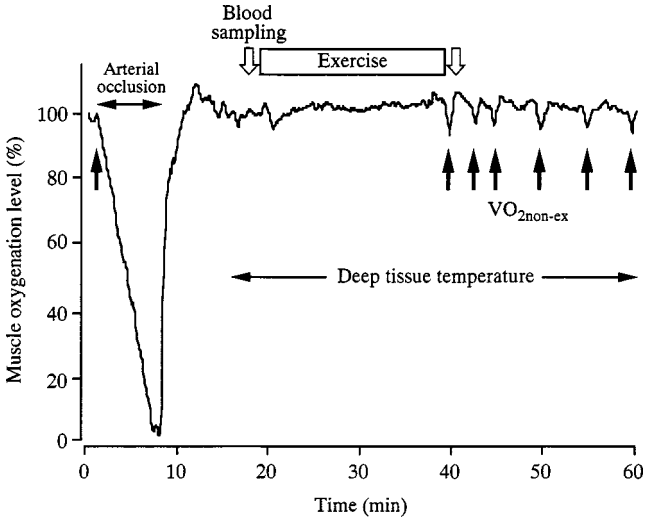

Fig. 1 Schematic representation of experimental protocol of experiment 2 and typical changes in muscle oxygenation level of nonexercising muscle. Exercise performed was a cycling exercise at a workload corresponding to 50% of peak pulmonary O_2 uptake for 20 min. $\dot{V}O_{2nonex}$, O_2 consumption of nonexercising muscle.

P-to-O_2 ratio *in vivo* skeletal muscle is 6, the resting muscle O_2 consumption was calculated by dividing the resting PCr breakdown rate in millimolar adenosine triphosphate per second (mM ATP/s) by 6, resulting in μM O_2/s. In this study, arterial occlusion was used to interrupt arterial blood flow by placing a pneumatic tourniquet on the upper arm at a pressure of 300 mmHg.

In experiment 2, the subjects performed a 20 min cycling exercise at a workload corresponding to 50% of peak pulmonary O_2 uptake in the laboratory, which was maintained at 22–24°C. The left upper extremities were kept at a resting state in the upright position on a hand rest while the subjects exercised. Electromyographic records confirmed the lack of significant contractile activity in the finger flexor muscles. The changes in the oxygenation level of the finger flexor muscles were monitored continuously at rest, including 6–8 min of arterial occlusion, during exercise, and for 20 min following exercise using NIR_{cws} (HEO-100, OMRON Inc.; a 3 cm separation between light source and detector)[5,8] (Figure 1). The parameters measured by NIR_{cws} were oxy-hemoglobin (HbO_2) and total hemoglobin. We defined changes in HbO_2 as the muscle oxygenation level. Muscle oxygenation level represents a dynamic balance between O_2 supply and O_2 consumption. Therefore, the initial rate of decline of the muscle oxygenation level during an arterial occlusion reflects the muscle O_2 consumption.[5] The values of $\dot{V}O_{2nonex}$ at rest, immediate postexercise, and 3, 5, 10, 15, and 20 min following exercise were determined by the rate of decline of the muscle oxygenation level during 20 s of arterial occlusion. The initial rate of decline at rest indicates the resting $\dot{V}O_{2nonex}$ as calibrated with the resting PCr breakdown rate obtained in experiment 1. The $\dot{V}O_{2nonex}$ values during the recovery periods were expressed relative to the slope of $\dot{V}O_{2nonex}$ at rest. Parameters measured by NIR_{cws} are relative values and are expressed as arbitrary units. Absolute O_2 concentration or saturation determination is impossible because of unquantifiable parameters such as optical path length. Therefore, we determined the functional anoxic condition by using arterial occlusion so as to obtain a physiological calibration to reduce individual variation. The muscle oxygenation level at rest was defined as 100% and the minimum value during arterial occlusion as 0%.

We also monitored deep tissue temperature (T_D) in the same area in which we measured the $\dot{V}O_{2nonex}$ from the resting state to 20 min following exercise by using a deep temperature monitor (CORETEMP: CTM-205, Terumo, Japan).[9] When a deep temperature monitor is utilized to determine T_D, the skin surface is covered with thermal insulation probe using the electronic servo-control system (zero-heat-flow method) protecting the skin surface from the effects of the outside air temperature. Thus, the surface temperature under such conditions is considered to be equal to the deep tissue temperature. Therefore, a simple surface temperature measurement can be taken to determine the deep tissue temperature. In this study, the temperature monitor probe, which is 3 cm in diameter, was placed over a region of the finger flexor muscles, near the NIR_{cws} probe. The depth into the tissue of the measurement area was approximately equal to half of the diameter. Thus, because the depth was 1.5 cm, it can be presumed that the temperature was that of the forearm muscles.

