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Time required for the restoration of normal heavy exercise $\dot{V}O_2$ kinetics following prior heavy exercise

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Burnley, Mark, Jonathan H. Doust, and Andrew M. Jones. Time required for the restoration of normal heavy exercise $\dot{V}O_2$ kinetics following prior heavy exercise. *J Appl Physiol* 101: 1320–1327, 2006. First published July 20, 2006; doi:10.1152/jappphysiol.00475.2006.—Prior heavy exercise markedly alters the O_2 uptake ($\dot{V}O_2$) response to subsequent heavy exercise. However, the time required for $\dot{V}O_2$ to return to its normal profile following prior heavy exercise is not known. Therefore, we examined the $\dot{V}O_2$ responses to repeated bouts of heavy exercise separated by five different recovery durations. On separate occasions, nine male subjects completed two 6-min bouts of heavy cycle exercise separated by 10, 20, 30, 45, or 60 min of passive recovery. The second-by-second $\dot{V}O_2$ responses were modeled using nonlinear regression. Prior heavy exercise had no effect on the primary $\dot{V}O_2$ time constant (from 25.9 ± 4.7 s to 23.9 ± 8.8 s after 10 min of recovery; $P = 0.338$), but it increased the primary $\dot{V}O_2$ amplitude (from 2.42 ± 0.39 to 2.53 ± 0.41 l/min after 10 min of recovery; $P = 0.001$) and reduced the $\dot{V}O_2$ slow component (from 0.44 ± 0.13 to 0.21 ± 0.12 l/min after 10 min of recovery; $P < 0.001$). The increased primary amplitude was also evident after 20–45 min, but not after 60 min, of recovery. The increase in the primary $\dot{V}O_2$ amplitude was accompanied by an increased baseline blood lactate concentration (to 5.1 ± 1.0 mM after 10 min of recovery; $P < 0.001$). Baseline blood lactate concentration was still elevated after 20–60 min of recovery. The priming effect of prior heavy exercise on the $\dot{V}O_2$ response persists for at least 45 min, although the mechanism underpinning the effect remains obscure.

priming exercise; lactate; oxygen uptake slow component

DURING HEAVY CONSTANT-WORK RATE cycle exercise (above the lactate threshold), following a short delay of ~15–20 s, pulmonary O_2 uptake ($\dot{V}O_2$) rises in an exponential fashion with a time constant of ~20–35 s to attain an amplitude that is largely dependent on the external power requirement (39). This “primary” or “fundamental” phase (phase II) is supplemented after ~2 min by a “slow component,” which results in a continued increase in $\dot{V}O_2$ as exercise progresses (2, 39). It has been demonstrated that both the primary and slow components of the $\dot{V}O_2$ response reflect events occurring within the exercising muscle (24, 42, 44, 45). Interestingly, when heavy exercise is performed under conditions of an exercise-induced elevation in blood lactate concentration ([lactate]), the $\dot{V}O_2$ kinetic response is markedly altered (23). Specifically, the primary $\dot{V}O_2$ response is elevated and the slow component amplitude is reduced with there being no change in the primary time constant (Refs. 3, 7–11, 21, 33, 34, 48, 51, 55; but see also Ref. 53).

It is surprising, given the extensive investigation of the effects of prior exercise on $\dot{V}O_2$ kinetics, that no study has systematically varied the recovery duration between bouts of heavy exercise to establish the time course over which the effect diminishes. Previous investigations have used discrete recovery durations of between 3 and 15 min to either maximize the treatment effect or to minimize the influence of elevations in baseline $\dot{V}O_2$ on the subsequent expression of the primary amplitude (e.g., Refs. 7, 8, 48, 57). Insight into the mechanism that underpins the effect of prior heavy exercise should result from treating recovery duration as the independent variable. This is because any candidate mechanism must fulfill two criteria to remain under consideration. First, it must account for the observed effect of prior heavy exercise (an increased primary $\dot{V}O_2$ amplitude and reduced $\dot{V}O_2$ slow component). Second, its recovery time course must be similar to that of the decay in the effect of prior heavy exercise.

The prior exercise effect has been most consistently observed following an exercise-induced elevation in blood [lactate] (17), with the effect being considerably greater when the same muscle group is utilized in both exercise bouts (6, 21, 32). It has been suggested that an exercise-induced metabolic acidosis might enhance muscle O_2 availability by increasing muscle vasodilatation (23). However, recent estimates of capillary blood flow suggest that muscle blood flow returns to resting levels within ~10 min after the cessation of heavy exercise (19), and, therefore, it might be possible to rule out enhanced bulk O_2 delivery to muscle as a candidate mechanism if the effects of prior exercise on $\dot{V}O_2$ kinetics remain evident beyond this time frame. In a similar fashion, it should be possible to eliminate other putative determinants of the effects of priming exercise (e.g., pyruvate dehydrogenase activity, muscle fatigue) by relating the time course over which the “priming” effect on $\dot{V}O_2$ kinetics decays to the recovery kinetics of other metabolites and metabolic processes.

