Creatine enhances oxygen uptake and performance during alternating intensity exercise

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ABSTRACT

RICO-SANZ, J. and M. T. MENDEZ MARCO. Creatine enhances oxygen uptake and performance during alternating intensity exercise. Med. Sci. Sports Exerc., Vol. 32, No. 2, pp. 379–385, 2000. Purpose: The main purpose of the present study was to measure the total oxygen consumed, accumulation of blood metabolites, and performance during alternating intensity exercise before and after a period of creatine (Cr) loading in well-trained humans. Methods: Fourteen males were randomly assigned to two groups of seven males and were tested before and after 5 d of placebo (PL) or Cr monohydrate (CR) loading (20 g d⁻¹). Oxygen uptake was measured using a breath-by-breath system during bicycle exercise alternating every 3 min between bouts at 30%(-30%) and 90% (-90%) of the maximal power output to exhaustion. Blood samples were also obtained at rest, before the end of each cycling load, at exhaustion, and 5-min postexercise. Results: The oxygen consumed during 1–90% (5.08 ± 0.39 L) and 2–90% (5.32 ± 0.30 L) was larger after CR (5.67 ± 0.34 and 5.78 ± 0.35 L, P < 0.01 and P < 0.05, respectively). Blood ammonia accumulation at the end of 1–90% (23.1 ± 6.5 μmolL⁻¹) and 3–30% (64.7 ± 15.2 μmolL⁻¹) was lower after CR (P < 0.05), whereas plasma uric acid accumulation was lower at exhaustion (P < 0.05) and 5-min postexercise (P < 0.01). Time to exhaustion increased (P < 0.05) from 29.9 ± 3.8 to 36.5 ± 5.7 min after CR, whereas it remained the same after PL. Conclusions: The results indicate that Cr feeding increases the capacity of human muscle to perform work during alternating intensity contraction, possibly as a consequence of increased aerobic phosphorylation and flux through the creatine kinase system. Key Words: ENERGY, FATIGUE, MUSCLE CONTRACTION, OXIDATIVE METABOLISM

It has recently been demonstrated that regimens of creatine (Cr) supplementation of 3 to 30 g·d⁻¹ for 3 (higher doses) to 14 d (lower doses) can increase the intramuscular levels of phosphocreatine (PCr) and primarily free Cr in humans (3,8,10,13,15,16,27,28,39). Associated with the increments in total Cr (TCr), some studies have reported increases in muscle performance after Cr supplementation (1,3,7,8,14), although others have not found significant changes (2,23,27,39). The extent of the increment of TCr appeared to influence PCr levels after 2 min of recovery from ischemic or sprint exercise (13,39). These results indicated enhanced oxidative phosphorylation after Cr loading because the resynthesis of PCr in human muscle is believed to occur solely in the presence of oxygen. Also, lower PCr degradation and pH drop during repeated isometric exercise in humans have been found, which suggests that oxidative phosphorylation is enhanced during the exercise periods (28). However, in one study a decrease in oxygen uptake during repeated maximal sprints was observed after Cr supplementation (1). In two other studies, the whole-body oxygen consumption during continuous supramaximal and submaximal (2) as well as submaximal incremental exercises (40) was not altered after Cr feeding. In the first study (1), the oxygen uptake measurements were made from analysis of gas expired in Douglas bags obtained after the seventh exercise bout of supramaximal intensities of cycling. In the latter two studies, the oxygen uptake measurements were obtained only every 30 s during a treadmill run to exhaustion at about 120% of maximal oxygen uptake (2) and during the last 30 s of 6-min exercise bouts at different intensities ranging from 50% to 90% of maximal oxygen uptake (40). Examination of the oxygen uptake with these procedures cannot accurately determine the dynamic changes in the rate of oxygen uptake and the total oxygen consumed during the entire exercise periods. Thus, the main purpose of the present study was to determine changes in oxygen uptake before and after a period of Cr loading in highly trained humans using a breath-by-breath system that permitted a precise quantification of the kinetics of oxygen consumption and the total oxygen consumed during alternating intensity exercise.