Furthermore, at rest and immediate postexercise blood samples from the intermediate cubital vein were drawn directly for determination of epinephrine, norepinephrine, and lactate concentrations. Plasma epinephrine and norepinephrine concentrations were analyzed by the diphenylethylenediamine method (HLC-8030, TOSOH, Japan). Plasma lactate concentration was analyzed by the lactate oxidase method (Hitachi 7170 automatic analyzer, Hitachi, Japan).

Student's t-test for paired observations was used to compare the resting value with the postexercise value. Statistical significance was accepted at $p<0.05$. All values were presented as means±standard error (SE).

3 Results

The resting PCr breakdown rate obtained in experiment 1 was 0.0068 ± 0.0005 mM ATP/s on average among the seven subjects. The resting $\dot{V}O_{2nonex}$ calculated from the resting PCr breakdown rate was $1.1\pm0.1\,\mu$M O_2/s (Table 1). The $\dot{V}O_{2nonex}$ increased ($p<0.05$) after exercise and began to gradually decrease towards the resting levels after 5 min of recovery. The peak $\dot{V}O_{2nonex}$ of each subject after exercise increased $59.6\pm7.2\%$ ($p<0.001$) from their respective resting values. Each of the parameters obtained from the blood samples increased, $147.7\pm20.5\%$ ($p<0.01$) in epinephrine, $39.4\pm12.6\%$ ($p<0.05$) in norepinephrine, and $191.4\pm64.9\%$ ($p<0.01$) in lactate, from their respective resting values (Table 1). T_D increased 0.8°C ($p<0.01$) after exercise and did not change remarkably during the recovery period. The relationships between the increase in $\dot{V}O_{2nonex}$ and the increase in epinephrine, norepinephrine, lactate, and T_D are shown in Figure 2. There were significant correlations between the increase in $\dot{V}O_{2nonex}$ and the increase in epinephrine concentration ($r^2=0.814$; $p<0.01$), and between the increase in $\dot{V}O_{2nonex}$ and the increase in lactate concentration (r^2

Table 1 $\dot{V}O_{2nonex}$, T_D, and epinephrine, norepinephrine, and lactate concentrations in the blood at rest and during postexercise recovery period.

		Postexercise					
	Rest	0 min	3 min	5 min	10 min	15 min	20 min
$\dot{V}O_{2nonex}$, $\mu MO_2/s$	1.1±0.1	1.5±0.1[a]	1.5±0.1[a]	1.5±0.2	1.2±0.1	1.2±0.2	1.1±0.1
T_D, °C	34.7±0.4	35.4±0.3[a]	35.5±0.3[b]	35.5±0.3[b]	35.5±0.3[b]	35.5±0.3[b]	35.5±0.3[a]
Epinephrine, ng/mL	0.04±0.01	0.09±0.01[b]					
Norepinephrine, ng/mL	0.57±0.05	0.78±0.09[a]					
Lactate, mg/dL	10.7±1.7	25.9±2.9[b]					

Exercise performed was a cycling exercise at a workload corresponding to 50% of peak pulmonary O_2 uptake for 20 min. Values are means±SE for seven men. $\dot{V}O_{2nonex}$, O_2 consumption of the finger flexor muscles (nonexercising muscle); T_D, deep tissue temperature.

[a] Significant difference compared with the resting value, $p<0.05$.

[b] Significant difference compared with the resting value, $p<0.01$.

= 0.637; $p<0.05$). No significant correlations between the increase in $\dot{V}O_{2nonex}$ and the increase in norepinephrine concentration or T_D were observed ($r^2=0.431$, $r^2=0.530$, respectively).

