

Creatine supplementation increases muscle total creatine but not maximal intermittent exercise performance

MICHAEL J. McKENNA,¹ JUDITH MORTON,² STEVE E. SELIG,¹ AND RODNEY J. SNOW³

¹Department of Human Movement, Recreation, and Performance, Centre for Rehabilitation, Exercise, and Sports Science, Victoria University of Technology, Melbourne, Victoria 8001;

²Department of Medicine, Monash Medical School, Alfred Hospital, Prahran, Victoria 3181;

and ³School of Human Movement, Deakin University, Burwood, Victoria 3125, Australia

McKenna, Michael J., Judith Morton, Steve E. Selig, and Rodney J. Snow. Creatine supplementation increases muscle total creatine but not maximal intermittent exercise performance. *J. Appl. Physiol.* 87(6): 2244–2252, 1999.—This study investigated creatine supplementation (CrS) effects on muscle total creatine (TCr), creatine phosphate (CrP), and intermittent sprinting performance by using a design incorporating the time course of the initial increase and subsequent washout period of muscle TCr. Two groups of seven volunteers ingested either creatine [$6 \times (5 \text{ g Cr-H}_2\text{O} + 5 \text{ g dextrose})/\text{day}$] or a placebo ($6 \times 5 \text{ g dextrose}/\text{day}$) over 5 days. Five 10-s maximal cycle ergometer sprints with rest intervals of 180, 50, 20, and 20 s and a resting vastus lateralis biopsy were conducted before and 0, 2, and 4 wk after placebo or CrS. Resting muscle TCr, CrP, and Cr were unchanged after the placebo but were increased ($P < 0.05$) at 0 [by 22.9 ± 4.2 , 8.9 ± 1.9 , and 14.0 ± 3.3 (SE) mmol/kg dry mass, respectively] and 2 but not 4 wk after CrS. An apparent placebo main effect of increased peak power and cumulative work was found after placebo and CrS, but no treatment (CrS) main effect was found on either variable. Thus, despite the rise and washout of muscle TCr and CrP, maximal intermittent sprinting performance was unchanged by CrS.

ergogenic aids; creatine washout; muscle performance; fatigue

CREATINE SUPPLEMENTATION (CrS) in humans has been reported to elevate muscle total creatine content (TCr), as well as enhance maximal intermittent exercise performance (6, 15, 19). Demonstrated mechanisms for this performance enhancement include a reduced ATP degradation during maximal exercise, due to elevated muscle Cr phosphate (CrP) content, particularly in type II muscle fibers (6). In addition, an accelerated rate of CrP resynthesis has been reported in some individuals after CrP depletion induced by electrical stimulation (16) but not voluntary exercise (6, 33).

Three studies have reported an ergogenic effect of CrS on maximal intermittent exercise performance, together with verification of an elevated muscle TCr or CrP (2, 6, 37). The first two studies employed an ordered, single-group, nonblinded experimental design. Therefore, it cannot be excluded that their reported performance enhancement resulted from a placebo effect (2, 6). Although an ergogenic effect was

found in one study (37), no such gain was found after CrS in a similar study by the same authors (38). Enhanced performance has also been reported during maximal intermittent cycling exercise after CrS, but these studies failed to sample skeletal muscle and thus verify the efficacy of their supplementation protocol (1, 4, 9, 10). This is an important omission, because the potential ergogenicity of CrS is thought to depend on the magnitude of increase in muscle TCr after CrS (6, 15, 16). The lack of muscle data in these studies would not be a major limitation if the nature of the improvement in intermittent exercise performance after CrS were similar between studies. However, this varies markedly, therefore confounding interpretation of these studies. For example, performance was enhanced in the initial exercise bout in one study (4) but in the later exercise bouts in others (1, 17). Similarly, studies reporting no ergogenic effects of CrS may also be criticized for having failed to verify an increased muscle TCr (3, 5, 7, 8, 28, 31, 36). Therefore, to properly investigate the effects of CrS on intense intermittent exercise performance, it is also necessary to verify a large gain in muscle TCr. No studies have combined measurements of muscle TCr and performance during brief (≤ 10 s), maximal, repeated efforts.

A good model for investigating the possible benefits of CrS on intermittent exercise performance is to measure both muscle TCr and peak muscular performance before CrS and, on several occasions over a number of weeks, afterward. If CrS does enhance maximal intermittent sprinting performance, then performance should be initially improved with CrS but then decline over time back toward the control levels, as muscle TCr also returns to normal. The time course for normalization of muscle TCr and CrP after CrS in humans was reported to be 4 wk or less (11, 21, 38). Normalization of muscle CrP was incomplete 1 wk after cessation of CrS (38), but TCr had returned to basal levels by 2 wk post-CrS (21). Only one of these studies has also reported muscle performance data (11). They found that muscle TCr did not significantly differ from resting levels at 4 wk after cessation of CrS, but the exact time course of this recovery was not determined (11). In addition, the magnitude of increase in TCr after CrS in that study was relatively small. Furthermore, the intermittent performance model did not use maximal exercise but rather used constant-load exercise, and performance was unchanged after CrS.