METHODS

Subjects. Fourteen highly trained cyclists volunteered to participate in the study, which was performed during 2
wk of the preparation of their competitive season. Subjects were completing about 400–700 km of cycling in a 5–7 d-wk⁻¹ training period, and they had been involved in cycling for at least 3 yr. One of the subjects had competed in the Giro de Italia and Tour de France. Before the initiation of the study, subjects were informed of the procedures involved with the experiment, and they gave a signed consent to participate in the study. The procedures were approved by the local ethics committee.

**Max test protocol.** On a familiarization visit to the laboratory during the first week, subjects performed an incremental test to exhaustion on an electronically-braked bicycle ergometer (Ergoline, Germany) to determine maximal oxygen uptake rate (VO₂max). Before the maximal test, subjects warmed up for 5 min at a load of 50 W and rested on the bicycle for 1 min. Toe clips were used to secure the subjects’ feet to the pedals. During the test, the load was incremented by 20 W every min until volitional exhaustion. Subjects pedaled at 75 rpm and the criteria for termination of the test was defined as the time when subjects dropped pedaling below 70 rpm. Whole body VO₂ and VCO₂ were measured continuously breath by breath with a CPX system (Medical Graphics, St. Paul, MN). The system was calibrated before each test with standard gases.

**Alternating intensity exercise protocol.** On the two experimental visits before and after supplementation, subjects performed an alternating intensity bicycle protocol. Subjects’ body mass was obtained with a clinical scale before each test with standard gases.

**RESULTS**

**Blood metabolites.** Before each test, a Teflon catheter (Perfusend, Sendal SA, Caceres, Spain) was inserted into a forearm vein and was kept patent during exercise with an infusion of heparin-free isotonic saline (Farmacia Antibioticos Farma SA, Madrid, Spain). Before the commencement of the exercise protocol and while the subject was resting on the bicycle, a baseline blood sample was taken. During the exercise, blood samples were taken 5 s before every change of exercise intensity with the exception of the change from warm-up to the first 30% (1–30%) exercise bout. Blood lactate was analyzed using an automated lactate analyzer (YSI 23 L, Yellow Springs Instruments, Yellow Springs, OH) and blood ammonia was analyzed with an Ammonia Checker II (Menarini Diagnostics, Kyoto, Japan). Plasma uric acid, nonesterified fatty acids (NEFA) and glycerol were analyzed in an autoanalyzer (RA-500, Technicon, Quimica Farmaceutica, Bayer, SA, Barcelona, Spain). Uric acid was measured using a method reported by Fossati et al. (11), and NEFA and glycerol were determined using the methods of Duncombe (9) and Nägele et al. (24), respectively.

**Supplementation period.** Subjects were requested to follow their habitual daily training and diet during the 2 wk of the experiment. Subjects’ daily activity and dietary intake during the 24 h preceding the experimental tests were recorded by one experimenter in a detailed interview with the subjects. The records were thoroughly examined to check for similarity of activity and diet in both experimental visits. During 5 d before the second experimental visit, subjects were randomly assigned based on the results of the max test and the alternating intensity tests to either ingest 20 g d⁻¹ of creatine monohydrate (CR) (Laboratorios Rubió S.A., Barcelona, Spain) or 20 g d⁻¹ of lactose (PL) in a double-blind design. Subjects were instructed to ingest 5 g of Cr or lactose in powder in easily dissolvable capsules (0.5 g each) with 250 mL of fruit juice immediately after breakfast, lunch, late afternoon snack, and dinner.

**Statistical analysis.** Values are expressed as mean ± SE. Repeated-measures ANOVA was used to evaluate changes after CR or PL in the variables examined. A post hoc Scheffé F-test was used whenever statistical significance was found. Statistical significance level was P < 0.05.