4 Discussion

The data from the present study demonstrated that (1) the resting $\dot{V}O_{2nonex}$ of the finger flexor muscles was 1.1

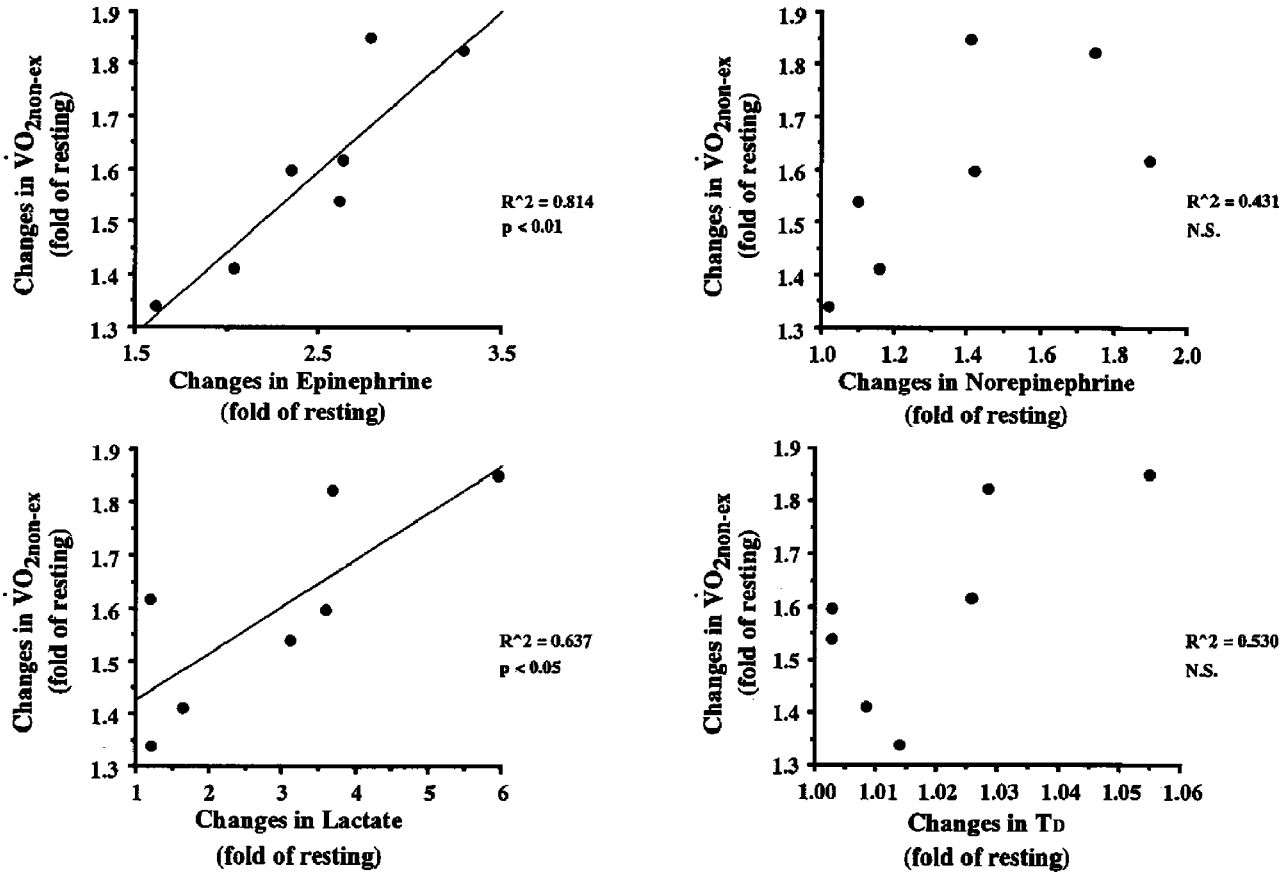

Fig. 2 Relationships between changes in $\dot{V}O_{2nonex}$ and changes in epinephrine, norepinephrine, lactate, and T_D after exercise at 50% of peak pulmonary O_2 uptake for 20 min. Each plot represents individual data. $\dot{V}O_{2nonex}$, O_2 consumption of nonexercising muscle; T_D, deep tissue temperature.

$\pm 0.1\ \mu M\ O_2/s$; 2) the peak $\dot{V}O_{2nonex}$ of each subject after exercise increased $59.6 \pm 7.2\%$ from the respective resting values; and (3) the changes in epinephrine and lactate concentrations in the blood were important $\dot{V}O_{2nonex}$ stimulant factors.