The present study had two major purposes. First, we wanted to provide further information on the time course of Cr disappearance from human skeletal muscle,

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by measuring muscle TCr and CrP before, and at 0, 2, and 4 wk after, CrS. Second, we wanted to investigate the effects of CrS on performance during maximal intermittent cycle sprinting, by determining whether changes in performance after CrS correspond temporally with the initial increase and subsequent decline in muscle TCr and CrP.

METHODS

Subjects

Fourteen healthy, young, recreationally active male or female physical education students were randomly allocated into two groups of seven subjects and received either creatine (Cr) or placebo supplements. None of the subjects was specifically trained in sprint cycling events. Diet and physical activity were not monitored, but subjects were requested to maintain their normal dietary and physical activity habits throughout the duration of the study. Physical characteristics of the groups are shown in Table 1. All subjects were informed of the risks involved and gave written informed consent. The study was approved by the Human Research Ethics Committee, Victoria University of Technology. Subjects refrained from food and caffeine intake for at least 4 h before exercise testing. Exercise was avoided on the day of the test, with only light exercise permitted on the previous day.

Experimental Design

Each subject performed a maximal intermittent exercise session on a cycle ergometer on five separate occasions, comprising familiarization, control, and at 0, 2, and 4 wk postsupplementation (Fig. 1). All exercise tests were conducted in the afternoon, at similar times in all trials. A muscle biopsy was taken at ~8 AM on the morning after each of the four intermittent sessions (Fig. 1). Although muscle sampling has been shown not to interfere with exercise performance, the biopsy was taken on days separated from the exercise test as a precautionary measure. Exercise performance was assessed after 4.5 days of supplementation, whereas a muscle biopsy sample was taken after 5 days of supplementation. Because muscle was sampled 15–17 h after the second sprint trial, it is possible that further Cr loading may have occurred in the CrS group between the second sprint trial and muscle sampling. The second sprint trial was performed 2 h after a 5-g dose of Cr, and a further two or three 5-g doses of Cr were ingested between the exercise bout and muscle sampling. Thus 90–93% of the total Cr dose preceded the sprint exercise trial (i.e., 135–140 g of 150 g; see *Supplementation Procedure*). Therefore, the muscle uptake of only 10–15 g of Cr (7–10%) could have been influenced by the sprint exercise trial. Furthermore, the facilitatory effects of acute endurance exercise on muscle Cr loading appears to occur only during the first few days of CrS (19). Thus a significant increase in muscle TCr and CrP stores between the second exercise trial and biopsy seems unlikely. Therefore, the short time delay (overnight) between performance measures and muscle sampling does not invalidate a comparison between performance and muscle TCr.

Table 1. *Subjects' physical characteristics*

	<i>n</i> (F, M)	Age, yr	Ht, cm	Body Mass, kg
Creatine	7 (4,3)	19 ± 3	170.3 ± 10.8	63.29 ± 5.49
Placebo	7 (2,5)	21 ± 3	176.5 ± 8.6	67.25 ± 9.76

Values are means ± SD. *n*, No. of subjects; F, female; M, male.

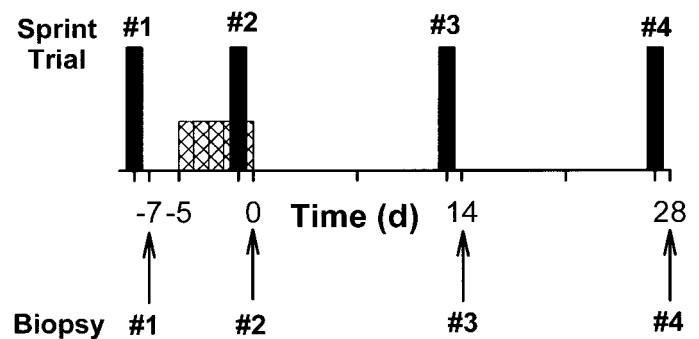


Fig. 1. Experimental overview. Filled bars, exercise trials; cross-hatched bars, 5-day supplementation period; arrows, muscle biopsies.

Supplementation Procedure

A double-blind procedure was used, with subjects randomly allocated to either a CrS or placebo supplementation group. When entering the study, all subjects were informed that they would receive either a placebo or Cr supplement, that Cr is thought to enhance intermittent sprinting performance, and that the time course for this positive effect to diminish is unknown. The CrS procedure was based on the work of Harris et al. (19). The supplements were taken as a dry powder in pre-labeled packets, with instructions to consume a packet at ~2-h intervals during the day. Because three packets were taken at mealtimes, it is highly likely that ~50% of the Cr supplements were taken with additional carbohydrate. Subjects consumed 5 g of Cr monohydrate plus 5 g dextrose in 200 ml of fluid, six times/day, for 5 days before each test. The total Cr intake was 30 g/day and 150 g overall. For the placebo supplement, 5 g dextrose in 200 ml of fluid were taken six times/day, for 5 days before each test.