**Subject characteristics and muscular performance.** Subjects’ average ages were 22.8 ± 1.2 yr (CR) and 24.5 ± 1.7 yr (PL). Their max VO₂ was 4.43 ± 0.23 L·min⁻¹ (CR) and 4.29 ± 0.04 L·min⁻¹ (PL), and their maximal power output was 352 ± 16 (CR) and 361 ± 11 W (PL). Body weight increased after CR supplementation (67.6 ± 2.3 kg preCR and 68.0 ± 2.5 kg postCR), but the change was not significant. The body weight in the PL group was 68.0 ± 2.7 and 68.0 ± 2.5 kg before and after treatment, respectively. The time to exhaustion preCR was 29.9 ± 3.8 min and increased to 36.5 ± 5.7 min postCR (P < 0.05). In the PL group, subjects fatigued after 38.1 ±
Baseline levels of blood ammonia before and after CR were 16.5 ± 2.4 and 12.4 ± 2.4 μmol·L⁻¹, respectively. The blood ammonia accumulation at the end of 1–90% (23.1 ± 6.5 μmol·L⁻¹) and 3–30% (64.7 ± 15.2 μmol·L⁻¹) was lower ($P < 0.05$) after CR (10.5 ± 3.7 and 42.3 ± 9.2 μmol·L⁻¹, respectively) (Fig. 2a). The accumulation of blood ammonia at exhaustion was 88.0 ± 15.2 and 66.5 ± 6.7 μmol·L⁻¹ before and after CR, respectively (NS). Before CR, the concentrations of blood ammonia at exhaustion

5.6 and 40.8 ± 5.7 min pretreatment and posttreatment, respectively (NS). The time to exhaustion at only 90% of MPO (317 ± 15 W for CR and 325 ± 10 W for PL) was 12.0 ± 1.8 min preCR and increased to 15.2 ± 2.8 postCR ($P < 0.05$). The corresponding times in the PL group were 16.0 ± 2.8 and 17.4 ± 2.8 min (NS).

**Ventilatory parameters.** The oxygen consumed during warm-up at 20% of MPO and the first 30% (1–30%) bout were not altered after Cr supplementation. Similarly, the time constants of the rate of oxygen consumption of 18.3 ± 1.1 s at 20% MPO and 24.8 ± 2.3 s at 1–30% were not different compared with those of the PL group; they were not altered after supplementation. However, during the first and second 90% work bouts, the oxygen uptake increased significantly ($P < 0.01$, $P < 0.05$, respectively) after CR (Table 1). The sum of oxygen uptake during the two bouts at 90% (10.40 ± 0.65 L) was also significantly higher ($P < 0.05$) after CR (11.45 ± 0.71 L). On the other hand, the oxygen consumed throughout the two bouts at 90% did not change significantly after PL (11.31 ± 0.50 vs 11.82 ± 0.34 L). The sum of the oxygen uptake during the exercise bouts that all subjects completed (the warm-up, three bouts at 30%, and two bouts at 90% MPO) was significantly larger ($P < 0.05$) after CR (18.20 ± 0.84 vs 19.28 ± 0.98 L). However, the corresponding values for the PL group were not significantly different. The rate constant of the oxygen uptake of the PL group during the 1–90% and the 2–90% were not different than those of the CR group (30.9 ± 1.9 and 24.9 ± 1.4 s, respectively). The decay constants of the CR group for the 2–30% and 3–30% bouts (38.7 ± 1.8 and 39.2 ± 3.3 s, respectively) were not different in the PL group. These time constants were not affected by the supplementation. The rate of ventilation and of carbon dioxide production throughout the protocol did not change after CR or PL.

