

Applied nutritional investigation

Effects of creatine on thermoregulatory responses while exercising in the heat

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Abstract

Objective: We hypothesized that creatine supplementation would interfere with normal body fluid shifts that occur during exercise in a hot environment due to its osmotic effect intracellularly. This study examined the effects of acute creatine loading (20 g/d for 5 d) on the thermoregulatory response of the body during a bout of exercise at 39°C.

Methods: Subjects (15 men and 1 woman) performed a cycle test of maximum oxygen consumption to determine the proper work rate for the heat-stress test (40 min at 55% maximum oxygen consumption at 39°C) and were assigned to a creatine group ($n = 8$) or a placebo group ($n = 8$) in a double-blind fashion. Each group performed the heat-stress test on two separate occasions: before supplementation and after supplementation (20 g/d of creatine with Gatorade or Solka-floc plus Gatorade). Dependent variables included rectal temperature, mean skin temperature, mean body temperature, and perceived thermal sensation.

Results: Repeated measure analysis of variance showed a significant ($P \leq 0.05$) increase in body weight in the group supplemented with Gatorade. Core temperature was significantly lower after supplementation for both groups combined (before supplementation at 37.85°C and after supplementation at 37.7°C), with no difference between groups. A significant three-way interaction (group \times trial \times time) was also found for rectal temperature, with both groups having significantly lower rectal temperature after supplementation. Mean body and mean skin temperatures showed no differences.

Conclusions: Short-term creatine supplementation (20 g/d for 5 d) did not have a negative effect on thermoregulatory responses during exercise at 39°C. © 2005 Elsevier Inc. All rights reserved.

Keywords

Creatine; Heat; Submaximal exercise; Thermoregulation; Ergogenic aid

Introduction

Many creatine (Cr) studies [1–4] have been conducted over the past years because of the role of Cr in energy

metabolism. During high-intensity exercise (of short duration), the energy for resynthesis of adenosine triphosphate is supplied from the breakdown of phosphocreatine (PCr) and anaerobic glycolysis [5]. The amount of available PCr appears to correlate with force development and may contribute to the delay of fatigue in high-intensity exercise [6]. It has been documented that acute Cr supplementation is effective in anaerobic performance by increasing free Cr and PCr within skeletal muscle cells [7]. Greenhaff et al. [8] evaluated this effect of Cr supplementation on PCr resynthesis. After 20 electrically evoked isometric contractions of the quadriceps muscle, the results supported an increased

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Table 1
Descriptive characteristics of subjects*

Variable	Cr	Pl	P
Age (y)	26 (3.6)	26 (1.9)	0.9998
Height (cm)	177.5 (11.8)	174.8 (7.66)	0.5843
Body mass (kg)	84.7 (14.3)	83.2 (7.82)	0.7948
Body mass index (kg/m ²)	26.8 (3.57)	27.4 (4.19)	0.3404
VO _{2max} (mL · kg ⁻¹ · min ⁻¹)	41.8 (4.12)	43.2 (5.27)	0.5395

Cr, creatine; Pl, placebo; VO_{2max}, maximum oxygen consumption

* Values are mean (standard deviation).

rate of PCr resynthesis, with the supplemented group having 20% higher PCr values than the controls after 2 min of recovery.

Cr is an osmotically active substance, and research has suggested that an increased concentration of Cr in the muscle leads to an increase in intracellular water [9]. When its concentration is increased inside the cell, it increases intracellular osmotic pressure and draws water into the cell, thereby increasing cellular volume. Assuming that is the case, an increase in cellular volume must come, at least initially, at the expense of extracellular volume. This decrease in extracellular volume might affect the body's ability to thermoregulate while exercising for a prolonged period in a hot environment.

There is an abundance of support on the positive ergogenic effects of Cr supplementation for anaerobic (high-intensity, short-duration) exercise, but none of this literature has suggested that Cr supplementation would be effective for aerobic (submaximal) type of exercise. Engelhardt et al. [10] concluded that Cr supplementation has positive effects on short-term exercise that includes aerobic endurance exercise but not aerobic exercise itself. In other words, one may be able to perform more sprints or a longer duration of sprints (high intensity, short duration) within an aerobic (submaximal) session. This is classically known as *interval training*.