Exercise Performance

All exercise trials were conducted on a modified air-braked cycle ergometer (RepcO, Melbourne, Australia). The operating principles of the air-braked cycle ergometer and their application in "all-out" exercise tests have been described and validated elsewhere (24, 35). Briefly, subjects pedal against air resistance caused by air vanes attached perpendicularly to the axis of rotation of the flywheel. Subjects attain their peak pedal cadence and thus, peak power output, during the first few seconds of a maximal effort, with both then declining rapidly as the subject fatigues, making this ergometer well suited to maximal power output testing (27, 33, 35). Power output was determined from the cube of pedaling velocity (35), which was sampled at 83 Hz, using a tachometer (Hall effect device and a cog at the wheel hub). The peak power, cumulative work output, and fatigue index were calculated for each sprint bout by a computer. Peak power and work are expressed relative to body mass, because independent groups were used. The fatigue index was defined as the relative decline in power output from the peak power attained in the first few pedal strokes to the final power at the end of each individual 10-s sprint bout and was expressed as a percentage. Because of a technical error, performance data in the Cr group are reported for *n* = 6 subjects, with *n* = 7 for the placebo group.

Subjects were weighed before exercise (Sauter type E 1200 balance). Each sprint bout was conducted with the subject remaining seated at a comfortable saddle height, with feet secured to the pedals by toeclips. The subjects were verbally encouraged to produce their maximum effort as rapidly as possible and to maintain this throughout each bout. Maximal

intermittent sprint performance was assessed by performing five, maximal-effort 10-s sprint bouts, with the following variable recovery intervals: 3 min after the first sprint bout, 50 s after the second bout, and then 20-s recovery intervals after the third and fourth bouts. A high-intensity, intermittent exercise protocol was chosen because such protocols are most likely to respond beneficially to CrS (e.g., Refs. 2, 6, 38). Repeated maximal-effort 10-s sprint bouts were utilized because the highest rates of CrP hydrolysis occur during brief, maximal exercise and because repeated maximal efforts induce large decreases in muscle CrP content (13). The protocol was also selected to replicate peak demands expected in intermittent field sports such as Australian-rules football, as this duration represents the longest high-intensity efforts required during such sports (26). The reproducibility of the 5×10 -s intermittent sprint test protocol was tested in five healthy subjects (4 men, 1 woman). Excellent reproducibility was found for peak power and work, for each 10-s maximal sprint bout, expressed per kilogram body mass. The coefficient of variation and intraclass correlation coefficients were 3.4% and $r = 0.977$ for peak power and 2.3% and $r = 0.998$ for work, respectively. This variability was similar to or less than that reported for peak power and/or cumulative work during a single (25) or repeated maximal 30-s sprint bouts (6). Higher variability was found for the fatigue index in each 10-s exercise bout, with a coefficient of variation of 11.7% and an intraclass correlation coefficient of 0.523.

Muscle Biopsy Procedure and Analyses

The resting muscle biopsy was obtained with the subject supine on a laboratory bed. Under local anesthesia (1% lignocaine injection) a small incision was made in the skin overlying the middle one-third of the vastus lateralis muscle, and a needle biopsy was taken. The excised muscle was rapidly frozen and stored in liquid nitrogen until later analyses. All muscle was freeze-dried, weighed, dissected free of any connective tissue, and powdered. The powdered tissue [2 mg dry mass (dm)] was extracted according to Harris et al. (18) and assayed enzymatically for ATP, CrP, and Cr by using fluorometric detection (23), as previously described (34). All Cr and CrP data were corrected to the highest ATP content for that individual, to minimize variation due to connective tissue or other nonmuscle constituents. The normal correction to the highest TCr obviously could not be conducted in this study, but ATP is a suitable alternative because CrS does not influence muscle ATP content (6, 19, 21).

Statistics

All experimental data are presented as means $\pm$ SE. Exercise performance data were analyzed by a three-way analysis of variance (treatment: Cr vs. placebo; trial: control, 0, 2, and 4 wk postsupplementation; bout: sprint bouts 1–5),

with repeated measures for two factors (trial, bout). All muscle data were analyzed by a two-way analysis of variance with repeated measures (treatment, trial). Post hoc analyses used the Newman-Keuls procedure. Significance was accepted at $P < 0.05$.

RESULTS

Body Mass

A significant trial main effect was found for body mass, with a greater mass at 4 wk postsupplementation compared with control ($P < 0.05$). No significant increase in body mass due to CrS was found (Table 2).

Exercise Performance

Peak power. A significant exercise bout main effect was found; peak power did not differ between the first two sprint bouts but then declined successively during the three subsequent sprint bouts ($P < 0.05$, Fig. 2). A significant trial main effect was found; peak power during the control (presupplementation) trial was lower ($P < 0.05$) than for the two subsequent trials (0 and 2 wk postsupplementation trials) but similar to the final trial (4 wk postsupplementation). No significant treatment main effects or interactions were found, indicating that CrS did not significantly influence peak power output.

Cumulative work. A significant exercise bout-by-trial interaction was found. A consistent finding for all four trials was that work output was similar for the first two sprint bouts but then declined successively during the three subsequent sprint bouts ($P < 0.05$, Fig. 3). The work performed in the first and second exercise bouts in the first (presupplementation) trial was less than in the three subsequent trials (0, 2, and 4 wk postsupplementation, $P < 0.05$), between which work output did not differ. The work performed in the third and fifth exercise bouts did not differ for the four trials. However, the work performed in the fourth exercise bout was higher in the 0-wk postsupplementation trial compared with the control and 4-wk postsupplementation trials ($P < 0.05$). No significant treatment main effects or interactions were found, indicating that CrS did not significantly influence work output.