The purpose of the present study, therefore, was to measure the time required to restore the normal $\dot{V}O_2$ kinetic response to heavy exercise following a prior priming bout of heavy exercise. We reasoned that this approach would provide evidence against one or more of the candidate mechanisms for the effect of priming exercise on $\dot{V}O_2$ kinetics and, in so doing, help to elucidate the mechanistic basis for the effect.

METHODS

Nine healthy male volunteers (mean \pm SD: age 29 ± 9 yr; height 179.6 ± 6.1 cm; body mass 77.7 ± 11.3 kg) gave written, informed

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consent to participate in this study, which was approved by the ethics committee of the University of Wales, Aberystwyth. The subjects included competitive cyclists and students who were familiar with laboratory testing procedures. They were instructed to arrive at the laboratory in a rested (no heavy exercise in the preceding 24 h), well-hydrated state, having consumed no food, caffeine, or alcohol in the 3 h before exercise testing. Subjects visited the laboratory on 11 occasions over a 3-wk period, with at least 24 h separating each visit. The first laboratory visit involved a ramp test to establish the peak $\dot{V}O_{2\text{peak}}$ and the gas-exchange threshold (GET). The remaining 10 visits involved "double square-wave" exercise tests, in which subjects performed two bouts of heavy exercise separated by 10, 20, 30, 45, or 60 min of recovery, with each test being performed twice in a random order.

Experimental procedures. All testing was performed on an electromagnetically braked cycle ergometer (Lode Excalibur Sport, Groningen, The Netherlands) in a well-ventilated laboratory at 19–24°C. The ergometer was adjusted for comfort, which included fitting the subject's own pedals if necessary, and the adjustments were recorded and replicated in subsequent tests. The first experimental test was designed to establish $\dot{V}O_{2\text{peak}}$ and the GET. Subjects self-selected a cadence of 85–95 rpm and maintained this cadence (± 2 rpm) throughout all subsequent tests. The test began with a 3-min period of unloaded pedaling, followed by a ramp increase in power output of 30 W/min until volitional exhaustion. The test was terminated when the cadence fell by 5 rpm and could not be increased despite strong verbal encouragement. In all cases, this fall was precipitous. Throughout this and all other tests, pulmonary gas exchange was measured breath-by-breath as described below. The breath-by-breath data were averaged over 10-s intervals, and the $\dot{V}O_{2\text{peak}}$ was established as the highest $\dot{V}O_2$ measured over 30 s. The GET was determined using the V slope method as a disproportionate increase in CO_2 output when plotted against $\dot{V}O_2$ (5). From the result of the ramp test, a work rate designed to elicit a $\dot{V}O_2$ that was 70% of the difference between the GET and $\dot{V}O_{2\text{peak}}$ (70% Δ) was calculated from linear regression of $\dot{V}O_2$ against power output, with account taken of the lag in $\dot{V}O_2$ relative to the increase in power output (55).

The subjects subsequently performed 10 further tests to complete the experimentation. Each of these tests involved two bouts of heavy exercise separated by between 10 and 60 min of recovery. These tests required subjects to perform 3 min of unloaded pedaling, followed by a step change in power output to 70% Δ , which was maintained for 6 min. At the end of exercise, subjects were allowed to continue unloaded cycling for 1 min before dismounting the ergometer and resting passively in a seated position. The recovery periods between the end of the first and the beginning of the second square wave exercise bouts were 10, 20, 30, 45, and 60 min, and these were presented in a random order. In each of these tests, the subjects repeated the 3-min unloaded pedaling phase before the second square wave increase in power output, again lasting 6 min, was completed. Pulmonary gas exchange and heart rate were measured throughout the tests (including the unloaded pedaling phase) and 1 min before and immediately after exercise a capillary blood sample was drawn from the fingertip and immediately analyzed to determine whole blood [lactate] (YSI Stat 2300, Yellow Springs Instruments, Yellow Springs, OH). Each of the five variations of the double square wave test was performed twice.

Measurements. Pulmonary gas exchange and ventilation were measured breath by breath with subjects wearing a nose clip and breathing through a low-dead space (90 ml), low-resistance ($0.75 \text{ mmHg} \cdot \text{l}^{-1} \cdot \text{s}$ at 15 l/s) mouthpiece and impeller turbine assembly (Jaeger Triple V). The inspired and expired gas volume and gas concentration signals were continuously sampled at 100 Hz, the latter using paramagnetic (O_2) and infrared (CO_2) analyzers (Jaeger Oxycon Pro, Hoechberg, Germany) via a capillary line connected to the mouthpiece. The gas analyzers were calibrated before each test with gases of known concentration, and the turbine volume transducer was calibrated using a 3-liter syringe (Hans

Rudolph, Kansas City, MO). The volume and concentration signals were time aligned by accounting for the delay in the capillary gas transit and the analyzer rise time relative to the volume signal. Calculations of $\dot{V}O_2$, CO_2 output, and minute ventilation were made using standard formulas (4) and displayed breath by breath. Heart rate was measured every 5 s using short-range radio telemetry (Polar S610, Polar Electro Oy, Kempele, Finland).