**Blood metabolites.** The average blood lactate at rest was 1.3 ± 0.2 mmol·L⁻¹ preCR and was 1.2 ± 0.2 mmol·L⁻¹ postCR. The average resting lactate values before and after PL were 1.3 ± 0.2 and 1.2 ± 0.2 mmol·L⁻¹, respectively. The accumulation of lactate remained the same throughout the exercise protocol in both protocols (Fig. 1). At exhaustion, the lactate concentrations in the CR group before and after supplementation were 10.0 ± 1.1 and 8.9 ± 1.0 mmol·L⁻¹, respectively. The corresponding values in the PL group were 8.8 ± 0.8 and 9.3 ± 0.9 mmol·L⁻¹, respectively.

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**Table 1.** Mean ± SE data for oxygen consumed (L) during 5 min of warm-up (W-UP), and 3 min alternating 30% and 90% of the max power output before and after creatine monohydrate (CR) or placebo (PL). Values are shown for those intensities during which all subjects were able to sustain the work load.

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<td>PRE</td>
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<td>W-UP</td>
<td>2.59 ± 0.16</td>
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<td>1-30%</td>
<td>0.98 ± 0.08</td>
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<td>1-90%</td>
<td>5.08 ± 0.39</td>
<td>5.67 ± 0.34†</td>
<td>5.63 ± 0.25</td>
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<td>2-30%</td>
<td>2.12 ± 0.11</td>
<td>2.17 ± 0.18</td>
<td>1.97 ± 0.18</td>
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<td>2-90%</td>
<td>5.52 ± 0.30</td>
<td>5.78 ± 0.35††</td>
<td>5.68 ± 0.27</td>
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<td>3-30%</td>
<td>2.10 ± 0.12</td>
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<td>1.96 ± 0.14</td>
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* $P < 0.05$.
† $P < 0.01$.

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![Figure 1](image-url) **Figure 1**—Blood lactate accumulation (mean ± SE) during alternating intensity bicycling exercise to exhaustion precreatine and postcreatine monohydrate (CR) (a) or placebo (PL) (b) loading. The data points correspond to rest, end of 1–30% (8 min), 1–90% (11 min), 2–30% (14 min), 2–90% (17 min), 3–90% (20 min), at exhaustion, and 5-min postexhaustion. At exhaustion and 5-min postexhaustion are shown because some subjects fatigued during the 3–90%. The exhaustion point in the figure corresponds to 29.9 ± 3.8 min (PRE) and 36.5 ± 5.7 (POST) in the CR group, and to 38.1 ± 5.6 (PRE) and 40.8 ± 5.7 (POST) in the PL group.
and 5 min after exhaustion were 104.1 ± 15.3 and 85.3 ± 12.9 μmol·L⁻¹, respectively, and after CR they were 78.8 ± 6.5 and 64.1 ± 8.2, respectively. The resting blood ammonia concentration before and after PL was 8.8 ± 1.8 and 14.1 ± 2.9 μmol·L⁻¹, respectively. The accumulation of ammonia during the entire protocol followed the same time-course before and after PL (Fig. 2b). The blood ammonia concentration at exhaustion was 68.8 ± 10.6 and 85.3 ± 10.0 μmol·L⁻¹ before and after PL, respectively. Also in PL, 5 min of recovery decreased the ammonia concentration to 48.2 ± 8.8 and 65.9 ± 6.7 μmol·L⁻¹ before and after treatment, respectively.

Uric acid accumulation after CR was significantly lower at exhaustion (47.8 ± 8.6 vs 34.1 ± 5.5 μmol·L⁻¹, \(P < 0.05\)) and 5 min postexercise (43.5 ± 5.9 vs 25.5 ± 4.2 μmol·L⁻¹, \(P < 0.01\)) (Fig. 3). On the other hand, NEFA and glycerol remained unchanged during the exercise protocol after treatment, although for some unknown reason the glycerol accumulation was higher (\(P < 0.05\)) at exhaustion after PL.

