Influence of endurance training on muscle [PCr] kinetics during high-intensity exercise

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Submitted 25 January 2007; accepted in final form 26 April 2007

Influence of endurance training on muscle [PCr] kinetics during high-intensity exercise. Am J Physiol Regul Integr Comp Physiol 293: R392–R401, 2007. First published May 2, 2007; doi:10.1152/ajpregu.00056.2007.—We hypothesized that a period of endurance training would result in a speeding of muscle phosphocreatine concentration ([PCr]) kinetics over the fundamental phase of the response and a reduction in the amplitude of the [PCr] slow component during high-intensity exercise. Six male subjects (age 26 ± 5 yr) completed 5 wk of single-legged knee-extension exercise training with the alternate leg serving as a control. Before and after the intervention period, the subjects completed incremental and high-intensity step exercise tests of 6-min duration with both legs separately inside the bore of a whole-body magnetic resonance spectrometer. The time-to-exhaustion during incremental exercise was not changed in the control leg [preintervention group (PRE): 19.4 ± 2.3 min vs. postintervention group (POST): 19.4 ± 1.9 min] but was significantly increased in the trained leg (PRE: 19.6 ± 1.6 min vs. POST: 22.0 ± 2.2 min; \( P < 0.05 \)). During step exercise, there were no significant changes in the control leg, but end-exercise pH and [PCr] were higher after vs. before training. The time constant for the [PCr] kinetics over the fundamental exponential region of the response was not significantly altered in either the control leg (PRE: 40 ± 13 s vs. POST: 43 ± 10 s) or the trained leg (PRE: 38 ± 8 s vs. POST: 40 ± 12 s). However, the amplitude of the [PCr] slow component was significantly reduced in the trained leg (PRE: 15 ± 7 s vs. POST: 7 ± 7% change in [PCr]; \( P < 0.05 \)) with there being no change in the control leg (PRE: 13 ± 8 s vs. POST: 12 ± 10% change in [PCr]). The attenuation of the [PCr] slow component might be mechanistically linked with enhanced exercise tolerance following endurance training.

31P phosphorus magnetic resonance spectroscopy; time constant; phosphocreatine dynamics; slow component; fatigue

THE DETERMINANTS OF THE RESPONSE dynamics of muscle O2 uptake (\( \Delta V_O2 \)) following the onset of exercise are the source of considerable debate. Although the availability of both O2 and metabolic substrate in the form of NADH have the potential to influence muscle \( \Delta V_O2 \), it is generally agreed that the principal “drivers” to mitochondrial oxidative phosphorylation are likely to be associated with the rate of ATP hydrolysis needed to generate the requisite muscle power. Candidate mechanisms therefore include muscle [ATP], [ADP], [Pi], [PCr], and [creatinine] (where concentration is denoted by the square brackets), either in isolation or in combination (7, 11, 37, 43, 64). Rossiter et al. (52, 56) have reported close agreement between the time constant (\( \tau \)) describing the fall in muscle [PCr] [measured noninvasively by \( ^{31} \)P magnetic resonance spectroscopy (31P-MRS)] and the \( \tau \) of the phase II increase in pulmonary \( \Delta V_O2 \) (which has been shown to closely reflect the kinetics of muscle \( \Delta V_O2 \)) (4, 19) during knee-extension exercise in humans. Moreover, Kindig et al. (33) reported that acute inhibition of creatine kinase results in a more rapid fall in intracellular \( P_O2 \) in isolated myocytes. Collectively, these results suggest that the control of oxidative phosphorylation is intimately linked to the kinetics of PCr hydrolysis in the transition from one metabolic rate to another, as originally proposed in the PCr-Cr shuttle concept (7, 37, 43). It appears that the creatine kinase reaction serves as a temporal buffer for the [ATP]-[ADP] ratio following the onset of muscle contractions, thereby abating the rise in putative controllers of mitochondrial respiration.