Data analysis. The breath-by-breath data from the square wave tests were used to estimate the $\dot{V}O_2$ kinetics. The data were first manually filtered to remove outlying breaths, defined as breaths deviating by more than three standard deviations from the preceding five breaths. The data were subsequently interpolated to provide second-by-second values, and the two double square wave tests under each condition were time aligned and averaged to provide one file per condition. As a result, all 10 transitions to the first bout of exercise ("control") were averaged to provide the highest possible confidence in the data subsequently modeled, whereas, for the subsequent bouts of exercise, the average of two transitions in each condition were used to characterize the response. The data were modeled using a modification of the procedure described by Rossiter et al. (45). The first 20 s of data following the onset of exercise were removed to eliminate the phase I component from the analysis. The first 2 min of data (20–120 s) were then modeled with a monoexponential function of the form:

$$\dot{V}O_2(t) = \dot{V}O_2(b) + A[1 - e^{-(t-TD)/\tau}] \quad (1)$$

where $\dot{V}O_2(t)$ is the $\dot{V}O_2$ at time t ; $\dot{V}O_2(b)$ is the baseline $\dot{V}O_2$ measured in the 60 s preceding the transition in work rate; and A , TD , and τ are the amplitude, time delay, and the time constant of the primary (phase II) response, respectively. The slow component amplitude was determined by averaging the $\dot{V}O_2$ in the last 30 s of the transition ("end-exercise $\dot{V}O_2$ ") and subtracting the "absolute" primary amplitude [i.e., $\dot{V}O_2(b) + A$] from this value. We chose to constrain the model fit to 120 s in an attempt to isolate the primary component rather than "iteratively optimizing" the fit (45), because the criteria for iterative optimization cannot be reliably applied to responses that contain a small slow component (such as those following prior heavy exercise in the present study). Additionally, the parameter estimates are little affected when a slow component emerges earlier than 120 s using a 20- to 120-s fitting window because the contribution a slow component makes to the amplitude of the response is very small over this time frame.

Statistical analysis. Main effects for all variables were determined using one-way repeated-measures analysis of variance. Statistical significance was accepted at $P < 0.05$. Specific differences between recovery durations were determined using 95% paired-samples confidence intervals, with intervals not including the null value being significantly different. The time course of recovery in blood [lactate] and the absolute primary $\dot{V}O_2$ amplitude was determined using an equation of the form:

$$y(t) = y_0 - A(1 - e^{-t/\tau}) \quad (2)$$

where $y(t)$ is the value of the variable at time t ; y_0 is the value of the variable at time 0; A is the amplitude of the response; and τ is the time constant. The Pearson product-moment correlation coefficient was used to examine the relationship between baseline blood [lactate] and the primary $\dot{V}O_2$ amplitude. All data are presented as means \pm SD unless otherwise stated.

RESULTS

The subjects' $\dot{V}O_{2\text{peak}}$ was 4.09 l/min ($52 \pm 9 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$), which was associated with a peak power output at the end of the ramp test of $383 \pm 46 \text{ W}$. The GET occurred at $2.44 \pm 0.32 \text{ l/min}$ ($60 \pm 4\% \dot{V}O_{2\text{peak}}$). The power output used for the double square wave exercise tests (70% Δ) was $286 \pm 33 \text{ W}$ (requiring an end-exercise $\dot{V}O_2$ of $\sim 97\% \dot{V}O_{2\text{peak}}$).

Table 1 shows the parameters of the $\dot{V}O_2$, heart rate, and blood lactate responses before, during, and at the end of heavy exercise in each condition. Baseline blood [lactate] was significantly elevated above the control value in all conditions [$F(4,8) = 99.27, P < 0.001$] but fell to within ~ 0.4 mM of it after 60 min of recovery. In contrast, baseline $\dot{V}O_2$ was elevated only after 10 min of recovery [$F(4,8) = 3.63, P = 0.008$], being similar to control values thereafter. Like blood [lactate], baseline heart rate was elevated after 10 min of recovery and remained so in all other conditions [$F(4,8) = 22.82, P < 0.001$], being ~ 5 beats/min higher after 60 min of recovery than before the first exercise bout.