Nonexercising muscles play various important roles during exercise of other muscle groups.[1–3] Although research has been conducted on the effect of aerobic exercise from many angles, until now there have been few studies on the changes in nonexercising muscle metabolism during aerobic exercise. In this study, we investigated the metabolic changes in the nonexercising muscle and their stimulant factors in a 20 min moderate intensity cycling exercise, which is commonly used in exercise therapy. Although the exercise protocol used in our research was different from that of previous studies by Ahlborg[10] and Richter,[2] the change in the immediate postexercise $\dot{V}O_{2nonex}$ (1.6 times resting) that we observed was consistent with the changes observed by Ahlborg (1.5 times resting) and Richter (2.2 times resting). Therefore, we believe that our $\dot{V}O_{2nonex}$ data obtained immediately postexercise is a reflection of the data during exercise. Particularly, we examined the effects of catecholamines, lactate, and T_D, respectively, on the $\dot{V}O_{2nonex}$ as follows.

Catecholamines: We recognized a strong correlation between the changes in $\dot{V}O_{2nonex}$ and the changes in blood epinephrine concentration (Figure 2). It has been suggested that the systemic increase in epinephrine which occurs as a result of the sympathoadrenal response to exercise results in a concomitant increase in intramuscular glycogen utilization of nonexercising muscles because glycogen phosphorylase activity is enhanced by β-adrenergic stimulation.[11] In addition, it has also been demonstrated that glycogen loss is reduced in exercising adrenalectomized rats and in rats with β blockade.[12] Thus, during exercise, the degree of glycogen depletion in nonexercising muscle depends on the availability of epinephrine. In light of these previous studies, it seems reasonable to suppose that the epinephrine causes the increase in $\dot{V}O_{2nonex}$. In our study, however, exercise intensity is lower and exercise duration is shorter than those of previous studies. Furthermore, as we did not measure the direct evidence of glycogenolysis, such as glycogen depletion and lactate efflux, we could not assert whether the β-adrenergic stimulation by epinephrine increased the $\dot{V}O_{2nonex}$. We must examine those factors by biopsy or administration of β blocker in a subsequent study in order to clarify the mechanism of the increase in $\dot{V}O_{2nonex}$.

Lactate: During exercise, blood lactate concentration represents a dynamic balance between production and removal. It has been clearly shown that the nonexercising muscles take up lactate and increase oxygen consumption during contraction of remote muscle groups.[2,13] Chance et al.[4] reported that there is a proportionality between the Hb/Mb resaturation time of exercising muscle during recovery measured by NIR_{cws} and lactate concentration. We clarified for the first time a correlation between the changes in $\dot{V}O_{2nonex}$ measured by NIR_{cws} and the changes in blood lactate concentration. In this study, the $\dot{V}O_{2nonex}$ began to decrease after 5 min of recovery (Table 1), despite the fact that blood lactate concentration must be higher than resting values through the recovery period.[1] Regarding this point, it has been reported that a significant removal of lactate from the blood by nonexercising muscles stops approximately 5 min after the cessation of exercise.[13,14] Our result agrees with these data that lactate oxidation is thought to be one of the important factors which is involved in the increase in $\dot{V}O_{2nonex}$.

Temperature: The effects of temperature on muscle metabolism *in vitro* and *in vivo* have been well established.[15] It is generally thought that the increase in O_2 consumption is caused by an increase in T_D in the surrounding muscle groups. However, we did not find any significant correlations between the change in $\dot{V}O_{2nonex}$ and the change in T_D (Figure 2). One possible reason is that an increase in T_D may be caused by an increase in O_2 consumption. Furthermore, in spite of T_D increasing significantly after the exercise and maintaining a steady state in the recovery period, the $\dot{V}O_{2nonex}$ began to decrease after 5 min of recovery (Table 1). This result suggests that factors other than the increase in T_D have a strong effect on the change in $\dot{V}O_{2nonex}$ during recovery. The validity and reliability of noninvasive deep temperature measurement methods during exercise were controversial at first. However, the effects of the change in skin blood flow due to an increase in outside temperature and exercise on T_D measurement have been corrected and proved to be valid with the development of a probe using the electronic servo-control system (zero-heat-flow method).[9] In this study, we measured both T_D and skin surface temperature noninvasively by using CORETEMP (CTM-205; Terumo, Japan). At rest before exercise, skin surface temperature (33.1°C on average) was lower than T_D (34.7°C on average). Additionally, although T_D maintained a higher level (35.5°C on average) during the 20 min recovery period after exercise, skin surface temperature soon after exercise declined gradually to the resting temperature from 34.3 to 33.2°C in approximately 15 min. This difference in T_D and skin surface temperature also provides indirect evidence that the use of CORETEMP is a valid measure of T_D.