Endurance exercise training causes a myriad of muscle metabolic and systemic adaptations that enhance the supply and utilization of O2 during exercise and result in improvements in indexes of aerobic fitness, such as the maximal \( \Delta V_O2 \), peak work rate (PWR) during incremental exercise, exercise economy, and the lactate and gas-exchange thresholds (26, 29). For the same submaximal work rate, PCr hydrolysis, lactate accumulation, and glycogen depletion (as assessed with muscle biopsy procedures) are all reduced after endurance training (e.g., Refs. 20, 31, 48). The higher [PCr] and lower [Pi] and [ADP] with training result in a higher phosphorylation potential, such that the same rate of mitochondrial respiration is accomplished with a reduced perturbation of adenine nucleotides (20, 26, 48). Endurance training also results in faster initial muscle (34) and pulmonary (6, 30, 47, 67) \( V_O2 \) kinetics and a reduction in the amplitude of the \( V_O2 \) “slow component” during heavy exercise (6, 9, 10). These adaptations might be expected to reduce the components of the muscle O2 deficit and result in enhanced exercise tolerance (29, 30).

Given the above, if the control of muscle \( \Delta V_O2 \) kinetics is indeed linked in some fashion to the kinetics of [PCr], as suggested by the results of several studies (2, 33, 40, 52, 54, 56), then one might expect that endurance training would result in a speeding of muscle [PCr] kinetics over the fundamental phase of the response and a “trimming out” of the so-called [PCr] slow component (16, 22, 54). Indeed, the electrical analog model of respiratory control proposed by Meyer (43) predicts that an increase in muscle mitochondrial content with endurance training will result in a speeding of muscle [PCr] kinetics and a reduced fall in [PCr] for the same oxidative metabolic rate. However, to our knowledge, the influence of endurance training on muscle [PCr] dynamics after the onset of high-intensity “step” exercise has not been reported. Therefore, the purpose of the present study was to use 31P-MRS to test the
hypotheses that endurance exercise training would result in 1) a speeding of muscle [PCr] kinetics over the fundamental phase of the response and 2) a reduction in the magnitude of any [PCr] slow component, during heavy-intensity single-legged, knee-extension exercise.

METHODS

Subjects. Six healthy male subjects (means ± SD: age 26 ± 5 yr, stature 1.82 ± 0.03 m, mass 80.7 ± 7.3 kg) volunteered and gave written, informed consent to participate in the study, which was approved by the local Research Ethics Committee. None of the subjects had participated in structured exercise activities for at least 6 mo before their involvement in the study. The subjects were instructed to arrive at the laboratory for each of their tests in a well-hydrated state and had not consumed food, caffeine, or alcohol during the previous 3 h.

Experimental protocol. The subjects completed a 5-wk intensive, structured program of single-legged endurance training on a knee-extensor ergometer. For each subject, the leg to be trained was randomly assigned as left or right, and the other leg served as a control. Before and after the training intervention period, the subjects completed two incremental exercise tests (one for each leg) and six step tests (three for each leg) from rest to a work rate calculated to require 80% of that achieved during the initial incremental tests. All tests were performed on separate days within a 10-day period before and after the training intervention.

The single-legged, knee-extension exercise tests were conducted in the prone position with the subjects positioned inside a whole body MRI system. A 6-cm 31P transmit-receive surface coil was placed within the subject bed, and the subject was asked to lie on it such that the coil was centered over the quadriceps muscle of the leg to be exercised. Subjects were then secured to the ergometer bed with Velcro straps at the thigh, buttocks, and lower back to minimize extraneous movement during the protocol. The foot of the leg to be exercised was connected to a pulley system that permitted a nonmagnetic strain gauge present within the pulley to which they were attached. Before exercise, during exercise, and during recovery, data were acquired every 1.5 s, with a spectral width of 1,500 Hz and 1,000 data points. Phase cycling with four phase cycles was employed, leading to a spectra being acquired every 6 s. The subsequent spectra were quantified via peak fitting, assuming prior knowledge, using the jMRUI (version 2) software package and the AMARES fitting algorithm. Spectra were fitted assuming the presence of the following peaks: P i, phosphodiester, phosphocreatine (PCr), α-ATP (2 peaks, amplitude ratio 1:1), γ-ATP (2 peaks, amplitude ratio 1:1), and β-ATP (3 peaks, amplitude ratio 1:2:1). In all cases, relative amplitudes were corrected for partial saturation because of the short repetition time relative to the longitudinal relaxation time constant T1. The ratio of P i to PCr was determined from the respective P i and PCr spectral areas as obtained during the quantification procedure. Intracellular pH was calculated with the use of the chemical shift of the P i, spectral peak relative to the PCr peak. For both incremental and step exercise, resting and end-exercise values of PCr, P i/PCr, and pH were measured over the last 30 s of the rest or exercise period, respectively. To determine the intracellular threshold (IT) during incremental exercise, piecewise linear regression was used. Briefly, different two-line combinations were fitted to the [P i/PCr]-work rate and pH-work rate relationships until the lowest sum of squared residuals was found (24, 39). The point at which this particular two-line combination intersected was accepted as the IT.