Prior heavy exercise had no effect on the time constant of the primary component [$F(4,8) = 1.15, P = 0.348$; Table 1] but resulted in a significant increase in the primary $\dot{V}O_2$ amplitude after 10, 20, 30, and 45 min of recovery [$F(4,8) = 5.05, P = 0.001$]. By 60 min, the primary amplitude had returned to the control value. The absolute primary amplitude (the asymptote, i.e., including baseline $\dot{V}O_2$) was also significantly elevated following prior heavy exercise [$F(4,8) = 7.24, P < 0.001$], but this elevation was no longer evident following 45 min of recovery. The 95% confidence interval for the primary time constant across all conditions was 3.0 ± 1.5 s, and the 95% confidence interval for the primary amplitude was 0.04 ± 0.02 l/min. The $\dot{V}O_2$ responses in a representative subject are shown in Fig. 1, in which the subsequent bouts of heavy exercise are each superimposed on the control $\dot{V}O_2$ response. From this figure, the increased primary amplitude can be seen after 10, 20, and 30 min of recovery, whereas it is more difficult to discern after 45 min, and the response appears to be identical to the control bout after 60 min of recovery. The amplitude of the $\dot{V}O_2$ slow component was significantly reduced by prior heavy exercise after 10 min of recovery (by 0.23 ± 0.04 l/min) and was also reduced after 20 min (by 0.08 ± 0.09 l/min) and 30 min of recovery [by 0.11 ± 0.09 l/min; $F(4,8) = 23.67, P < 0.001$]. After 45 and 60 min of recovery, the slow component was similar to the response observed in the control bout. The end-exercise blood [lactate] was similar across conditions [$F(4,8) = 1.89, P = 0.12$], as was the $\dot{V}O_{2\text{peak}}$, which attained a value of $\sim 97\%$ of the $\dot{V}O_{2\text{peak}}$ measured during the ramp test [$F(4,8) = 1.18, P = 0.338$]. The end-exercise heart rate was significantly increased by prior heavy exercise in all subsequent exercise bouts by ~ 3 – 5 beats/min [$F(4,8) = 4.31, P = 0.003$; Table 1].

Figure 2 shows the time course of decline in baseline blood [lactate] (Fig. 2A), the primary $\dot{V}O_2$ amplitude (Fig. 2B), and the absolute primary amplitude (Fig. 2C). A monoexponential curve applied to the mean data demonstrated that the baseline blood [lactate] and absolute primary amplitude recovered with a broadly similar time course (time constants of 13.7 and 15.4 min for baseline blood [lactate] and the primary $\dot{V}O_2$ amplitude, respectively). Although the fit to the blood lactate data demonstrated reasonable confidence (95% confidence intervals = 3.1 min), the fit to the $\dot{V}O_2$ data was poor (95% confidence intervals = 24.4 min). The elevated baseline $\dot{V}O_2$ observed after 10 min of recovery distorted the recovery profile of the primary amplitude data presented in Fig. 2B, although the effect of priming exercise on the primary amplitude declined linearly from 20 min onward. When the absolute primary amplitude (which is not distorted by changes in the baseline $\dot{V}O_2$) was plotted against baseline blood [lactate] (Fig. 3), there was a strong positive correlation between these two variables ($r = 0.98, P < 0.003$).

DISCUSSION

The principal new finding of the present investigation was that the effect of prior heavy exercise persisted for not more than ~ 45 min and was temporally associated with the fall in blood [lactate]. The increase in the absolute primary $\dot{V}O_2$ amplitude and blood [lactate] at the onset of exercise recovered with time constants of ~ 14 – 15 min, and these changes were highly correlated.

The effect of prior heavy exercise has received a great deal of empirical attention in the last decade (3, 7–11, 21, 23, 33, 37, 40, 51). Besides being simple to administer, this intervention has profound and, as shown in the present investigation, long-lasting effects on the $\dot{V}O_2$ response. The present study demonstrated that the characteristic effects of priming exercise on $\dot{V}O_2$ kinetics (i.e., increased primary $\dot{V}O_2$ amplitude and reduced $\dot{V}O_2$ slow component) occurred only when there was a physiologically significant elevation in the baseline blood [lactate]; when blood [lactate] recovered to within ~ 0.5 mM of its initial baseline, the $\dot{V}O_2$ kinetics were not different from those observed in the control or “unprimed” condition. However, we would stress that there is no obvious mechanistic basis for an association between $\dot{V}O_2$ kinetics and blood [lactate], and we therefore consider that blood [lactate] serves only as a “proxy

Table 1. Parameters of the oxygen uptake, blood lactate, and heart rate responses to exercise

Parameter	Control	10 min	20 min	30 min	45 min	60 min
Baseline						
Baseline blood [lactate], mM	0.9±0.1	5.1±1.0*	3.1±0.9*	2.1±0.5*	1.6±0.2*	1.3±0.3*
Baseline $\dot{V}O_2$ l/min	1.11±0.11	1.20±0.12*	1.08±0.14	1.10±0.14	1.09±0.14	1.12±0.11
Baseline HR beats/min	89±11	113±7*	103±10*	98±12*	97±10*	94±12*
Primary phase						
Primary τ , s	25.9±4.7	23.9±8.8	23.2±4.7	26.4±5.9	24.6±6.8	26.0±6.0
Primary amplitude, l/min	2.42±0.39	2.53±0.41*	2.54±0.39*	2.52±0.41*	2.48±0.39*	2.43±0.40
Absolute primary amplitude, l/min	3.52±0.37	3.72±0.41*	3.62±0.40*	3.61±0.38*	3.56±0.41	3.55±0.41
End exercise						
Slow component amplitude, l/min	0.44±0.13	0.21±0.12*	0.37±0.09*	0.33±0.12*	0.43±0.17	0.44±0.14
End-exercise blood [lactate], mM	7.9±1.1	7.9±1.6	7.7±1.3	7.6±1.2	7.5±1.1	7.3±1.0
End-exercise $\dot{V}O_2$ l/min	3.97±0.39	3.93±0.42	3.99±0.43	3.94±0.39	3.99±0.39	4.00±0.42
End-exercise HR, beats/min	173±9	178±7*	176±9*	177±8*	177±8*	176±9*

Values are means \pm SE. HR, heart rate; τ , time constant; $\dot{V}O_2$, oxygen uptake; [lactate], lactate concentration. *Significantly different from the corresponding control value (95% paired-samples confidence intervals do not include zero).