5 Conclusions

This study produced the following important findings: (1) the resting $\dot{V}O_{2nonex}$ of the finger flexor muscles was $1.1 \pm 0.1\ \mu M\ O_2/s$; (2) the peak $\dot{V}O_{2nonex}$ of each subject after exercise increased $59.6 \pm 7.2\%$ from the respective resting values; and (3) the changes in epinephrine and lactate concentrations in the blood were important $\dot{V}O_{2nonex}$ stimulant factors.

In this study, we were able to quantitatively evaluate $\dot{V}O_{2nonex}$ by using ^{31}P-MRS and NIR_{cws}, and to clarify one of the factors involved in the metabolic control of nonexercising human skeletal muscle after aerobic exercise. Finally, NIR_{cws}, unlike most previous techniques used to determine muscle O_2 consumption, is noninvasive, without deleterious effects, can be used to measure repeatedly and relatively rapidly, and thus was found to be suitable for *in vivo* human studies.

References

1. G. Ahlborg, J. Wahren, and P. Felig, ''Splanchnic and peripheral glucose and lactate metabolism during and after prolonged arm exercise,'' *J. Clin. Invest.* **77**, 690–699 (1986).
2. E. A. Richter, B. Kiens, B. Saltin, N. J. Christensen, and G. Savard, ''Skeletal muscle glucose uptake during dynamic exercise in humans: Role of muscle mass,'' *Am. J. Physiol.* **254**(17), E555–E561 (1988).
3. G. Ahlborg, ''Mechanism for glycogenolysis in nonexercising human muscle during and after exercise,'' *Am. J. Physiol.* **248**(11), E540–E545 (1985).
4. B. Chance, T. M. Dait, C. Zhang, T. Hamaoka, and F. Hagerman, ''Recovery from exercise-induced desaturation in the quadriceps muscle of elite competitive rowers,'' *Am. J. Physiol.* **262**, C766–C775 (1992).
5. T. Hamaoka, H. Iwane, T. Shimomitsu, T. Katsumura, N. Murase, S. Nishio, T. Osada, Y. Kurosawa, and B. Chance, ''Noninvasive measures of oxidative metabolism on working human muscles by near-infrared spectroscopy,'' *J. Appl. Physiol.* **81**(3), 1410–1417 (1996).
6. American College of Sports Medicine, ''ACSM's Guidelines for Exercise Testing and Prescription, 5th ed., Williams and Wilkins, Philadelphia (1995).
7. M. L. Blei, K. E. Conley, and M. J. Kushmerick, ''Separate measures of ATP utilization and recovery in human skeletal muscle,'' *J. Physiol. (London)* **465**, 203–222 (1993).
8. T. Shiga, K. Yamamoto, K. Tanabe, Y. Nakase, and B. Chance, ''Study of an algorithm based on model experiments and diffusion theory for a portable tissue oximeter,'' *J. Biomed. Opt.* **2**(2), 154–161 (1997).
9. R. H. Fox, A. J. Solman, R. Isaacs, A. J. Fry, and I. C. MacDonald, ''A new method for monitoring deep body temperature from the skin surface,'' *Clin. Sci.* **44**, 81–86 (1973).
10. G. Ahlborg, L. Hagenfeldt, and J. Wahren, ''Substrate utilization by the inactive leg during one-leg or arm exercise,'' *J. Appl. Physiol.* **39**(5), 718–723 (1975).
11. A. Bonen, G. W. Ness, A. N. Belcastro, and R. L. Kirby, ''Mild exercise impedes glycogen repletion in muscle,'' *J. Appl. Physiol.* **58**(5), 1622–1629 (1985).
12. J. C. McDermott, G. C. B. Elder, and A. Bonen, ''Adrenal hormones enhance glycogenolysis in nonexercising muscle during exercise,'' *J. Appl. Physiol.* **63**(3), 1275–1283 (1987).
13. M. I. Lindinger, G. J. F. Heigenhauser, R. S. McKelvie, and N. L. Jones, ''Role of nonworking muscle on blood metabolites and ions with intense intermittent exercise,'' *Am. J. Physiol.* **258**, 1486–1494 (1990).
14. J. R. Poortmans, J. D. Bossche, and R. Leclercq, ''Lactate uptake by inactive forearm during progressive leg exercise,'' *J. Appl. Physiol.: Respir., Environ. Exercise Physiol.* **45**(6), 835–839 (1978).
15. G. A. Brooks, K. J. Hittelman, J. A. Faulkner, and R. E. Beyer, ''Temperature, skeletal muscle mitochondrial functions, and oxygen debt,'' *Am. J. Physiol.* **220**(4), 1053–1059 (1971).