Modeling procedures. For analysis of the [PCr] kinetics during step exercise, the [PCr] data were first expressed as the percent change relative to the resting baseline, which was assumed to represent 100%. For each of the legs in each of the subjects, the three like transitions were then time aligned and averaged together to increase the signal-to-noise ratio and to improve confidence in the parameter estimates derived from the subsequent model fits (51). The parameter values...
derive with this approach were indistinguishable from the parameter values derived when each of the individual responses was modeled separately and then averaged together.

The [PCr] responses were then modeled by nonlinear, least-squares regression techniques. We used two approaches to characterize the [PCr] kinetics. In the first approach (model 1; see Fig. 1A), we used a similar procedure to that described by Rossiter et al. (53). Briefly, an exponential function of the form

$$\Delta[PCr]_{(0)} = [PCr]_o - \Delta[PCr]_{(1)}(1 - e^{-\tau}) \quad (1)$$

where $[PCr]_o$ is the value of [PCr] at time 0 (onset of exercise), $\Delta[PCr]_{(1)}$ is the projected asymptotic value, and $\tau$ is the time constant of the response, was fit to the data. The first fit contained only the first 60 s of exercise data, but the fitting window was then increased iteratively until there was a clear departure of the measured data from the model fit, as judged from inspection of a plot of the residuals. In this way, the best-fit exponential for the fundamental component of the response was established. The magnitude of the [PCr] slow component was then calculated as the difference between the asymptotic amplitude of the fundamental [PCr] response and the average [PCr] measured over the last 30 s of exercise. The mean response time was also calculated by fitting a single-exponential function (see Eq. 1) from the onset of exercise (time 0) through the entire data set.

In the second approach (model 2; see Fig. 1B), we used a procedure similar to that described by Barstow and Mole (5). In this approach, the [PCr] kinetics were described by a model that incorporated two exponential terms that began together after a common time delay, as described in the following equation:

$$\Delta[PCr]_{(0)} = [PCr]_o - \Delta[PCr]_{(1)}(1 - e^{-\tau_1}) - \Delta[PCr]_{(2)}(1 - e^{-\tau_2}) \quad (2)$$

where $\Delta[PCr]_{(1)}$ and $\Delta[PCr]_{(2)}$ are the asymptotic values to which [PCr] projects for the faster and slower components of the [PCr] response, respectively, and $\tau_1$ and $\tau_2$ are the time constants associated with those processes. In Eq. 2, it is assumed that the slower component of the response begins simultaneously with the faster component or close to the onset of exercise (5). It was pertinent to include Eq. 2 in the analysis of these data because it is currently unknown whether the fundamental and slow components of the muscle [PCr] response occur in series or in parallel.

Statistics. Differences between the trained and control legs were tested by a two-way ANOVA with repeated measures. When a significant interaction was detected, data were subsequently analyzed with a Newman-Keuls post hoc test to locate differences. Significance was accepted at $P < 0.05$. Values are expressed as means ± SD unless otherwise indicated.