However, it is becoming increasingly evident that many aerobic (endurance) participants consume Cr supplements for as yet undetermined benefits. No literature has focused on whether or not the osmotic effect of Cr might affect the thermoregulatory processes during exercise. This study examined the effect of short-term Cr supplementation on the body's ability to thermoregulate while aerobically exercising in the heat without fluid replacement.

Materials and methods

Subjects ($n = 16$) were 15 men and 1 woman, with an age range of 22 to 33 y (Table 1). No available research has suggested that fluid changes might be affected by sex or racial differences. Subjects were untrained but recreationally active (maximum oxygen consumption [VO_{2max} ≤ 52 mL · kg⁻¹ · min⁻¹]) and non-acclimatized to the heat. Sub-

jects were excluded from the study if they had taken Cr supplements within the previous 2 mo. Previous research has shown that this is an appropriate time frame for the washout of exogenous Cr [11]. Before testing, all subjects were required to fill out a health history form that was reviewed for contraindications to participate in accordance with guidelines for maximum exercise testing by the American College of Sports and Medicine. These contraindications included more than one cardiovascular risk factor, pregnancy, and metabolic disorders such as diabetes [12]. The female subject was required to take a home pregnancy test before testing and to repeat testing 1 mo later to account for the same time period in the menstrual cycle. The project was approved by the institutional review board of Kent State University (Kent, OH, USA). Subjects were dressed in shorts, t-shirts, socks, and shoes during the tests, with no fluid ingestion permitted during the exercise tests. Subjects reported to the laboratory and performed each trial at the same time of day (± 30 min).

An environmental chamber (Model EW-146, Western Environmental Chamber, Napa Valley, CA, USA) was used to induce heat stress. Temperature was maintained at $39 \pm 0.5^\circ\text{C}$ during testing. The chamber was turned on for at least 6 h before testing to stabilize radiant heat within the chamber. Due to the passive nature of this system, humidity could not be precisely controlled but was monitored (23% to 28%, mean = 26%).

Graded exercise tests were performed on a cycle ergometer (Lode, Groningen, Netherlands) to determine VO_{2max}. The protocol consisted of increasing the work rate in an incremental manner until maximal voluntary exhaustion. The test began at 50 W for 3 min followed by a 5-min rest period. The test continued in this manner, with the workload being increased by 50 W for 3 min and a 5-min rest thereafter. Expired respiratory air samples were collected continuously and averaged at 30-s intervals throughout testing by using a VacuMed system (Vacumetrics, Ventura, CA, USA). The subject breathed through a one-way valve for the duration of the test to analyze the expired air to measure oxygen consumption per unit time (VO₂), volume of expired air, carbon dioxide consumption per unit time, and respiratory exchange ratio (RER).

Heart rate was recorded at 30-s intervals. Maximal oxygen uptake was accepted as the highest 30-s VO₂ value recorded during the test. This maximal oxygen uptake was accompanied by the accepted criteria for determination of maximal effort, which included a heart rate within 10 beats of age-predicted maximum heart rate, a rate of perceived exertion (RPE) of at least 17, an RER of at least 1.1, a lactate level above 7.9 mM, and a plateau of the VO₂ response curve [13]. Lactate measurements were also obtained 3 min after exercise from a finger stick and analyzed with a hand-held Accusport lactate analyzer (Boehringer Mannheim GmbH, Mannheim, Germany). All subjects met at least two of the accepted criteria for maximal effort. RPE exceeded 17 and all lactate levels exceeded 7.9 mM.

The cycle ergometer was chosen as the mode of exercise because of the ease of maintaining a constant and predetermined workload. Moreover, previous research has shown that cycle exercise affects fluid responses more than running or walking [14–18]. The test was a continuous 40-min bout with the subject working at an intensity that elicited 55% of $\dot{V}O_{2\max}$. The appropriate workload was determined from the $\dot{V}O_{2\max}$ test by plotting $\dot{V}O_2$ versus workload. A regression equation was then used to calculate the work rate that elicited 55% of $\dot{V}O_{2\max}$. This was achieved $\pm 3\%$ of $\dot{V}O_{2\max}$.

