Effect of creatine supplementation on oxygen uptake kinetics during submaximal cycle exercise

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Jones, Andrew M., Helen Carter, Jamie S. M. Pringle, and Iain T. Campbell. Effect of creatine supplementation on oxygen uptake kinetics during submaximal cycle exercise. J Appl Physiol 92: 2571–2577, 2002.—The purpose of this study was to test the effect of oral creatine (Cr) supplementation on pulmonary oxygen uptake (\( \dot{V}\)O\(_2\)) kinetics during moderate [below ventilatory threshold (VT)] and heavy (above VT) submaximal cycle exercise. Nine subjects (7 men; means ± SD: age 28 ± 3 yr, body mass 73.2 ± 5.6 kg, maximal \( \dot{V}\)O\(_2\) 46.4 ± 8.0 ml·kg\(^{-1}\)·min\(^{-1}\)) volunteered to participate in this study. Subjects performed transitions of 6-min duration from unloaded cycling to moderate (80% VT; 8–12 repeats) and heavy exercise (50% change; i.e., halfway between VT and maximal \( \dot{V}\)O\(_2\); 4–6 repeats), both in the control condition and after Cr loading, in a crossover design. The Cr loading regimen involved oral consumption of 20 g/day of Cr monohydrate for 5 days, followed by a maintenance dose of 5 g/day thereafter. \( \dot{V}\)O\(_2\) was measured breath by breath and modeled by using two (moderate) or three (heavy) exponential terms. For moderate exercise, there were no differences in the parameters of the \( \dot{V}\)O\(_2\) kinetic response between control and Cr-loaded conditions. For heavy exercise, the time-based parameters of the \( \dot{V}\)O\(_2\) response were unchanged, but the amplitude of the primary component was significantly reduced with Cr loading (means ± SE: control 2.00 ± 0.12 l/min; Cr loaded 1.92 ± 0.10 l/min; \( P < 0.05\)) as was the end-exercise \( \dot{V}\)O\(_2\) (control 2.19 ± 0.13 l/min; Cr loaded 2.12 ± 0.14 l/min; \( P < 0.05\)). The magnitude of the reduction in \( \dot{V}\)O\(_2\) with Cr loading was significantly related to the percentage of type II fibers in the vastus lateralis (\( r = 0.87; P < 0.01; n = 7\)), indicating that the effect might be related to changes in motor unit recruitment patterns or the volume of muscle activated.

Many athletes supplement their diet with creatine (Cr) monohydrate to increase intramuscular phosphocreatine (PCr) concentration ([PCr]) and Cr concentration ([Cr]) and to improve performance in multiple-sprint activities (8, 12, 18). Relatively few studies have examined the influence of Cr supplementation on oxygen uptake (\( \dot{V}\)O\(_2\)) during exercise, and the results of these studies have been inconclusive. In one study, a reduction in whole body \( \dot{V}\)O\(_2\) was observed during repeated, maximal sprint exercise after Cr loading (1). In contrast, Rico-Sanz and Marco (30) reported a significant increase in \( \dot{V}\)O\(_2\) during high-intensity submaximal exercise at ~90% of the power output at maximal \( \dot{V}\)O\(_2\) (\( \dot{V}\)O\(_2\)\(_{max}\)). Two other studies have reported no effect of Cr loading on \( \dot{V}\)O\(_2\) during submaximal incremental exercise (37) or continuous submaximal and supramaximal exercise (2). Most of these studies measured the \( \dot{V}\)O\(_2\) response on just one occasion, and the measurement tended to be discontinuous (e.g., one measurement every 30 s) (1, 2, 37). Accurate determination of exercise \( \dot{V}\)O\(_2\) requires consideration of the measurement error, and confidence in the data may require several repeat transitions to sufficiently enhance the signal-to-noise ratio (24).