Fatigue index. A significant exercise bout main effect was found; the fatigue index rose progressively from the first through the fourth bout ($P < 0.05$), with no further change the fifth bout (Fig. 4). A significant

Table 2. Body mass and resting vastus lateralis muscle ATP content determined before (control), after 5 days of supplementation, and at 2 wk and 4 wk postsupplementation

Variable	Control	0 wk Postsupplementation	2 wk Postsupplementation	4 wk Postsupplementation
Placebo group				
Body mass, kg	67.25 $\pm$ 3.69	67.38 $\pm$ 3.80	67.45 $\pm$ 3.64	67.94 $\pm$ 3.72*
ATP, mmol/kg dm	23.4 $\pm$ 0.9	22.9 $\pm$ 1.3	23.8 $\pm$ 1.1	22.6 $\pm$ 0.6
Cr group				
Body mass, kg	63.29 $\pm$ 2.08	64.02 $\pm$ 2.09	64.22 $\pm$ 2.02	64.31 $\pm$ 2.22*
ATP, mmol/kg dm	22.0 $\pm$ 0.8	22.6 $\pm$ 1.2	22.1 $\pm$ 1.3	23.5 $\pm$ 1.1

Values are means $\pm$ SE; $n = 7$ subjects/group. Cr, creatine. Supplements were either Cr monohydrate (5×30 g/day) or a placebo (dextrose). *Significant main effect for trial, week 4 $>$ control, $P < 0.05$.

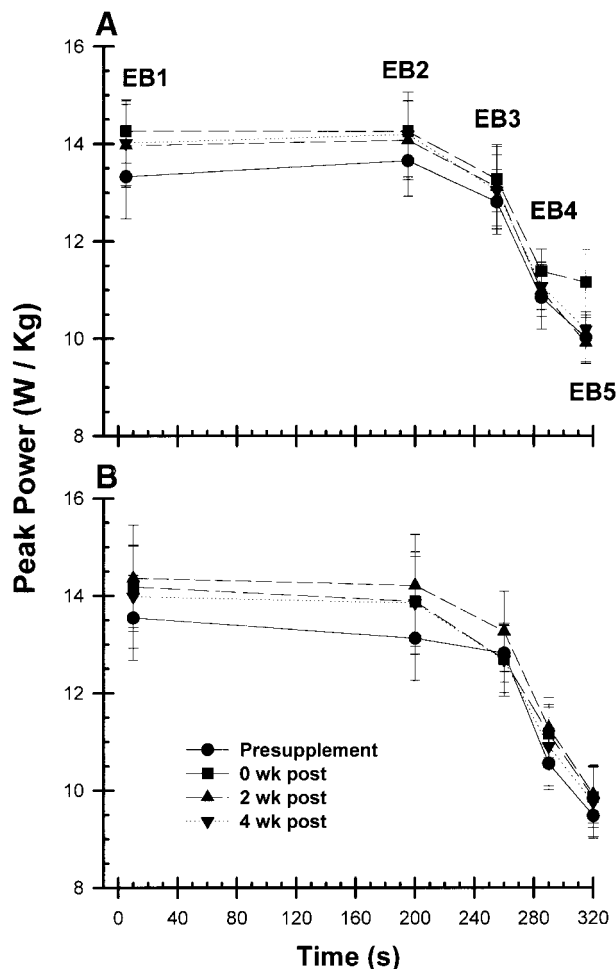


Fig. 2. Peak power output during maximal intermittent exercise, which comprised 5, 10-s exercise bouts (EB1-EB5), with intervening recovery intervals of 180, 50, 20, and 20 s. Exercise trials were conducted on 4 occasions: presupplementation and at 0, 2, and 4 wk after (post) 5 days of creatine (Cr) monohydrate (CrS; A; 30 g/day) or placebo (B; dextrose) supplementation. Values are means $\pm$ SE; Cr: $n = 6$; placebo: $n = 7$. No significant CrS treatment effects were found. See text for details.

trial-order effect was found, with a higher fatigue index found in the 0- and 2-wk postsupplementation trials than in the control (presupplementation) trial ($P < 0.05$). No significant treatment effects or interactions were found for the fatigue index (Fig. 4).

Muscle Substrates and TCr

Muscle ATP was unchanged after either CrS or placebo treatment and did not differ between the groups (Table 2). Consequently, muscle CrP, Cr, and TCr were corrected to the highest ATP content for that individual. Significant trial-by-treatment interactions were found for muscle CrP, Cr, and TCr ($P < 0.05$). None of the muscle Cr, CrP, or TCr contents varied significantly in the placebo group over the four measurement times (Fig. 5). In addition, there were no significant differences in these measurements in the control (presupplementation) biopsy between the Cr and placebo groups. For the Cr group, Cr, CrP, and TCr were each elevated at 0 and 2 wk after CrS ($P < 0.05$) but did

not differ from presupplementation levels 4 wk after CrS (Fig. 5). Muscle Cr, CrP, and TCr were greater at 0 wk after CrS than at all times in the placebo group ($P < 0.05$). In addition, muscle Cr, but not CrP, was greater at 2 wk post-CrS than in the placebo group presupplementation trial ($P < 0.05$). Thus CrS significantly increased muscle TCr relative to both Cr and placebo group control levels, and this increase comprised elevations in both Cr and CrP ($P < 0.05$).