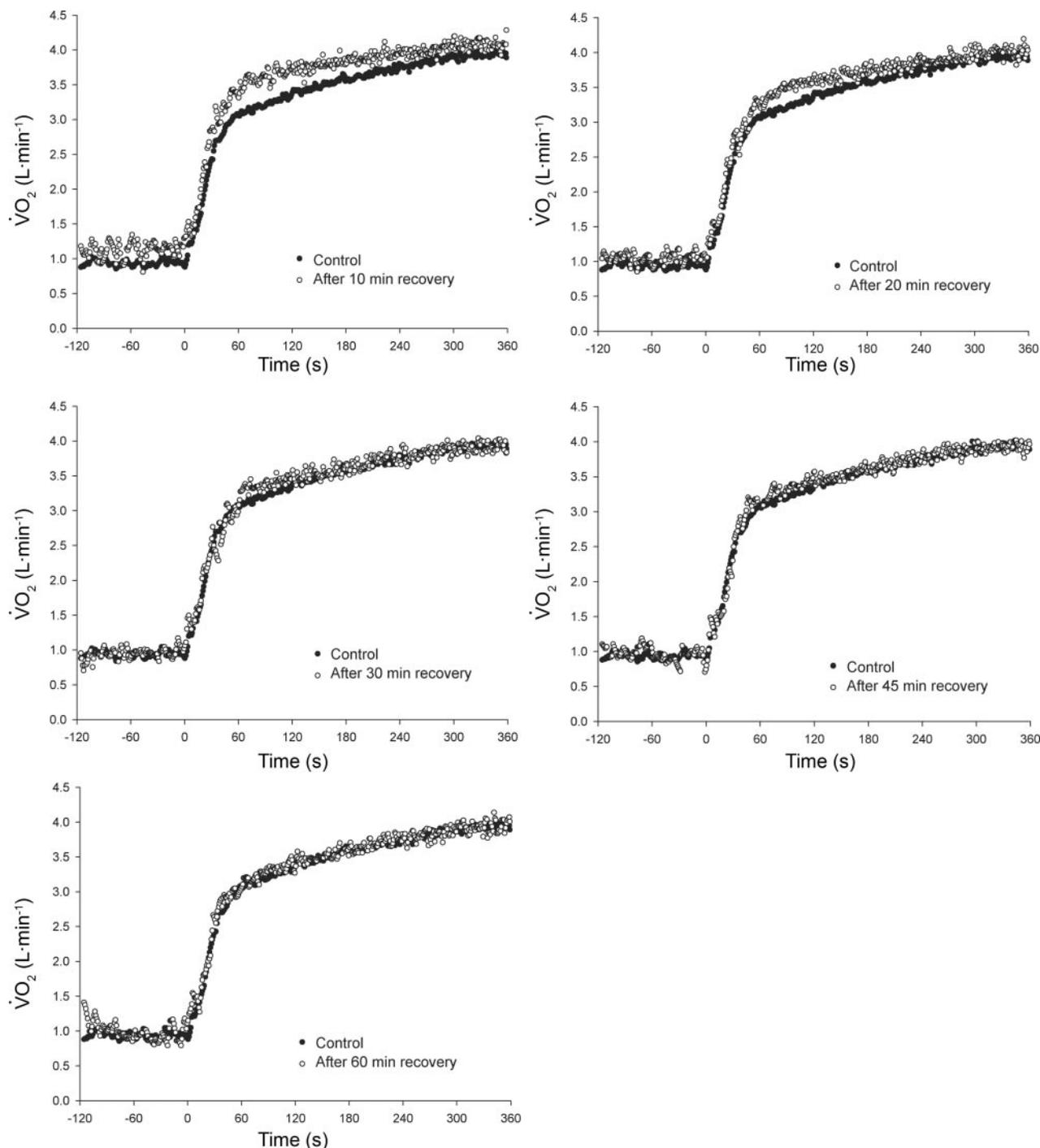


Fig. 1. Superimposed second-by-second oxygen uptake ($\dot{V}O_2$) responses during repeated bouts of heavy exercise in a representative subject. Note the elevated primary $\dot{V}O_2$ amplitude after 10 min of recovery compared with the control condition and the gradual reduction in the magnitude of the effect as the duration of the recovery between the 2 bouts is extended. After 60 min of recovery, no effect of prior heavy exercise can be observed.

variable" for another process that modulates the $\dot{V}O_2$ response to exercise.