No previous studies have examined the kinetics of the \( \dot{V}\)O\(_2\) adaptation from rest to either moderate [below lactate threshold (LT)] or heavy (above the LT) submaximal exercise after Cr loading. In the transition from rest to exercise, the rate at which \( \dot{V}\)O\(_2\) adjusts to the anticipated steady-state requirement is reciprocally related to the splitting of PCr (31), but it is presently unknown what effect, if any, Cr loading has on the rate of adaptation of \( \dot{V}\)O\(_2\) at the onset of exercise. The purpose of this study, therefore, was to examine the effect of Cr loading on \( \dot{V}\)O\(_2\) kinetics, including the “steady-state” \( \dot{V}\)O\(_2\), during moderate and heavy exercise. We hypothesized that Cr loading would increase \( \dot{V}\)O\(_2\) during heavy (30) but not moderate exercise but have no effect on the time constant of the primary \( \dot{V}\)O\(_2\) response.

METHODS

Subjects. Nine healthy subjects (7 men) volunteered to participate in this study, which was approved by Manchester Metropolitan University Ethics Committee. The subjects were (means ± SD) 28 ± 3 yr of age, their body mass was 73.2 ± 5.6 kg, and their \( \dot{V}\)O\(_2\)\(_{max}\) was 46.4 ± 8.0 ml·kg\(^{-1}\)·min\(^{-1}\). The subjects were recreationally active but not highly trained. The subjects were all fully familiar with laboratory exercise.

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testing procedures. None of the subjects had ingested Cr as a supplement within 18 mo of the start of the study. The subjects were instructed to arrive at the laboratory in a rested and fully hydrated state, at least 3 h postprandial, and to avoid strenuous exercise in the 48 h preceding a test session. For each subject, tests took place at the same time of day (±2 h) to minimize the effects of diurnal biological variation on the results.

Methods. The subjects first performed a ramp exercise test (30 W/min) to the limit of tolerance on an electrically braked cycle ergometer (Ergoline, Jaeger, Germany) for the determination of the ventilatory threshold (VT) and the \( V_{\text{O2 max}} \). All tests were performed at a cadence of 75 revolutions/min. The breath-by-breath data were collected and displayed at 10-s intervals. The VT was determined visually as an increase in \( V_{\text{CO2}} \) production relative to \( V_{\text{O2 max}} \). Each exponential curve was used to describe one phase of the \( V_{\text{O2}} \) response with and without Cr loading. The subjects performed 8–12 bouts of moderate exercise and 4–6 bouts of heavy exercise in each condition (i.e., control and Cr loaded). Each square-wave exercise bout included a baseline of 3 min of unloaded cycling, 6 min of either moderate or heavy exercise, and 6 min of unloaded cycling in recovery. In any one test session, subjects performed a maximum of two transitions to moderate exercise and one transition to heavy exercise. The moderate exercise bouts always preceded the heavy exercise bouts. No more than two test sessions were performed on any day, and, where this occurred, test sessions were separated by at least 1 h. Pulmonary gas exchange was measured breath by breath during all square-wave tests (see below), and heart rate was measured every 5 s with a telemetric heart rate monitor (Polar Sports Tester, Kempele, Finland). A fingertip capillary blood sample was collected immediately before and immediately after two bouts of moderate exercise and two bouts of heavy exercise in each condition to determine change (Δ) in blood lactate concentration ([lactate]) (YSI 1500, Yellow Springs Instruments).

The subjects performed repeated bouts of moderate and heavy exercise, both in the control condition and after Cr loading. The Cr loading regimen involved the consumption of 20 g of Cr monohydrate (Highfive, Leicester, UK) per day for 5 days. The subjects dissolved the Cr in 250 ml of warm orange squash and consumed the Cr in four equally spaced doses of 5 g. It is known that this loading regimen results in a significant increase in intramuscular [Cr] and [PCr] (19, 21). The subjects then consumed a maintenance dose of 5 g Cr per day until they had completed all of the exercise bouts required in the Cr-loaded condition. The conditions were presented in a crossover design. Five subjects performed the control condition exercise bouts first before loading with Cr and performing the exercise bouts in the Cr-loaded condition. The other four subjects first loaded with Cr and were tested in this condition; these subjects were then tested in the control condition 35–50 days later to allow for Cr washout, it having been demonstrated that the time required for total muscle Cr to return to basal levels is ~4 wk (16, 25). Body mass was recorded before each exercise test session by using balance scales.