**DISCUSSION**

The main purpose of this study was to investigate the effects of Cr loading on oxygen uptake, accumulation of blood metabolites, and performance during alternating intensity exercise in highly aerobically trained humans. The results of the study showed that blood accumulation of ammonia decreased and oxygen consumption and performance increased after Cr loading. To our knowledge, this is the first study reporting *in vivo* changes in oxygen consumption with decreased blood ammonia accumulation and improvements in performance in humans during relative long duration muscular contraction after Cr supplementation.

The Cr supplementation regimen used in the present study was similar to that used by others who have shown increments of the intramuscular levels of total Cr after Cr feeding (3,10,13,15,16). Contrary to the results of Balsom et al. (2) and Stroud et al. (40), who observed no significant alteration in the oxygen uptake during running after Cr loading, the results of the present study showed an elevation of the oxygen consumed during exercise after Cr. One

![Figure 2](image1.png)

**Figure 2**—Blood ammonia \((\text{NH}_3)\) accumulation (mean ± SE) during alternating intensity bicycling exercise to exhaustion precreatine and postcreatine monohydrate (CR) (a) or placebo (PL) (b) loading. The data points correspond to rest, end of 1–30% (8 min), 1–90% (11 min), 2–30% (14 min), 2–90% (17 min), 3–90% (20 min), at exhaustion, and 5-min postexhaustion. At exhaustion and 5-min postexhaustion are shown because some subjects fatigued during the 3–90%. The exhaustion point in the figure corresponds to 29.9 ± 3.8 min (PRE) and 36.5 ± 5.7 (POST) in the CR group, and to 38.1 ± 5.6 (PRE) and 40.8 ± 5.7 (POST) in the PL group. Significantly different from PRE: * \(P < 0.05\), ** \(P < 0.01\).

![Figure 3](image2.png)

**Figure 3**—Plasma uric acid accumulation (mean ± SE) during alternating intensity bicycling exercise to exhaustion precreatine and postcreatine monohydrate supplementation (CR) (a) or placebo (PL) (b) loading. The data points correspond to rest, end of 1–30% (8 min), 1–90% (11 min), 2–30% (14 min), 2–90% (17 min), 3–90% (20 min), at exhaustion, and 5-min postexhaustion. At exhaustion and 5-min postexhaustion are shown because some subjects fatigued during the 3–90%. The exhaustion point in the figure corresponds to 29.9 ± 3.8 min (PRE) and 36.5 ± 5.7 (POST) in the CR group, and to 38.1 ± 5.6 (PRE) and 40.8 ± 5.7 (POST) in the PL group. Significantly different from PRE: * \(P < 0.05\), ** \(P < 0.01\).
possible explanation for the conflicting findings might be the difference in the frequency of the oxygen consumption measurements. Whereas in the studies of Balsom et al. (2) and Stroud et al. (40) expired gas samples were collected for 30 s and one value for oxygen uptake was obtained, in the present study, we measured the rate of oxygen consumption breath by breath. We averaged the breath-by-breath data every 5 s in each experiment to have the same number of points in each curve, which permitted a standardized description of the timecourse of the rate of oxygen uptake and a more accurate determination of the total oxygen consumed throughout the entire exercise protocol and before and after treatment. There were a total of 36 points to describe the kinetic changes and to compute the total oxygen consumed for each subject during the 3-min exercise periods. The integral of the individual oxygen uptake rate curves showed an enhancement of the total oxygen consumed supporting a role for Cr in the control of oxidative phosphorylation in exercising human muscle.