The increase in TCr at 0 wk after CrS was 22.9 ± 4.2 (range 7.2–40.3) mmol/kg dm ($18.0 \pm 3.6\%$, $P < 0.05$). The increase in TCr at 0 wk after CrS was ≥ 20 mmol/kg dm in five of seven subjects, with gains of ~ 7 and 14 mmol/kg dm in the remaining two subjects. The gain in TCr comprised increases in CrP of 8.9 ± 1.9 mmol/kg dm ($9.8 \pm 2.1\%$, $P < 0.05$) and in free Cr of 14.0 ± 3.3 mmol/kg dm ($40.9 \pm 11.3\%$, $P < 0.05$).

Muscle TCr-Performance Relationships

Regression analyses were performed with the Cr group data, between the percent increases in muscle TCr ($\% \Delta \text{TCr}$) and in performance, at 0 wk postsupplementation compared with presupplementation. The

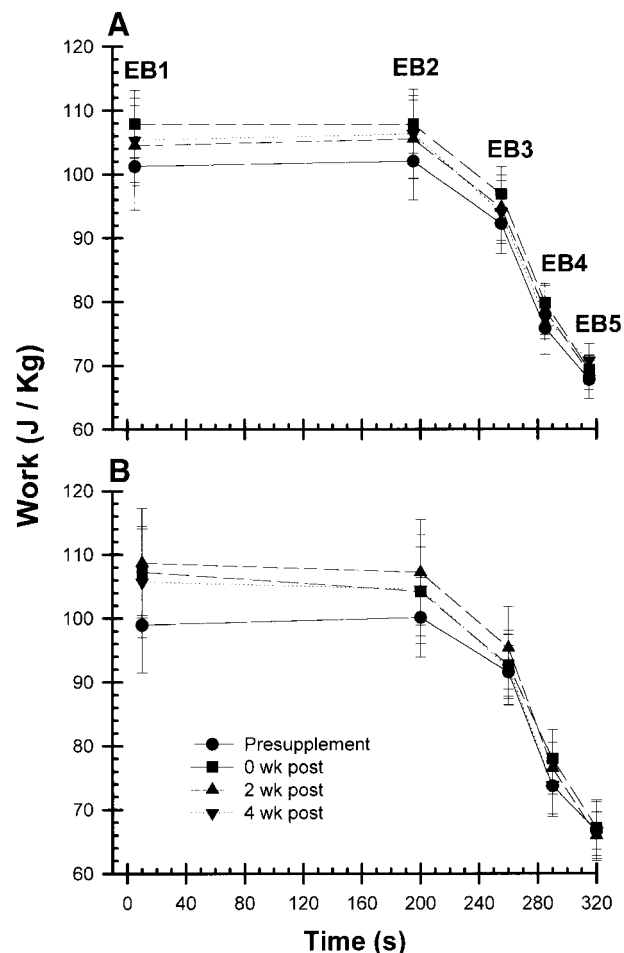


Fig. 3. Cumulative work production during maximal intermittent exercise, which comprised 5, 10-s EBs, with intervening recovery intervals of 180, 50, 20, and 20 s. Protocol, data analysis, and significance are as described in Fig. 2.

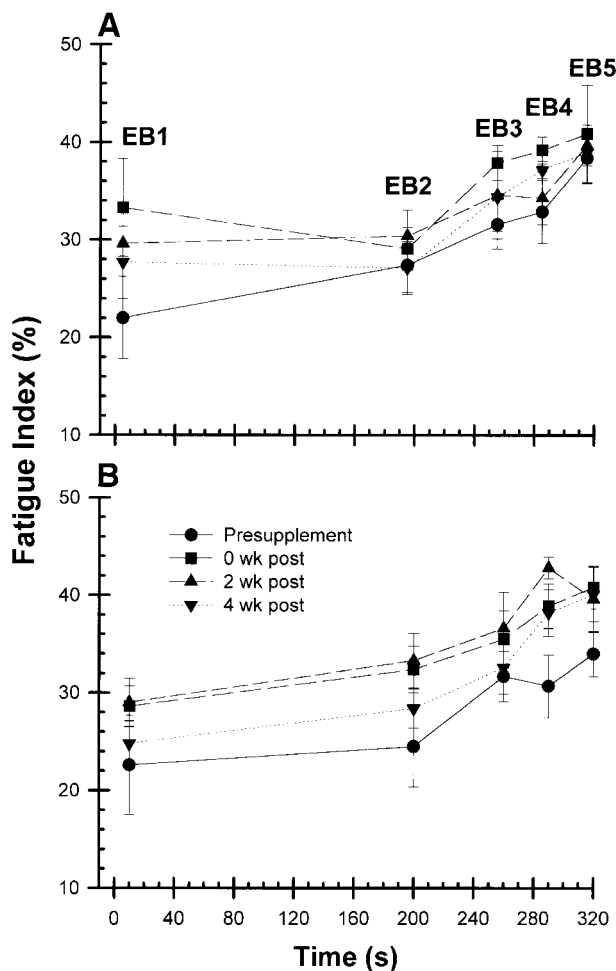


Fig. 4. Fatigue index during maximal intermittent exercise, which comprised 5, 10-s EBs, with intervening recovery intervals of 180, 50, 20, and 20 s. Protocol, data analysis, and significance are as described in Fig. 2.