In agreement with previous work, the primary $\dot{V}O_2$ amplitude was elevated by prior heavy exercise in the present study, and this could be detected after recovery durations of 10–45 min but not thereafter. The $\dot{V}O_2$ slow component was reduced after 10–30 min of recovery but had returned to control values after 45 and 60 min of recovery. The decay in the effect of prior heavy exercise on the primary amplitude is in contrast to

the effect of prior exercise on other parameters of the $\dot{V}O_2$ response: baseline $\dot{V}O_2$ returned to its control value after 20 min of recovery, in agreement with our previous work (8), confirming that the effects are not an artifact of an unchanged response superimposed on an elevated baseline $\dot{V}O_2$. The primary time constant was unaffected regardless of recovery duration, confirming that the effect of prior heavy exercise on the $\dot{V}O_2$ response is not, at least for upright cycle exercise, related to the rate at which $\dot{V}O_2$ adjusts in phase II of the

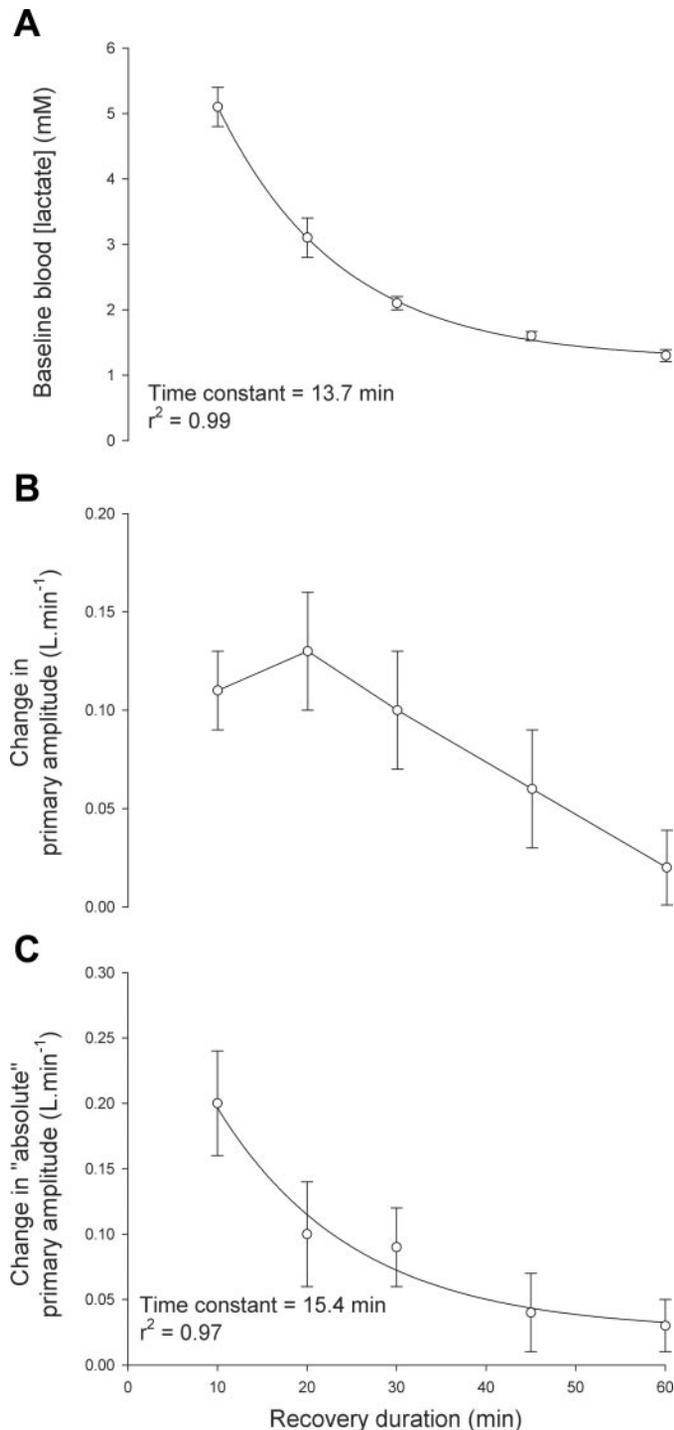


Fig. 2. Time course of recovery of baseline blood lactate concentration ([lactate]) (A), the elevation in the primary amplitude (B), and the elevation in the "absolute" primary amplitude (C). The change in the primary amplitude was calculated by subtracting the increase in $\dot{V}O_2$ above baseline in the first heavy bout from the increase in $\dot{V}O_2$ above baseline during the subsequent heavy bouts, whereas the absolute primary amplitude was calculated by subtracting the absolute primary amplitude (the increase in $\dot{V}O_2$ including the baseline $\dot{V}O_2$) in the control bout from that of the second heavy bout to prevent the increase in baseline $\dot{V}O_2$ after 10 min obscuring the relationship between the change in the primary amplitude and recovery duration. Note the exponential decay associated with the recovery of baseline blood [lactate] (A), the linear decline evident after 20 min in the primary amplitude (B), and the approximately exponential time course of recovery in the absolute primary amplitude (C). Values are means \pm SE.