**RESULTS**

Incremental exercise. The results for incremental exercise are presented in Table 1. The time to exhaustion during the incremental exercise test was not significantly altered in the control leg (PRE: 19.4 ± 2.3 vs. POST: 19.4 ± 1.9 min) but was significantly ($P < 0.05$) increased in the leg that underwent training (PRE: 19.6 ± 1.6 vs. POST: 22.0 ± 2.2 min). Accordingly, the PWR attained in the test was increased in the trained leg but not in the control leg (Table 1). The end-exercise pH and [PCr] values were not significantly different before compared with after the intervention period in either the control leg or the trained leg. The time courses for the changes in [PCr], pH, and [P]/[PCr] during incremental exercise were similar in the control leg before and after the intervention.
period; however, the [PCr], pH, and [Pi]/[PCr] relationships were “right-shifted” in the trained leg. These relationships are illustrated for a typical subject in Figs. 2–4. The IT (see METHODS) was not altered in the control leg (PRE: 17 ± 4 vs. POST: 18 ± 4 W) but was significantly increased in the trained leg (PRE: 16 ± 3 vs. POST: 20 ± 2 W; \( P < 0.05 \); Fig. 3). For all work rates above the IT, muscle [PCr] and pH were higher and the [Pi]/[PCr] ratio was lower after the training intervention in the trained leg (Figs. 2–4).

**Step exercise.** The results for step exercise are presented in Table 2. In model 1, the \( \tau \) for the fundamental decrement in [PCr] was not significantly altered in either the control leg (PRE: 40 ± 13 vs. POST: 43 ± 10 s) or the trained leg (PRE: 38 ± 8 vs. POST: 40 ± 12 s). The 95% confidence interval surrounding the estimate of \( \tau \) was 6 ± 3 s. The amplitude of the fall in [PCr] over the fundamental phase of the response was not significantly influenced by the intervention period in either the control leg or the trained leg. However, the amplitude of the [PCr] slow component was significantly reduced in the trained leg (PRE: 15 ± 7% vs. POST: 7 ± 7%; \( P < 0.05 \)) but not in the control leg (PRE: 13 ± 8% vs. POST: 12 ± 10%). The mean response time was not significantly altered in either the control leg (PRE: 74 ± 30 s vs. POST: 91 ± 38 s) or the trained leg (PRE: 74 ± 24 s vs. POST: 59 ± 33 s). The reduced [PCr] slow component after training resulted in a significant sparing of [PCr] at the end of exercise (Table 2). The higher end-exercise [PCr] following endurance training is evident in Fig. 5, which shows the muscle [PCr] responses to exercise in the control and trained legs of a representative subject. Figure 5 shows that the blunting of the [PCr] response after training can be primarily attributed to a reduced fall in [PCr] over the slow component phase of the response.

The essential results were not appreciably different when model 2 was applied (Table 2). Again, neither the time constant nor amplitude of the faster exponential response was altered by the intervention period (for control \( \tau \), PRE: 35 ± 11 s vs. POST: 33 ± 11 s for training \( \tau \), PRE: 34 ± 10 vs. POST: 36 ± 16 s). Moreover, neither the time constant nor amplitude of the slower exponential response was altered by the intervention period. As would be expected (5), the \( \tau \) of the faster process tended to be shorter, the amplitude of the faster process tended to be smaller, and the amplitude of the slower process tended to be greater with model 2 than with model 1 (see Table 2). As per model 1, the amplitude of the slower exponential process was attenuated after endurance training (PRE: 36 ± 12% vs. POST: 27 ± 24%); however, greater interindividual variability

![Fig. 2](image_url) [PCr] changes before (●) and after (○) the intervention period in the control leg (CON) and the trained leg (TRA) in a representative subject during incremental one-legged, knee-extension exercise. Notice the rightward shift of the [PCr]-time relationship and the enhanced exercise tolerance posttraining in the TRA leg.

![Fig. 3](image_url) Intramuscular pH changes before (●) and after (○) the intervention period in the CON leg and the TRA leg in a representative subject during incremental one-legged, knee-extension exercise. Notice the rightward shift of the pH-time relationship and the enhanced exercise tolerance posttraining in the TRA leg. The intracellular pH threshold is marked with vertical arrows.
with this approach precluded the attainment of statistical significance. The total fall in [PCr] from rest to end exercise was significantly reduced in the trained leg only (Table 2).

In addition to effects on the muscle [PCr] responses to exercise, endurance training also had important effects on muscle pH and [Pi]/[PCr]. The end-exercise pH was not altered in the control leg but was significantly higher after training in the trained leg. This is illustrated in Fig. 6, which clearly shows a different pattern of response for pH after training in the trained leg compared with the other conditions.