Pulmonary gas exchange was measured breath by breath during all exercise tests. Subjects breathed through a low-resistance turbine volume transducer (Jaeger Triple V), which had a dead space of 90 ml. Gas was continuously drawn down a capillary line into rapid response gas analyzers (Jaeger Oxycon Alpha, Hoechberg, Germany). \( V_{\text{O2}}, V_{\text{CO2}} \), and minute ventilation were calculated and displayed breath by breath once the delay between the volume and concentration signals had been accounted for. The volume transducer was calibrated before each test with a 3-liter calibration syringe (Hans Rudolph), and the analyzers were calibrated with certified standard gases.

The breath-by-breath data were linearly interpolated to provide second-by-second values. For each subject, the data from the repeated exercise bouts were time aligned and averaged to provide one set of second-by-second data for each variation of the protocol (i.e., control moderate, control heavy, Cr moderate, and Cr heavy). The time course of the \( V_{\text{O2}} \) response after the onset of exercise was described in terms of a two-component (moderate exercise) or three-component (heavy exercise) exponential function, by using iterative nonlinear regression techniques in which minimizing the sum of squared error was the criterion for convergence. Each exponential curve was used to describe one phase of the response. The first phase began at the onset of exercise, whereas the other terms began after independent time delays (4)

\[
\dot{V}_{\text{O2}}(t) = \dot{V}_{\text{O2}(b)} + A_i(1 - e^{-t/\tau_i}) + A_p[1 - e^{-t/T_{D2}p}] + A_s[1 - e^{-t/T_{D2}s}]
\]

where \( t \) is time; \( \dot{V}_{\text{O2}(b)} \) is the baseline \( V_{\text{O2}} \) measured in the 3 min preceding the onset of exercise; \( A_i, A_p, \) and \( A_s \) are the amplitudes of the exponential curves fitting the cardiodynamic, primary, and slow components, respectively; \( \tau_i, T_{D2}p, \) and \( T_{D2}s \) are the respective time constants; and \( T_{D1} \) and \( T_{D2} \) are the time delays. The cardiodynamic component was terminated at \( T_{D1} \) and given the value for that time. The amplitude of the primary response \( (A_p) \) was defined as the increase in \( \dot{V}_{\text{O2}} \) from baseline to the asymptote of the primary component. The absolute amplitude of the primary \( \dot{V}_{\text{O2}} \) response was calculated as the sum of baseline \( \dot{V}_{\text{O2}} \) and \( A_p \). The amplitude of the \( \dot{V}_{\text{O2}} \) slow component was determined as the increase in \( \dot{V}_{\text{O2}} \) from \( T_{D2} \) to the end of exercise, rather than from the asymptotic value \( (A_s) \), which may project beyond the value at 6 min (end exercise). In addition to the kinetic analysis, the absolute \( \dot{V}_{\text{O2}} \) values around 2 and 6 min were checked, but these did not differ from the parameters derived from the model.

Muscle biopsies. Seven of the subjects had undergone a muscle biopsy of the vastus lateralis within 12 wk of their participation in the present study as part of another experiment in our laboratory (28). Briefly, ~200 mg of muscle were obtained from the lateral portion of the right vastus lateralis muscle with a conchotome biopsy procedure under local anesthetic (1% lignocaine hydrochloride). Standard histochemical procedures were used for the determination of myofibrillar ATPase activity, and muscle fibers were subsequently classified as either type I or type II, according to their pH lability. Muscle fiber type was expressed as a percentage of the number of fibers of each type counted relative to the total number of fibers counted.

Statistical analysis. The results were analyzed by using two-tailed paired t-tests with significance accepted when \( P < 0.05. \) The relationship between muscle fiber type and changes in \( \dot{V}_{\text{O2}} \) with Cr loading was explored by using Pearson's product-moment correlation coefficient. The results are presented as means ± SE.
RESULTS

The Cr loading regimen caused a significant increase in body mass (from 73.2 ± 1.9 to 74.2 ± 1.8 kg; P < 0.05), whereas there was no change in the control condition (from 73.2 ± 1.9 to 73.3 ± 2.0 kg).

The results for moderate exercise are shown in Table 1. There were no significant differences in the parameters of the VO₂ kinetic response between the control and Cr-loaded conditions.