How this physiological phenomenon might have occurred in the working muscles of the subjects of the present study might be explained by compiling findings from animal and human muscle. Saks et al. (32) were the first to propose that limitation of diffusion of ADP through the outer mitochondrial membrane in cardiomyocytes and ST fibers of rats enabled Cr to increase the rate of oxidative phosphorylation by stimulating mito-CK because of the unrestricted diffusion of Cr in these fibers (32). Moreover, Meyer et al. (22) and Kushmerick et al. (20) argued for different regulation of oxygen consumption in slow twitch (ST) and fast twitch (FT) fibers. Rico-Sanz (28) proposed that Cr stimulated oxidative phosphorylation in human ST fibers when oxygen supply was not impeded after observing a reduced muscle PCr and pH drop measured with 31P magnetic resonance spectroscopy during low intensity but not during high intensity isometric muscle contraction. Indeed, it was later shown that Cr enhanced respiration in ST fibers but not in the FT fibers of rat muscle (21). Training also increased Cr-stimulated respiratory rate in human skinned fibers (25). Furthermore, the change in respiration of skinned fibers after exercise stimulated by Cr was related to the percentage of ST fibers (41). Because free Cr available for energy transport appears to be a small fraction of the TCr available in muscle (35), the increments of 25% to 40% in muscle free Cr potentially favor changes in oxidative phosphorylation in contracting human muscle fibers that are under control by Cr. Because our subjects were well endurance trained (average maximum oxygen uptake in the Cr group > 65 mL.kg.min⁻¹; training load, cycling 400–700 km wk⁻¹) with a muscle mass very likely composed primarily of ST fiber mass and a relatively large number of capillaries, oxidative enzymes, and mitochondria, the increased oxygen consumed after Cr might have been because of an amplification of aerobic phosphorylation via mito-CK on the subjects’ ST fibers. The results obtained in the present experiment support the role of the Cr-PCr shuttle in the regulation of respiration and transport of energy in muscle (4–6,32,33,36,37,38).

However, it was during the 90% exercise periods that the effect of Cr was observed, but not during the 30% or the warm-up, when oxidative fibers are almost exclusively recruited during contraction (12). One possible reason for not observing an increment in the total oxygen uptake during the 5 min of warm-up and the 1–30% after Cr might be because of the low relative number of fibers needed to sustain these workloads. The relatively low energy demand at 20% and 30% of MPO likely covered by ST fibers could have been covered equally by fewer ST fibers with an enlargement of oxidative phosphorylation after Cr. During the 1–90%, because all or most of the ST fibers had to be recruited and blood flow and transit time optimized to enable a high rate of energy supply, the effect of Cr on oxidative phosphorylation might have been potentiated, and this was first detected during the course of the 1–90% and later during the 2–90% MPO bouts. Possibly, this metabolic cost covered by larger oxidative metabolism after Cr had to be paid by larger flux through myokinase and/or protein catabolism before Cr, as indicated by the decrement in blood ammonia accumulation after Cr.

The fact that blood ammonia accumulation was significantly reduced already during the 1–90% and 2–90% MPO bouts suggests that the flux through myokinase and the adenine nucleotide degradation and/or amino acid deamination pathways was lower after Cr feeding. Muscle glutamate consumption and ammonia production has been observed during the first 10 min at 60% to 65% MPO (42). The adenine nucleotide degradation during intense exercise can lead to deamination of AMP to IMP and ammonia. Katz et al. (18) demonstrated that cycling at 97% of maximal oxygen uptake produced an increase in ammonia that was similar to the decrease in the adenine nucleotide pool. During high intensity exercise, glycogen breakdown is also more pronounced compared with low intensity exercise (34), and it is larger in FT fibers as exercise intensity increases (12). The IMP content at fatigue is also larger in FT fibers compared with ST fibers (17,30) and is elevated in glycogen-depleted but not in glycogen-filled type I and type II muscle fibers during prolonged exercise at 70% of maximal oxygen uptake (26). Furthermore, hypoxemia increased the accumulation of IMP in human muscle (31). Taking all these results together, it is possible that glutamate consumption occurred in the present study, and that a part of the ammonia accumulation arose from protein metabolism. However, it is most likely that most of the ammonia was produced by adenine nucleotide metabolism of FT and ST fibers because the muscle glycogen was probably being used in both fiber types, and these fibers experienced some local muscle hypoxia during the 90% MPO bouts. Previous studies have also shown lower blood ammonia accumulation after repeated bouts of maximal isokinetic exercise and swimming sprints (7,14,23), lower blood hypoxanthine accumulation after 10 supramaximal exercise bouts (1), and lower muscle adenine nucleotide degradation after Cr loading (8), which support a coupling between the CK and myokinase. Aside from a reduction in amino acid or/and adenine nucleotide degradation during exercise, as indicated