The effect of training on [P_i]/[PCr], which reflects the phosphorylation potential, is equally profound. Figure 7 shows that [P_i]/[PCr] reaches a stable value within ~2 min after the start of exercise in this representative subject, whereas, before training, and in the control leg, [P_i]/[PCr] continues to increase throughout exercise.

**DISCUSSION**

To our knowledge, this is the first study to investigate the effects of an endurance training intervention on skeletal muscle [PCr] kinetics in the transition from rest to constant-load, high-intensity exercise. The principal original findings of this study are that 5 wk of intensive training did not significantly alter the fundamental component [PCr] kinetics but did result in an attenuation of the fall in [PCr] over the slow-component phase of the response such that [PCr] at the end of exercise was significantly higher after training.

In the present study, we used two mathematical models to examine the influence of training on muscle [PCr] kinetics. Model 1 was similar to that used by Rossiter et al. (53) and involved iteratively fitting a single-exponential function to the first 1–3 min of exercise data until the residuals showed a consistent deviation from their previously “flat” profile. This model assumes that the initial response reflects a linear first-order control process and that the initial and subsequent slow phases occur in series, i.e., that the slow component is of delayed onset and its development therefore does not influence the kinetics of the initial phase (5). This model has the advantage of reducing the number of parameters and therefore increasing confidence in those that remain (i.e., the time constant and amplitude of the initial “fast” phase). Model 2 was similar to that described by Barstow and Molé (5) for VO₂ kinetics and involved fitting a biexponential model to the data from the onset of exercise. This model provides time constant and amplitude values for both the fast and slow components of the response and assumes that these components develop in par-

### Table 2. Effects of training on muscle metabolic responses during high-intensity step exercise

<table>
<thead>
<tr>
<th></th>
<th>CON-PRE</th>
<th>CON-POST</th>
<th>TRA-PRE</th>
<th>TRA-POST</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH, resting baseline</td>
<td>7.04±0.03</td>
<td>7.05±0.03</td>
<td>7.05±0.03</td>
<td>7.04±0.02</td>
</tr>
<tr>
<td>pH, end exercise</td>
<td>6.95±0.11</td>
<td>6.96±0.07</td>
<td>6.92±0.06</td>
<td>6.96±0.09*</td>
</tr>
<tr>
<td>[PCr] fundamental τ, s</td>
<td>40±13</td>
<td>43±10</td>
<td>38±8</td>
<td>40±12</td>
</tr>
<tr>
<td>[PCr] fundamental amplitude, %change</td>
<td>48±7</td>
<td>45±6</td>
<td>50±8</td>
<td>46±11</td>
</tr>
<tr>
<td>[PCr] slow component, %change</td>
<td>13±8</td>
<td>12±10</td>
<td>15±7</td>
<td>7±7*</td>
</tr>
<tr>
<td>[PCr], end exercise, % of baseline</td>
<td>39±11</td>
<td>43±15</td>
<td>35±8</td>
<td>47±16*</td>
</tr>
</tbody>
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**Model 1**

<table>
<thead>
<tr>
<th></th>
<th>Model 2</th>
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<tr>
<td>[PCr] fundamental τ, s</td>
<td>35±11</td>
</tr>
<tr>
<td>[PCr] fundamental amplitude, %change</td>
<td>31±7</td>
</tr>
<tr>
<td>[PCr] slow component τ, s</td>
<td>470±211</td>
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<tr>
<td>[PCr] slow component, %change</td>
<td>34±14</td>
</tr>
<tr>
<td>[PCr], end exercise, % of baseline</td>
<td>36±9</td>
</tr>
</tbody>
</table>

Values are mean ± SD. τ, time constant. For information on equations used for models 1 and 2, please see text. *P < 0.05 for TRA-PRE vs. TRA-POST.
allel such that the kinetics of the phases will be interdependent. Model 1 provided a statistically better fit to the data (as judged by the mean squared error of the model fits), but we are unable to conclude from the present study which of the models better reflects the physiological reality. However, the principal results of the study were essentially the same irrespective of the model used to analyze the data, and thus, for simplicity, the discussion will focus on the results derived from model 1.