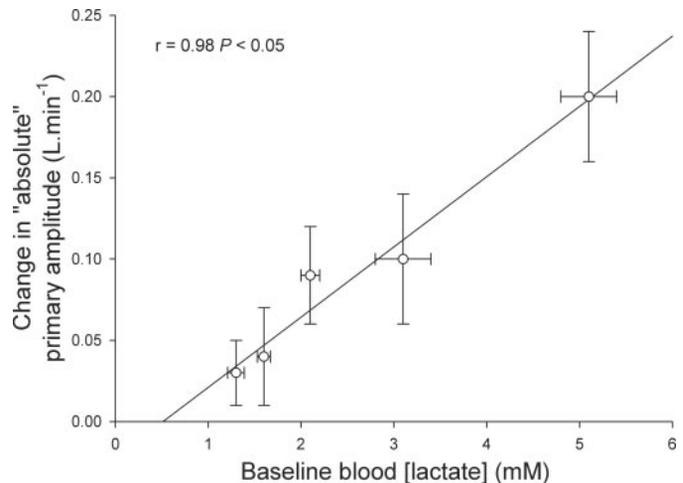


Fig. 3. Correlation between baseline blood [lactate] and the change in the primary amplitude. Each data point represents a different recovery duration. Note the strong positive correlation between the two parameters and that the x-axis intercept occurs at ~ 0.6 mM, which is close to the observed mean resting blood [lactate] (0.9 mM). Values are means \pm SE.

response. The present study has, therefore, added to previous work (8, 57) by demonstrating that the effect of prior heavy exercise decays gradually and is no longer evident after 60 min of passive recovery.

It has been suggested that prior exercise exerts its effect on the on-transient $\dot{V}O_2$ response by a number of possible mechanisms including increased muscle temperature, enhanced convective or diffusive O_2 delivery, enhanced substrate flux through pyruvate dehydrogenase, and/or increased motor unit recruitment (10). The absence of an effect of prior moderate exercise on heavy exercise $\dot{V}O_2$ kinetics (11, 23, 37) seems to rule out increased muscle temperature as a mediator, and indeed passive heating of the muscles has been shown to have no effect on the primary $\dot{V}O_2$ response (9, 30, 34). Earlier work (23, 37) suggested that an enhancement of muscle blood flow and/or O_2 unloading consequent to the lactacidosis imposed by the first heavy bout resulted in a speeded $\dot{V}O_2$ kinetic response. Both direct (35) and indirect (7, 15, 57) measurements of muscle perfusion and oxygenation demonstrate that muscle O_2 availability is indeed enhanced following prior heavy exercise. Interestingly, supine heavy exercise has been shown to reduce the primary $\dot{V}O_2$ amplitude (31), suggesting that reducing the perfusion pressure can influence the amplitude of the primary $\dot{V}O_2$ response, and hyperoxia has been shown to increase the primary $\dot{V}O_2$ amplitude (37). However, more recent work by Wilkerson et al. (56) suggests that hyperoxia had no effect on the primary $\dot{V}O_2$ amplitude, although it did reduce the amplitude of the slow component. Furthermore, neither hypoxia (18) nor recombinant erythropoietin administration (14, 58) alters the primary $\dot{V}O_2$ amplitude.

It is pertinent to consider the recovery time course of muscle blood flow in relation to the longevity of the effect of prior exercise. Although blood flow data during recovery from exercise are sparse, Van Beekvelt et al. (54) presented evidence that recovery of forearm blood flow is incomplete 20 min after heavy handgrip exercise, suggesting that the blood-flow kinetics at the cessation of exercise are considerably slower than those of the on-transient. This on-off asymmetry has also been

demonstrated in two reports using measurements of erythrocyte flux in rat spinotrapezius muscle during moderate contractions (on-transient half-time = ~ 11 s; Ref. 29) and recovery (off-transient half-time = ~ 26 s; Ref. 20). Furthermore, estimated capillary blood flow kinetics following the cessation of heavy cycle exercise in humans suggests that the response is biphasic, with a primary time constant of ~ 50 s (19). However, even assuming that, in extremis, the primary time constant for capillary blood flow was three times larger than this (four standard deviations above the mean), recovery of leg muscle blood flow would be complete within 15–20 min. Consequently, the recovery time course of muscle blood flow, although slower than the on-transient, appears to be too rapid for enhanced O_2 delivery to account for the priming effect of prior exercise.