The results for heavy exercise are shown in Table 2. There were no significant differences in the temporal features of the VO₂ response (i.e., time constants and time delays) between the two conditions. However, both the amplitude of the primary VO₂ response and the end-exercise VO₂ were significantly reduced in the Cr-loaded condition (P < 0.05; Fig. 1). The reduction in VO₂ with Cr loading was significantly correlated with the percentage of type II muscle fibers in the vastus lateralis (r = 0.87; P < 0.01; n = 7; Fig. 2). Blood lactate accumulation was also significantly reduced after Cr loading (P < 0.05; Table 2).

In the control condition, the time constant of the primary component was significantly longer (i.e., the kinetics were slower) for heavy exercise (27.1 ± 2.2 s) compared with moderate exercise (17.3 ± 1.7 s; P < 0.05). Furthermore, the gain of the primary component (A/5(power output)) was significantly lower in heavy exercise (9.9 ± 0.6 ml·min⁻¹·W⁻¹) than in moderate exercise (10.8 ± 0.5 ml·min⁻¹·W⁻¹; P < 0.05).

DISCUSSION

The primary original finding of this study is that Cr loading leads to a significant reduction in VO₂ during heavy, but not moderate, submaximal exercise, with no change in the time constant of the primary component.

It is perhaps not surprising that Cr loading had no effect on the time constant of the fundamental VO₂ response. It could be considered that a significantly greater contribution of PCr hydrolysis to the ATP turnover after Cr loading might spare O₂ demand and slow the VO₂ on-kinetics. Alternatively, because the fundamental increase in VO₂ at the onset of exercise is temporally linked to the splitting of PCr (31), additional PCr hydrolysis per unit time after Cr loading might be expected to speed the VO₂ kinetics. The Cr loading regimen that we used would be expected to increase total muscle Cr by 15–20% with 25–40% of this being stored as PCr (12, 21). However, there is presently no evidence that Cr loading increases the magnitude of PCr hydrolysis in a single rest-to-exercise transition (12, 35). For example, in the study of Snow et al. (35), the reduction in intramuscular [PCr] (from 86.1 mmol/kg dry mass at rest to 38.9 mmol/kg dry mass after 20 s of maximal cycle sprinting) after Cr loading was similar to the reduction in the control condition (from 83.8 mmol/kg dry mass at rest to 34.7 mmol/kg dry mass).

Our finding of an ~4% reduction in VO₂ during heavy exercise after Cr loading was in contrast to our hypothesis and is intriguing. Our subjects performed multiple repeats from unloaded cycling to moderate (8–12 transitions) and heavy exercise (4–6 transitions) in a crossover design, and we are, therefore, confident that this effect is real and is not the result of experimental error or noise in the data. A reduction in VO₂ during heavy exercise after Cr loading was evident in all nine subjects, although the effect was small in some subjects. On average, there was no difference between the response of the group that performed the control tests first and the group that performed the Cr-loaded tests first, indicating that 35–50 days were sufficient to allow muscle [Cr] to return to normal in the latter group (16, 25).

Only a limited number of previous studies have measured VO₂ during exercise with and without Cr loading (1, 2, 30, 37). Balsom et al. (1) reported a reduction in VO₂ after the seventh bout of repeated supramaximal cycling exercise with the use of Douglas bag collections of expired air. However, Balsom et al. (2) could detect no change in VO₂ during continuous running at ~120% VO₂max after Cr loading, and Stroud et al. (37) reported no difference in VO₂ during submaximal incremental treadmill exercise. In both of these studies, VO₂ was not analyzed breath by breath but was averaged over 30-s periods, and the exercise bouts were only performed once. It is possible that, with only one measurement,

Table 1. Response of oxygen uptake in the transition from unloaded cycling to moderate exercise in the control and creatine-loaded conditions