% Δ TCr after CrS was not significantly related to the percent increase (% Δ) in highest peak power attained after CrS (% Δ peak power = $0.05 \cdot \% \Delta \text{TCr} + 4.28$, $r = 0.10$, not significant). Similarly, the % Δ TCr was not related to the % Δ cumulative (i.e., 5×10 s) work (% Δ work = $0.07 \cdot \% \Delta \text{TCr} + 4.50$, $r = 0.11$, not significant).

Gender Effects on Muscle TCr and TCr Loading

The muscle TCr before CrS did not differ between women and men ($n = 6$, 125.3 ± 4.9 ; $n = 8$, 120.9 ± 1.7 mmol/kg dm, respectively). Furthermore, no gender differences were found in the magnitude of TCr loading after 5 days of CrS [women ($n = 4$) vs. men ($n = 3$), 23.8 ± 4.4 and 26.0 ± 6.6 mmol/kg dm, respectively].

DISCUSSION

Two major findings emanate from this study. First, we provide important additional information on the time course of Cr washout from skeletal muscle after CrS. The CrS procedure successfully increased muscle TCr and CrP contents, which remained elevated for at least 2 wk and had returned to control values at 4 wk

after cessation of CrS. Thus the Cr washout period was complete within the time period between 2 and 4 wk. Second, despite the initial increase and subsequent decline in muscle TCr and CrP, maximal intermittent exercise performance was unchanged relative to the placebo group. Significant increases in peak power and work output were found in the second trial, but this was true for both the CrS and the placebo supplementation groups. This strongly suggests that this increase in performance was due to a placebo effect, rather than an ergogenic effect of CrS. Thus no ergogenic effect was found for CrS with the intermittent exercise model used in this study.

Efficacy of Cr-Loading Protocol

The CrS procedure used was effective in elevating muscle TCr content in all subjects, with a mean increase of 23 mmol/kg dm and individual increases ranging from 7 to 40 mmol/kg dm. This was comparable to most other reports, in which the CrS protocol did not include a large carbohydrate intake (2, 6, 11, 14, 16, 19, 21). Considerable individual variability was found in the rise in muscle TCr after CrS. This variability did not appear to depend on gender, because both the presupplementation TCr and the magnitude of loading of TCr after CrS did not differ between men and women. Our finding that gender did not influence resting muscle TCr contrasts with that of Forsberg et al. (12), who found that women had a 10% higher muscle TCr than men. The reason for this is not clear

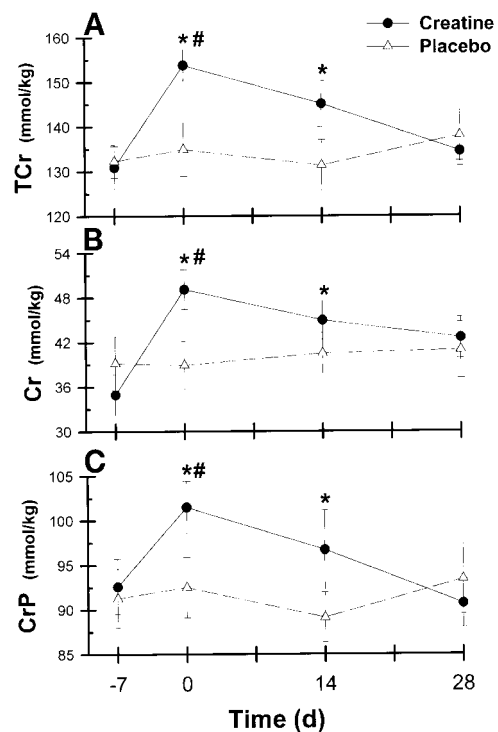


Fig. 5. Muscle total creatine (TCr; A), Cr (B), and creatine phosphate (CrP; C) contents before and at 0, 2, and 4 wk after 5 days of Cr monohydrate (30 g/day) or placebo (dextrose) supplementation. Values are means $\pm$ SE; $n = 7$ /group. *Significantly greater than pre-CrS trial, $P < 0.05$. #Significantly greater than all placebo trials, $P < 0.05$.

but may reflect the small sample size analyzed in this study. To our knowledge, no studies have specifically examined the possibility of gender differences in muscle Cr loading.

It is possible that the observed variation in the magnitude of Cr uptake in our study after CrS may be influenced by the effects of acute exercise (19) and by differences in training status. Although the subjects in the present study were all regular participants in physical activity and were all encouraged to maintain their normal activity levels throughout the duration of the study, we have no objective evidence that their activity levels remained constant. However, it is unlikely that variations in activity after the CrS period affected muscle Cr content, because neither endurance training (22) nor high-intensity sprint training (34) influenced muscle CrP or TCr contents.

Another factor that potentially might influence the extent of muscle Cr loading is fluctuations in dietary Cr intake (i.e., vegetarians vs. omnivores). Because we did not control for diet, we cannot account for the possible effect of any such fluctuations. It is unlikely, however, that this omission alters the interpretation of the findings in the present study, because others have found no differences between vegetarians and carnivores in either muscle TCr content or in changes in TCr after 5 days of CrS (20).