Our subjects completed 21–25 endurance training sessions, comprising a mixture of continuous and high-intensity interval training, over a 5-wk period. The physiological and metabolic adaptations to exercise training are known to be rapid, and significant improvements in muscle oxidative capacity would be expected from participation in such a program (20, 26, 29, 34, 48, 58, 59, 67). Indeed, the time-to-exhaustion and PWR achieved in the incremental exercise test increased by ~13% in the trained leg, with there being no significant change in the control leg. Moreover, the 31P metabolite responses to incremental and step exercise in the trained leg were consistent with the training intervention having been successful in enhancing muscle oxidative function.

During incremental exercise, the 31P metabolite responses and exercise performance were not significantly altered by the intervention period in the control leg. In contrast, training resulted in a right shift in the [PCr] and pH responses to incremental exercise such that the IT was increased by ~25% and, above the IT, [PCr] and pH were both higher for the same work rate (Figs. 2 and 3) and [Pi]/[PCr] was lower for the same work rate (Fig. 4). Interestingly, the [PCr] and pH values at the end of exercise were not different after training but were reached at a higher work rate. During step exercise, the end-exercise pH and [PCr] values were significantly higher and [Pi]/[PCr] was significantly reduced with training (Figs. 5–7). A stable [Pi]/[PCr] reflects adequate energy status and indicates that oxidative phosphorylation is able to meet the ATP requirement of the exercise task. These results are consistent with several previous studies that have documented the influence of training on MRS-derived indexes of muscle metabolism during exercise in a variety of human populations (12, 14, 32, 38, 44, 45).  

**[PCr] time constant.** The principal purpose of this study was to examine the influence of endurance training on [PCr] kinetics after the onset of high-intensity exercise. The results were
consistent with our second hypothesis (that training would reduce the magnitude of the [PCr] slow component) but not with our first hypothesis (that training would reduce τ for the fundamental component [PCr] kinetics). At the same absolute work rate, the end-exercise [PCr] was significantly higher after than before training, and this resulted from a reduction in the extent of PCr depletion over both the fundamental phase (mean Δ[PCr], PRE: 50% vs. POST: 46%) and the subsequent slow phase (mean Δ[PCr], PRE: 15% vs. POST: 7%) of the response (Fig. 5). The end-exercise pH was also significantly higher after training (Fig. 6).

Given the favorable alterations to muscle metabolism caused by the training intervention, the lack of any measurable effect of training on the τ for the fundamental component of [PCr] might be considered surprising. Indeed, our results are apparently inconsistent with the prediction of Meyer (43), based on an electrical analog model of respiratory control, that [PCr] kinetics will become faster if mitochondrial content (or the activity of mitochondrial enzymes) is increased with endurance training, as would certainly be expected in the present study (20, 31, 34, 58, 61). However, there may be several explanations for this apparent discordance.

First, Meyer’s model was developed to reflect a first-order linear system in which there is a single rate-limiting step and the response can be adequately described with a single exponential function. Although this is often considered to be true for the oxidative metabolic response to moderate-intensity exercise (i.e., at work rates that do not elicit a sustained increase in blood [lactate] and [H⁺]), it is possible that the response to higher work rates that elicit a reduction in pH (such as that applied in the present study) is additionally influenced by or limited by factors such as a disequilibrium in the creatine kinase reaction, a reduction in muscle O2 availability, or the recruitment of “higher-order,” less-efficient, muscle fibers (13, 49, 60). For example, at high work rates, in addition to its putative signaling role in the control of mitochondrial respiration, a fall in [PCr] might be required to buffer [ATP] if O2 supply is limiting. In this scenario, a training-induced increase in muscle O2 availability for the same high-intensity work rate might reduce the rate and extent to which [PCr] falls (22, 25). Certainly, there is evidence that the metabolic response to exercise (including [PCr], [P], and pH, as assessed by 31P-MRS) is sensitive to the fraction of inspired O2, which is likely to influence intracellular Po2 (22, 25). This, along with the other factors alluded to above, might confound the application of the electrical analog model to interpretation of the effects of training on [PCr] kinetics during high-intensity exercise.