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Creatine</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline VO₂, l/min</td>
<td>0.64 ± 0.03</td>
<td>0.61 ± 0.03</td>
<td>NS</td>
</tr>
<tr>
<td>TD₁, s</td>
<td>27.2 ± 2.1</td>
<td>19.0 ± 1.3</td>
<td>NS</td>
</tr>
<tr>
<td>Primary τ, s</td>
<td>17.3 ± 1.7</td>
<td>19.0 ± 1.3</td>
<td>NS</td>
</tr>
<tr>
<td>Primary amplitude, l/min</td>
<td>0.76 ± 0.05</td>
<td>0.73 ± 0.05</td>
<td>NS</td>
</tr>
<tr>
<td>Blood [lactate], mM</td>
<td>−0.05 ± 0.1</td>
<td>0.05 ± 0.1</td>
<td>NS</td>
</tr>
<tr>
<td>End-exercise HR,</td>
<td>106 ± 5</td>
<td>106 ± 4</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are means ± SE. VO₂, oxygen uptake; TD, time delay; τ, time constant; [lactate], lactate concentration; HR, heart rate; NS, not significant.

Table 2. Response of oxygen uptake in the transition from unloaded cycling to heavy exercise in the control and creatine-loaded conditions

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Creatine</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline VO₂, l/min</td>
<td>0.67 ± 0.03</td>
<td>0.64 ± 0.03</td>
<td>NS</td>
</tr>
<tr>
<td>TD₁, s</td>
<td>19.1 ± 1.5</td>
<td>18.1 ± 1.7</td>
<td>NS</td>
</tr>
<tr>
<td>Primary τ, s</td>
<td>27.1 ± 2.3</td>
<td>27.8 ± 2.2</td>
<td>NS</td>
</tr>
<tr>
<td>Primary amplitude, l/min</td>
<td>2.00 ± 0.12</td>
<td>1.92 ± 0.10</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>SC amplitude, l/min</td>
<td>115.7 ± 10.9</td>
<td>125.7 ± 9.4</td>
<td>NS</td>
</tr>
<tr>
<td>End-exercise VO₂,</td>
<td>0.20 ± 0.06</td>
<td>0.20 ± 0.04</td>
<td>NS</td>
</tr>
<tr>
<td>l/min</td>
<td>2.19 ± 0.11</td>
<td>2.12 ± 0.12</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Blood [lactate], mM</td>
<td>3.4 ± 0.4</td>
<td>2.8 ± 0.4</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>End-exercise HR,</td>
<td>158 ± 4</td>
<td>155 ± 4</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are means ± SE. SC, slow component.
noise in the data (24) obscured any difference in \( \dot{V}_O_2 \) between the conditions. Also, in running, an increase in body mass resulting from the Cr loading will increase the energy cost of running at a particular submaximal speed, and it is possible that this could counteract any reduction in \( \dot{V}_O_2 \) that might otherwise have been evident. Recently, Rico-Sanz and Marco (30) reported that the total volume of oxygen consumed by trained cyclists during 3-min periods of cycling at 90% of the power output at \( \dot{V}_O_2_{\text{max}} \) was greater after Cr loading. However, in that study, the order of testing in the experimental group was not randomized; i.e., subjects were always tested in the control condition first. In addition, there was a trend for total \( \dot{V}_O_2 \) to also be higher at the same exercise intensity in the group who consumed a placebo, and it is not clear whether this effect was accounted for in the statistical analysis.