Body mass was heavier in both CrS and placebo supplementation groups at 4 wk postsupplementation compared with control measurements. An explanation for this finding is not readily apparent but must involve an increased energy intake and/or a decreased energy expenditure. The lack of effect of CrS on body mass is consistent with some studies (3, 31, 37) but not others, in which an increase was found immediately after CrS (1, 2, 9, 14, 16, 28). However, because muscle TCr was elevated after CrS in the present study, a lack of change in body mass cannot be attributable to a failure to load the muscle with Cr.

Cr Washout Time

Our data confirm that muscle CrP, Cr, and TCr had returned to basal levels at 4 wk post-CrS, consistent with previous studies (11, 21, 38). Our data clearly indicate that muscle CrP, Cr, and TCr each remained significantly elevated above presupplementation levels at 2 wk postsupplementation. This is consistent with a recent report that muscle CrP remained elevated at 1 wk postsupplementation (38) but contrasts with a finding that muscle CrP, Cr, or TCr did not differ significantly from presupplementation levels at 2 wk postsupplementation (21). An important difference between the present and the former study (21) was that we found significant increases in muscle CrP, Cr, and TCr immediately after CrS. In the study by Hultman et al. (21), muscle TCr was elevated immediately after CrS in the six subjects in their *study 1*, but muscle CrP was only significantly increased when a larger pool of subjects was used. This apparent type II error with the small sample size in their *study 1* may also explain why their muscle TCr was not significantly elevated above

presupplementation levels at 2 wk after CrS. In the present study the muscle TCr declined toward the presupplementation levels at a rate of $\sim 0.68 \text{ mmol} \cdot \text{kg dm}^{-1} \cdot \text{day}^{-1}$. This rate is similar to that reported by Hultman et al. (Ref. 21; $\sim 0.43 \text{ mmol} \cdot \text{kg dm}^{-1} \cdot \text{day}^{-1}$) and to that calculated from the data presented by Febbraio et al. (Ref. 11; $\sim 0.67 \text{ mmol} \cdot \text{kg dm}^{-1} \cdot \text{day}^{-1}$).

Unchanged Performance After CrS

Muscle Cr, CrP, and TCr were elevated at 0 wk and remained elevated at 2 wk postsupplementation. On the basis of previous studies (2, 6, 37), an ergogenic effect might then be anticipated during the maximal intermittent exercise performance trials at these time points. The magnitude of increase in TCr was previously suggested to play an important role in any performance enhancement after CrS (6, 16). In the present study an increase in TCr $\geq 20 \text{ mmol/kg dm}$ occurred in five of seven subjects, with gains of 7 and 14 mmol/kg dm in the remaining two subjects (a woman and a man, respectively). However, we found no effects of CrS on peak power output, cumulative work production, or the fatigue index during five bouts of 10-s maximal intermittent cycling sprints. Furthermore, we found no significant relationships between the percent gain in muscle TCr and the percent improvements in the highest peak power, or the cumulative work output during sprint exercise. Peak power output was increased after the presupplementation trials (0 and 2 wk postsupplementation) in both the placebo and Cr groups. A similar order effect was seen for cumulative work production, with greater work in three of the five sprint bouts in the 0- and 2-wk postsupplementation trials. This may indicate a learning effect in both groups and suggests that the familiarization employed was insufficient for the purposes of stabilizing peak power development and work output. However, the low coefficients of variability for the intermittent protocol argue against this as a likely explanation. We cannot exclude the possibility that a learning effect occurred only for the placebo group, whereas a Cr-induced ergogenic effect occurred only for the Cr group. This would account for the greater peak power and work in the 0-wk postsupplementation trial for each group, but this seems quite unlikely. The stability in peak power and cumulative work observed for both placebo and Cr groups in *trials 2* and *3*, as well as the subject recruitment from a common recreationally active pool (physical education students), argues against differential effects for these groups. A more probable explanation for the order effect for peak power and work is that a placebo effect occurred for both groups, consistent with information given to subjects when entering the study.

Two recent studies in which CrS was shown to elevate muscle TCr and reported to enhance performance utilized a single-group, ordered design, such that control testing always preceded CrS testing (2, 6). Importantly, both studies did not report use of a placebo or employ a blinded design, and therefore subjects presumably knew that they were to receive Cr. The information and instructions given to the subjects were

not reported in either of these studies. Thus, despite the familiarization undertaken in these studies, there is a very strong possibility that the enhanced performance reported after CrS in both studies was due to a placebo effect, in line with subject expectations of a performance enhancement. Because CrS had no effect on peak power or cumulative work output, together with the low coefficient of variability for these measurements, our results cannot support an ergogenic effect of CrS for brief bouts of maximal-intensity, intermittent exercise. Alternately, if any ergogenic effect was derived from CrS, it must have been less than the sensitivity of the intermittent test protocol. Despite the excellent reproducibility of our test protocol, it is possible that small increases of <2–3% in peak power and cumulative work occurred after CrS but that we were unable to detect these. Thus we cannot exclude a possible type II error, due to the large intersubject variability, our small sample size, together with the minor limitation in test precision. A large number of subjects would be required to detect such small changes using the present experimental conditions. Our conclusions of unaltered performance after CrS are also consistent with those of numerous other reports (Table 3), who failed to detect any performance enhancement after CrS (1, 3, 5, 7–9, 30, 33, 37, 38), even when muscle TCr was elevated (30, 33). In contrast, several studies have reported enhanced performance after CrS, in studies in which muscle TCr was increased (6), or was not measured (4, 10, 17). Furthermore, although an ergogenic effect was found after CrS during 5 series of 30 maximal dynamic arm flexor contractions (37), no such gains were found in a later study by the same authors (38). Therefore, at best, the benefits of CrS on maximal sprint perfor-