Priming exercise has been shown to result in marked changes in the muscle metabolic profile, and Harris et al. (25) were the first to suggest that this may influence subsequent exercise metabolism and performance. Specifically, these authors showed that 4 min of intense cycle exercise substantially increased muscle acetylcarnitine concentration. This “acetyl group stockpiling” was suggested to be a major factor in the apparent speeding of $\dot{V}O_2$ kinetics observed by Campbell-O’Sullivan et al. (12). It has been demonstrated that acute activation of pyruvate dehydrogenase activity by dichloroacetate (DCA) reduces substrate-level phosphorylation during exercise in humans, which has been suggested to be a consequence of a reduction in the “acetyl group deficit” (52). Consistent with this interpretation are the complementary findings from two experiments demonstrating that both prior muscle stimulation (26) and treatment with DCA (27) resulted in speeded PO_2 kinetics in isolated myocytes. However, DCA administration does not result in any measurable change in $\dot{V}O_2$ kinetics during heavy-intensity cycle exercise in humans (28). Additionally, Rossiter et al. (44) showed that DCA administration during prone knee-extension exercise reduced the primary $\dot{V}O_2$ amplitude, in complete contrast to the effect of prior heavy exercise (7, 8). There also appears to be little correspondence between the recovery time course of the effects observed here and that of pyruvate dehydrogenase activity, because the latter has been shown to recover quite rapidly (half-time of ~ 4 min) following intense exercise (43). Therefore, the response profiles and recovery time course of the effects observed in the present study do not appear to be consistent with altered substrate flux through pyruvate dehydrogenase.

In the present study, there was a strong positive correlation between the recovery of baseline blood [lactate] and the increased primary $\dot{V}O_2$ amplitude following prior heavy exercise. Although such data can never establish causality, this relationship indicates that lactate or a related metabolite or metabolic control process with a similar recovery time course may play a role in the effect of prior heavy exercise. However, any role that lactate may have would almost certainly not be a direct one, because infusion of lactate into working dog muscle does not alter $\dot{V}O_2$ during submaximal electrical stimulation (41), and prior heavy exercise (11) or sodium lactate infusion (38) does not alter the steady-state $\dot{V}O_2$ response during moderate-intensity exercise in humans. In addition, epinephrine infusion increases blood [lactate] but does not increase $\dot{V}O_2$ during heavy exercise in humans (22). Thus, although there is a strong correlation between the time course of recovery in the $\dot{V}O_2$

response and baseline blood [lactate], we reiterate that there is no clear mechanistic link between these variables.

It has been suggested that the effect of prior heavy exercise on the $\dot{V}O_2$ response is related to an increase in motor unit recruitment at the onset of subsequent exercise, which would reduce the requirement for further motor unit recruitment as exercise continues (7). The consequence of these events when measured at the mouth might be an increased primary amplitude and a reduced $\dot{V}O_2$ slow component (7, 33, 48). The principal evidence for this notion stems from our observation of an increase in the integrated electromyogram (iEMG), which was proportional to the change in the primary $\dot{V}O_2$ amplitude with prior exercise (7). In addition, several studies have presented evidence that markers of muscle activity (iEMG, fiber-specific glycogen depletion, and magnetic resonance imaging and spectroscopy) increase in concert with the development of the $\dot{V}O_2$ slow component (36, 45, 46, 50). However, although it seems reasonable to argue that the additional recruitment of motor units as the slow component develops could be attributed to the need to support or replace fatigued muscle fibers to maintain the external power requirements (35, 44, 47), at first glance it seems unlikely that fatigue could explain the increased iEMG observed after 12 min of recovery from prior heavy exercise (7), or the time course of restoration of the primary $\dot{V}O_2$ amplitude in the present work. Maximal muscle power output has been shown to recover rapidly after a bout of heavy exercise (49), following similar kinetics to the restoration of muscle phosphorylcreatine content (45, 47). On the other hand, muscle force during low-frequency electrical stimulation (< 50 Hz) can remain depressed for many hours following fatiguing contractions (16). It has also been shown that prior muscle activity reduces the “recruitment threshold” of motor units during subsequent contractions (1, 13) and that restoration of the original thresholds may take considerably longer than the restoration of maximal voluntary force-generating capacity (13). Thus, although it is not possible to identify a mediator(s) of the priming effect in the present work, the prolonged influence of low-frequency fatigue (16) and/or alterations in motor unit recruitment strategy (1, 7, 13) cannot be ruled out.

In summary, the present study has shown that an increase in the primary $\dot{V}O_2$ amplitude with no change in the associated time constant and a reduced $\dot{V}O_2$ slow component during heavy exercise can still be observed 30–45 min following an initial heavy bout. After 60 min, however, the $\dot{V}O_2$ response had returned to its initial profile. The time course with which the effect of prior heavy exercise on the absolute primary $\dot{V}O_2$ amplitude decays is similar to the recovery time course of blood [lactate]. However, the mechanistic basis for an association between $\dot{V}O_2$ kinetics and blood [lactate] is obscure, and we therefore consider that blood [lactate] serves only as a proxy variable for another process that modulates the $\dot{V}O_2$ response to exercise. Based on the time course demonstrated herein, we suggest that factors such as O_2 delivery and pyruvate dehydrogenase activity are not likely to be responsible for the effects of prior exercise on the kinetics of $\dot{V}O_2$.

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