It has been demonstrated that the addition of Cr to skeletal or cardiac muscle cell cultures increases the rate of oxidative phosphorylation (7, 34, 41). It has been proposed that a Cr-PCr shuttle exists in which Cr is transported to the mitochondria and PCr is delivered to the sites at which energy is required (7). The activity of Cr kinase in the mitochondrial intermembrane space is coupled with the rate of aerobic respiration (32), and it has been suggested that the increased rate of oxidative phosphorylation after the addition of Cr to cultures of cardiomyocytes results from an increased sensitivity of respiration to ADP (33). The PCr-to-Cr ratio, which dictates the free ADP concentration, is reduced with Cr loading, and this should, in theory, stimulate mitochondrial respiration. ADP appears to be restricted to the outer mitochondrial membrane in cardiac and type I muscle fibers (32), and this restriction might explain the influence of Cr on the rate of respiration in these fibers (33). Differences in the regulation of respiration between type I and type II skeletal muscle fibers have been reported previously, and this appears to result from differences in mitochondrial function (13, 43). The addition of Cr to cultures of type II muscle fibers has not been shown to cause an increased respiratory rate (23). On the other hand, a positive correlation has been reported between the proportion of type I fibers and the increase in the rate of aerobic respiration when Cr was added to a culture of human skeletal muscle fibers (39). These observations might help to explain the discrepancy between the present study, in which \( \dot{V}_O_2 \) was reduced during heavy, submaximal exercise after Cr loading, and the study of Rico-Sanz and Marco (30), in which \( \dot{V}_O_2 \) appeared to be increased after Cr loading at a similar exercise intensity. The subjects in the study of Rico-Sanz and Marco were highly trained long-distance cyclists (\( \dot{V}_O_2_{\text{max}} \sim 64 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1} \)), whereas our subjects were recreationally active in a number of sports but not well trained (\( \dot{V}_O_2_{\text{max}} \sim 46 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1} \)). It is quite possible, therefore, that there were differences in the proportion of type I fibers in the active muscles between the subject groups. Seven of our subjects had undergone a muscle biopsy of the vastus lateralis within 12
of their participation in the present study as part of another experiment in our laboratory (28). There was a significant correlation between the percentage of type II fibers in the vastus lateralis and the reduction in $A_P$ (i.e., the $\dot{V}_\text{O}_2$ at the end of the primary adaptive phase) during heavy exercise (Fig. 2). In other words, subjects with a higher proportion of type II muscle fibers evidenced a larger reduction in $\dot{V}_\text{O}_2$ during heavy exercise after Cr loading.

It is unlikely that the energy turnover would have been reduced for the same power output after Cr loading. Therefore, it has to be considered that Cr loading alters muscle efficiency (i.e., it increases oxidative coupling efficiency, P/O) in some way. It has previously been demonstrated that subjects with a high proportion of type II fibers have a lower gain of the primary component (and a larger contribution of the $\dot{V}_\text{O}_2$ slow component to the end-exercise $\dot{V}_\text{O}_2$) than subjects with a low proportion of type II fibers (4). Pringle et al. (28) have also shown that the proportion of type II fibers is negatively related to the gain of the $\dot{V}_\text{O}_2$ primary component during heavy and severe, but not moderate, exercise. It is possible, therefore, that Cr loading affects the pattern of motor unit recruitment during heavy exercise. Evidence for this includes the following: 1) muscle fiber type is only related to the amplitude of the $\dot{V}_\text{O}_2$ primary component during exercise above the LT, where type II muscle fibers are likely to be recruited (4, 28), and Cr loading lowered $\dot{V}_\text{O}_2$ during heavy but not moderate exercise (Fig. 1); and 2) the effect of Cr loading was greater in subjects with a high proportion of type II fibers (Fig. 2). It is presently unclear why a predominance of type II muscle fibers is related to improved efficiency (i.e., lower $\dot{V}_\text{O}_2$ for the same power output) during both constant-load (4, 28) and incremental (5) exercise in humans when, in vitro, type II fibers produce greater heat and consume more oxygen for the same tension development (13, 17).

Whereas a greater recruitment of type II fibers during heavy exercise after Cr loading is one explanation for our results, an alternative explanation is that Cr loading causes a reduction in the total amount of muscle mass recruited. It is unclear whether the increase in fat-free mass seen with Cr loading (15) is the result of increased protein synthesis or is due simply to water retention. However, there is evidence that Cr loading reduces EMG activity during submaximal exercise (36). It has been suggested that the increase in muscle PCr availability resulting from Cr loading might reduce the rate of muscle fatigue by reducing the rate of anaerobic glycolysis and, therefore, the degree of intramuscular acidosis (29, 42). It has been estimated that a relatively high proportion of the energy cost of muscle contraction (30–50%) can be attributed to processes independent of the actomyosin-ATPase, such as the activities of the sarcoplasmic reticulum Ca$^{2+}$-ATPase and the sarcolemmal Na$^+$-K$^+$-ATPase (38). If fewer muscle fibers are recruited to meet the ATP requirement of performing the external work after Cr loading, the ATP cost of the “support processes” involved in maintaining intracellular homeostasis may be reduced. This, in turn, could explain a reduction in whole body $\dot{V}_\text{O}_2$. Additional studies are needed to clarify the mechanism by which $\dot{V}_\text{O}_2$ during heavy exercise is reduced after Cr loading.