OXYGEN UPTAKE AND AMMONIA AFTER CREATINE FEEDING
by the reduction in blood ammonia and uric acid accumulation, there was no indication of alterations in any other metabolic pathway after Cr loading because lactate, NEFA, and glycerol accumulation were the same. As a consequence of the potential effect of Cr on oxidative phosphorylation, the ST fibers were most likely able to rely for a longer time on oxidative metabolism after Cr supplementation. Alternatively or synergistically, possible enlargements in PCr contents might have buffered larger amounts of ADP at myofibrillar sites in both fiber types. Both of these conditions could have caused the lower ammonia accumulation. The increased oxygen uptake during the intense exercise bouts supports the first possibility, whereas the results of Casey et al. (8) support the second possibility. This latter possibility is not excluded as a partial explanation for the results of the present study.

The improvements in performance during relatively prolonged alternating intensity exercise open a new line of evidence that Cr might enhance the capacity of muscle in sport events with metabolic demands that alternate between aerobic and anaerobic metabolism and depend highly on aerobic metabolism (i.e., soccer, basketball, handball, and hockey). Endurance sport athletes like cyclists and triathletes might benefit from Cr supplementation because the metabolic demands during races are also of alternating nature—they are required to climb hills before and after a ride on flat areas. The lack of positive change in performance after Cr feeding during exercise protocols that depend primarily on anaerobic metabolism is understandable when there is lack of enhancement of muscle PCr (27,39). On the other hand, it is very difficult to accept the conclusions of Febbraio et al. (10) who showed enlarged PCr levels after Cr feeding, but argued that the absence of performance enhancement was because of the very low role of the CK system during the fifth repeated bout of 1-min of exercise after subjects had performed four other bouts at constant work separated by 4 min. Their own results demonstrated a drop in PCr of > 70% from the resting value at the end of the fourth bout, which indicated large participation of the CK system. Also, the results of Casey et al. (8) demonstrated that increased PCr levels in type I fibers mediated improvement in performance in repeated bouts of 30-s maximal exercise. The evidence from animal muscle that additional PCr in the presence of ADP can produce faster and stronger contractions and more complete relaxation than any externally generated ATP (36) suggest that an increased flux through the CK system might also increase the efficiency of contraction.

The negative results in performance after Cr reported by Balsom et al. (2) during endurance running might be a consequence of increments in body mass observed after Cr supplementation. Because the body has to be transported in space during running, any increment in body mass could be detrimental to performance unless it was functional muscle mass capable of overcoming the mass change. It is important to note that most experimenters to date have requested their volunteers to ingest the Cr doses with 500 mL of fluids four times a day. This is an additional 2 L of fluid consumption. Hyperhydration regimens can increment total body water (29). Contrary to common assumptions, athletes might be hypohydrated and fluid loading alone can cause water retention. It is also possible that Cr can cause water retention (16), although determinations of muscle water by 3H magnetic resonance spectroscopy have shown no change (19). We are not aware that any direct measure of total body water has been made yet after Cr loading. This is at present under investigation. In the present study, we tried to minimize this effect by asking the subjects to ingest only 250 mL of fluids with the Cr dose. Although there was an increment of 0.4 kg in body weight after Cr, the change was not significant. However, in our case, any change in body weight was not a critical factor because the subjects performed bicycle exercise in a stationary ergometer.

In conclusion, the results of this study demonstrate an increased oxygen uptake coupled to a reduction in ammonia accumulation in blood after Cr loading in humans, which suggests that Cr enhances oxidative phosphorylation and decreases protein and/or adenine nucleotide degradation, subsequently enhancing muscle performance during alternating intensity exercise.

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