Second, although mitochondrial volume and oxidative enzyme activity (equivalent to the resistor in Meyer’s model) were likely increased as a consequence of the training program completed by our subjects (20, 26, 34, 48), it is possible that muscle [PCr] (equivalent to the capacitance in Meyer’s model) may have also increased. Certainly, the training program completed by our subjects included a significant volume of high-intensity interval training, which might have increased the “anaerobic capacity,” including the total muscle PCr (28, 36). An increase in total muscle PCr would be predicted to result in slower [PCr] kinetics after the onset of exercise (43), which could functionally “off set” any speeding of [PCr] kinetics that might otherwise have occurred subsequent to increased mitochondrial volume. Also, although impressive physiological and muscle metabolic adaptations can be observed after only a few weeks of endurance training (6, 20, 29–31, 34, 58, 59, 67), it is possible that a longer period of training might have resulted in a speeding of the [PCr] on -kinetics. There is some evidence, mostly arising from cross-sectional studies, that endurance-trained athletes have faster [PCr] kinetics than sprint-trained or untrained subjects in the recovery from exercise (41, 42, 66) (see Ref. 27); however, to our knowledge, no previous studies have specifically examined the influence of a training intervention on [PCr] kinetics during exercise. Cross-sectional studies are unable to rule out a genetic influence on muscle metabolic responses (46), and it is possible that the control of [PCr] kinetics differs between exercise and subsequent recovery (33, 56). Therefore, there is presently no convincing evidence that [PCr] kinetics become faster following a period of endurance training.

The sensitivity of the methods used in the present study to detect an actual speeding of [PCr] kinetics had it occurred also requires comment. There is known to be considerable intrasample variability in [PCr] determination when 31P-MRS is used, and this “noise” can confound physiological interpretation of the data if appropriate steps are not taken (51). In the
present study, we attempted to enhance the signal-to-noise ratio by 1) examining the metabolic responses to high-intensity exercise and 2) averaging together the responses to three identical rest-to-exercise transitions (51). This approach resulted in 95% confidence interval for the estimated τ of approximately ±6 s, which is similar to previous studies (54, 56) and might be considered acceptably tight. However, we are unable to rule out the possibility that a speeding of [PCr] kinetics took place with training that could not be detected because of the inherent limitations of the exercise model utilized.

Several studies have indicated that the τ for [PCr] closely reflects the τ for VO2 in the transition from rest to exercise (2, 40, 52, 54, 56), consistent with suggestions that the control of oxidative phosphorylation is linked either directly or indirectly to PCr hydrolysis (37, 43). Our observations of an unchanged τ for [PCr] after endurance training therefore suggests either that VO2 kinetics were also not speeded or that the intervention resulted in a dissociation of, or disturbance to, the normal [PCr]-mediated control of VO2. We did not measure VO2 in the present study and therefore are unable to discriminate between these possibilities. However, VO2 kinetics are very sensitive to endurance training (6, 17, 30, 34, 47, 67), and the type of training program completed by our subjects would be expected to result in a reduction in the τ of the fundamental response (6, 34). Further research is clearly required to explore the possibility that [PCr] and VO2 kinetics might be dissociated by a short-term endurance training intervention. Interestingly, observation of a dissociation of [PCr] and VO2 kinetics would not be unprecedented. Rossiter et al. (53) measured [PCr] and VO2 kinetics simultaneously during repeated bouts of high-intensity exercise and reported that prior exercise speeded the phase II VO2 kinetics (τ was significantly reduced from ~47 to ~41 s) but did not alter the [PCr] kinetics (τ was ~35 and ~32 s in the first and second bouts). With training, a possible dissociation of [PCr] and VO2 kinetics might be hypothesized to be related to altered sensitivity of the mitochondria to, for example, [ADP] or [creatinine] (15, 59, 61).

[PCr] slow component. Consistent with several previous studies (22, 53, 54, 56), a slow component in the [PCr] response (equivalent to ~22% of the total [PCr] decrement) was evident in all subjects. Rossiter et al. (56) measured [PCr] kinetics and pulmonary VO2 kinetics simultaneously and reported that ~90% of the VO2 slow component was reflected in a slow component in the decline in [PCr] in the contracting muscles. These results indicated that the apparent reduction in muscle efficiency beyond ~3 min of high-intensity exercise was related to an increased phosphate cost of muscle force production. The mechanistic basis to the VO2 slow component remains obscure, although the recruitment of “low-efficiency” type II fibers, which might have a higher phosphate cost for force generation relative to type I fibers (8), has been frequently proposed as a likely mechanism (3, 18, 35, 49, 63).