There was no significant change in the respiratory exchange ratio during either moderate (~0.94) or heavy (~1.05) exercise after Cr loading. Therefore, the reduced $\dot{V}_\text{O}_2$ during heavy exercise cannot be explained by a shift in substrate utilization toward additional carbohydrate oxidation. Indeed, the accumulation of blood lactate over the 6-min bout of heavy exercise was significantly reduced after Cr loading. Assuming that a 1.0 mM increase in blood lactate above resting values is equivalent to the consumption of ~3.0 ml O$_2$/kg body mass (14) and that the increase in blood [lactate] reflects muscle lactate production to a similar extent in the two conditions, it can be estimated that Cr loading spared O$_2$ demand by an additional ~132 ml. It is interesting to speculate on whether the small reduction in the energy cost of heavy exercise after Cr loading (evidenced by significant reductions in both pulmonary $\dot{V}_\text{O}_2$ and $\Delta$blood (lactate)) might enhance exercise performance. In running, it is possible that any advantage from the Cr loading might be negated by the concurrent increase in body mass, which would tend to increase the energy cost of exercise. In cycling, where body mass is less important to performance, at least on the flat, it is feasible that Cr loading could enhance endurance exercise performance. To date, relatively few studies have examined this possibility. However, in the study of Rico-Sanz and Marco (30), subjects’ time to exhaustion during alternating cycling at 30 and 90% of the power output at $\dot{V}_\text{O}_2$ max was significantly increased from ~30 to ~37 min after Cr loading, with no significant change in the placebo group. Additional studies are needed to examine the influence of Cr feeding on performance in non-weight-bearing endurance activities.

An important issue in the study of $\dot{V}_\text{O}_2$ kinetics is whether the time constant of the primary component is increased (i.e., the kinetics are slowed) during heavy compared with moderate exercise. The literature is equivocal on this issue, with some studies demonstrating slower primary $\dot{V}_\text{O}_2$ kinetics during heavy exercise (e.g., Ref. 27) and others demonstrating no change (e.g., Ref. 6). Studies demonstrating slower kinetics have been interpreted as evidence that the primary kinetics are limited by O$_2$ availability during heavy exercise (40). It has been suggested that previous studies that have addressed this issue have used an insufficient number of transitions and/or subjects to allow confidence in the data (20). Given that we used a large number of transitions in the present study, it may be pertinent to comment on differences in the kinetic features of the $\dot{V}_\text{O}_2$ response to moderate and heavy exercise in the control condition. In the present study, the time constant of the primary component was significantly longer for heavy exercise (27.1 ± 2.2 s) than for moderate exercise (17.3 ± 1.7 s). It is unclear why these results differ from our laboratory’s previous observations of no difference in the primary time con-
stant between moderate and heavy cycle exercise (9, 10). It was also of interest that the gain of the primary component during heavy exercise is consistent with there being a greater recruitment of type II muscle fibers and, therefore, a greater contribution of the characteristics of VO2 in type II fibers to the overall pulmonary VO2 signal during heavy exercise. The time constant of VO2 at the onset of contraction is longer in isolated (rost) muscles with a predominance of type II fibers (22), and the time constant of the primary component during heavy exercise is longer in subjects with a high proportion of type II fibers in the vastus lateralis (28). Furthermore, ΔVO2/Δpower output is lower in subjects with a high proportion of type II muscle fibers during both ramp exercise (5) and constant-load exercise above the LT (4, 28).

In conclusion, this study has shown that Cr loading causes a small but significant reduction in VO2 during heavy, but not moderate, submaximal exercise, with no change in the primary time constant. The reduction in VO2 was present at the end of the primary component and persisted throughout the exercise bout. It is possible that Cr loading influences motor unit recruitment patterns or the volume of muscle mass recruited during heavy submaximal exercise, but additional studies are needed to clarify the mechanism responsible for this effect.

REFERENCES