mance are equivocal. We cannot exclude the possibility that the lack of ergogenic effect after CrS in the present study was due to the different exercise model used than in other intermittent exercise studies (e.g., 2, 6, 17, 37). The two purported mechanisms of performance enhancement after CrS are reduced ATP degradation during exercise due to increased muscle CrP content (6) and an accelerated postcontractile rate of CrP resynthesis (16). The repeated maximal sprint bouts together with the short intervening recovery intervals in the intermittent exercise model used in this study would be expected to induce large reductions in muscle ATP and CrP (2, 13). Given the marked fatigue evidenced by the decline in peak power and cumulative work during the latter sprint bouts (Figs. 2 and 4), it seems likely that the intermittent exercise model used in this study would respond positively to CrS. Because muscle biopsy data were not obtained before and after exercise we cannot make conclusions regarding the effects of CrS on muscle ATP degradation during exercise or on postexercise CrP resynthesis rates. However, it should be noted that neither of these variables nor performance during 20-s and 60-s maximal-effort sprints was improved after CrS in recent studies conducted in our laboratory (33; R. J. Snow, M. J. McKenna; unpublished observations). It is likely that numerous factors in addition to depletion of muscle CrP limit intense intermittent exercise performance, including impairments in sarcoplasmic reticulum calcium release and muscle membrane excitability (29, 39). Thus augmenting muscle CrP and Cr after CrS may attenuate only one of several mechanisms of exercise limitation and therefore fail to attenuate muscular fatigue during intense intermittent exercise.

Table 3. *Effects of Cr supplementation on resting muscle CrP, Cr, TCr, and maximal exercise performance in humans*

Study Design (Ref. No.)	<i>n</i>	Dose, g	CrP, %Δ	Cr, %Δ	TCr, Δ	TCr, %Δ	Performance Measurements	Performance Results
Ordered, single blind (11)	6	100	22‡	7	18‡	15‡	Cycle: 4 × 1 min at ~115% $\dot{V}O_{2\max}$, then single bout to fatigue	NS time to fatigue
Ordered, nonblinded (2)	7	120	10	29‡	23‡	18‡	Cycle: 5 × 6 s, 1 × 10 s, constant work (30-s rest)	Final bout ↓4% cadence decline‡
Ordered, nonblinded (6)	9	100	10‡	36‡	23‡	19‡	Vertical jump Cycle: 2 × 30-s sprint (4-min interval)	NS ↑4% peak work <i>bouts</i> 1 and 2§ ↑4% total work <i>bouts</i> 1 and 2‡
Crossover, double blind (37)	9	3*	4‡				Knee extension: isometric MVC	NS
Crossover, double blind (30)	9	60	NS†			13‡	Knee extension: 3 × 30, 4 × 20, 5 × 10 MVC Cycle: 1 × 30-s sprint	NS fatigue index; ↑ mean torque NS peak power, fatigue index, work
Ordered, double blind (38)	10	80	6‡				Arm flexion: 5 × 30 MVC	NS fatigue index; mean torque
Crossover, double blind (33)	8	150	3	22‡	12‡	9‡	Cycle: 1 × 20-s sprint	NS peak power, fatigue index, work
Independent groups, four repeated measures, double blind (present study)	7	150	10‡	41‡	23‡	18‡	Cycle: 5 × 10-s sprint (180-, 50-, 2 × 20-s intervals)	NS peak power, fatigue index, work

n, No. of subjects. Change (Δ) in total Cr (TCr) is expressed in mmol/kg dry mass (dm). CrP, creatine phosphate; $\dot{V}O_{2\max}$, maximal O_2 consumption; MVC, maximal voluntary contraction; NS, not significant; †, increase; ‡, decrease. Double-blind crossover studies are listed in order of trial washout period (3, 2, and 4 wk, respectively). Studies cited are those that measured both muscle Cr status as well as performance; these have a single-group design except where indicated. *Cr dose in g/kg. †Raw data not reported, CrP/ATP and TCr/ATP ratio. ‡ $P < 0.05$. § $P < 0.06$.

In conclusion, CrS significantly increased skeletal muscle TCr, CrP, and free Cr contents, and these remained significantly elevated 2 wk after cessation of supplementation. Each had returned to control levels by 4 wk after CrS. Despite these muscle adaptations, peak power and work output during five bouts of maximal 10-s cycle sprints were unchanged by CrS, either acutely or for up to 4 wk after supplementation, in comparison to the placebo group. Thus CrS did not increase maximal intermittent sprinting performance.

We thank Musashi Australia Pty, Ltd., for the kind donation of Cr-H₂O; Assoc. Prof. Damien Jolley for statistical advice; and our subjects for their efforts.

This study was supported by the Australian Sports Commission.

Address for reprint requests and other correspondence: M. J. McKenna, Dept. of Human Movement, Recreation and Performance (FO22), Victoria Univ. of Technology, PO Box 14428, MCMC, Melbourne, Victoria 8001, Australia (E-mail: michael.mckenna@vu.edu.au).

Received 27 April 1998; accepted in final form 22 July 1999.

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