Endurance training resulted in a significant (>50%) reduction in the magnitude of the [PCr] slow component during exercise at the same absolute work rate. To our knowledge, this is the first demonstration that training reduces the intramuscular [PCr] slow component. Several studies have demonstrated that the magnitude of the VO2 slow component is reduced after a period of endurance training (6, 9, 10). Given the close link between the [PCr] and VO2 slow component established previously (53, 54, 56) and evidence that the efficiency of muscle energy transfer (as P/O) does not appear to be altered by endurance training (59), our results suggest that the reduction in the VO2 slow component with endurance training is related to a reduction in the energy (and phosphate) turnover required for a given high-intensity work rate. It is possible that an increase in muscle mitochondrial volume with training reduced the number of muscle fibers (including higher-order, perhaps type II, fibers) that had to be recruited to meet the force requirements of the exercise task and that this was responsible for the observed reduced [PCr] slow component. Alternatively, an increased muscle O2 availability, and/or a reduction in the concentration of metabolites associated with the fatigue process, might also have altered muscle fiber recruitment patterns or reduced the phosphate (and O2) cost of ion pumping (49). Other interventions that appear to reduce the amplitude of the [PCr] slow component include the inspiration of hyperoxic gas (22), the performance of prior high-intensity exercise (53), the ingestion of sodium bicarbonate (16), and the infusion of dichloroacetate (55), all of which are known to reduce the accumulation of fatigue-related metabolites.

The reduced [PCr] slow component observed with endurance training in the present study resulted in a net sparing of [PCr] at the end of the 6-min period of high-intensity exercise (PRE: 35 ± 8% vs. POST: 47 ± 16%). Moreover, endurance training resulted in less of a fall in pH and less of an increase in [P]i/[PCr]. These adaptations are consistent with the development of tighter metabolic control, i.e., the achievement of the same (or similar) VO2 with less perturbation of the adenine nucleotides, with training (15, 23, 48). Moreover, because a low [PCr] and pH and a high P(i) (or H2PO4-3) have been associated with the fatigue process (50, 62, 65), these effects are likely to be important in the enhanced exercise tolerance that attends endurance training. The higher end-exercise pH suggests that endurance training resulted in a reduced activation of “anaerobic” glycolysis and/or a greater proton efflux from muscle to blood. The VO2 slow component is only manifest during exercise above the lactate threshold where there is a sustained metabolic acidosis (18, 63). Moreover, the reduction in the VO2 slow component with endurance training is associated with a reduced accumulation of blood lactate (6, 9, 10). Although the relationship between the VO2 slow component and metabolic acidosis is not believed to be causal (18, 49), it is interesting that the reduced [PCr] slow component observed after training in the present study was associated with a higher end-exercise pH. An explanation for this effect might be that, according to the creatine kinase equilibrium, [PCr] is required to fall more when pH is low to enable the attainment of an appropriately high level of [ADP] to sustain oxidative metabolism (1, 13).

Although the changes were not statistically significant, it was interesting that there was a tendency for some of the 31P indexes of muscle metabolism to be improved in the control leg after the training intervention. Improvements in muscle oxidative capacity and/or endurance in the contralateral limb during single-limb training programs have also been documented in previous studies (21, 45, 57). We cannot rule out the possibility that the subjects altered their levels of habitual physical activity during the training intervention period (although we consider this to be unlikely). Rather, it is possible that the subjects inadvertently performed isometric contractions of their control
leg to brace the body while the other leg was being trained or tested or that neural adaptations occurred that altered the metabolic response to exercise in both legs (21, 45).

In conclusion, 5 wk of endurance exercise training resulted in a significant improvement in IT and in time to exhaustion during incremental exercise, with no change in the control leg. During step transitions to high-intensity exercise, endurance training resulted in a significant reduction in the magnitude of this change. Further study is required to elucidate the effects of endurance training on the relationship between [PCr] and \(\dot{V}O_2\) kinetics during high-intensity exercise.

REFERENCES