Skin temperatures were monitored at four sites (chest, arm, thigh, and calf) with skin thermistors (Series 400, Yellow Springs Instrument, Beavercreek, OH, USA). The chest thermistor was located at the fourth intercostal space near the manubrium. The arm thermistor was located midway between the elbow and acromion over the triceps muscle. The thigh thermistor was located midway between the top of the patella and the inguinal crease on the anterior surface of the thigh. The calf thermistor was located on the dorsal surface of the belly of the gastrocnemius at the maximum circumference. All thermistors were connected to a switchbox interfaced with a telethermometer (Series 2100, Yellow Springs Instrument). Temperatures were recorded before exercise (time 0) and every 10-min during the exercise bout. Mean skin temperature (T_{sk}) was calculated by using the equation from Ramanathan [19]. The T_{sk} was subsequently used, in addition to rectal temperature (T_{re}), to compute mean body temperature [20] and heat storage [21].

$$T_{sk} = 0.3(T_{chest} + T_{arm}) + 0.2(T_{thigh} + T_{calf}) \quad (1)$$

$$T_B = (0.33 \times T_{sk}) + (0.67 \times T_{re}) \quad (2)$$

T_{re} was used as an index of core temperature and monitored during the exercise to prevent heat injury to the subject. The rectal thermistor was inserted 13 cm beyond the anal sphincter by the subject to obtain a measurement of core temperature (T_{re}). The maximum core temperature allowed was 39°C, but no subject reached this level. Disposable rectal probes were used to measure core temperature. Each subject had one probe and used it for both trials. Standard laboratory procedures were used for cleaning the probe between trials.

Subjects were given a supply of the supplement or placebo for the 5 d of the supplementation period. The substances were provided in five separate containers that contained the supplement, which was Cr in Gatorade (Gatorade, Quaker Oats, Chicago, IL, USA), or placebo, which was Solka-floc (International Fiber Corp., Nitro, WV, USA) in Gatorade. Solka-floc is a non-caloric purified form of cellulose ground to microparticles that replaces some or all of the fat in dairy-type products, sauces, frozen desserts, and salad dressings. Dosages consisted of 20 g of Cr or 10 g of Solka-Floc premixed with 60 g of Gatorade. Subjects loaded for a period of 5 d during which they consumed one container per day with as much water as desired. This quantity of Cr (20 g/d for 5 d) has been shown to increase PCr stores within skeletal muscle [22]. Carbohydrates, in beverages such as Gatorade, have

been shown to facilitate uptake of Cr by the skeletal muscle because of the insulin response it produces [23]. Administration of the supplements was done in a double-blind fashion. The premixed bags of experimental treatment or placebo were prepared by the investigator into five individual containers that were then combined into one container designated for each subject.

A thermal sensation scale was also employed. This scale is a modified Gagge scale [24] that was generated in our laboratory. It is an extension of a cold thermal sensation scale [25] that was modified from Gagge's original thermal sensation scale. The Gagge thermal sensation scale spans from "unbearably cold" to "unbearably hot." This study was concerned only with temperatures above neutral, so a new scale was needed. The newly modified Gagge scale was anchored at 0.0 "neutral" and increased at intervals of 1 except for the initial increase of 0.5 from "neutral" to "moderately warm." The scale terminated at 10 with "unbearably hot." This measurement was also taken at 10-min intervals before the cardiac output measurement.

Statistica software (StatSoft, Tulsa, OK, USA) was used to analyze all data. A three-way (2 group \times 2 trial \times 5 time) mixed-model analysis of variance with repeated measures on the factors trial and time was used to determine the effects of Cr supplementation on thermoregulation during prolonged exercise in the heat. A significant three-way interaction was evaluated with a test of simple effects according to procedures described by Bruning et al. [26]. If the F ratio for the simple effects was significant ($P \leq 0.05$), between-mean comparisons were made with *t* ratios with the level of probability ($P \leq 0.05$) adjusted for the number of comparisons made according to Bonferroni's correction.

Results

Weight changes due to exercise in the heat are presented in Table 2. There was a significant difference across time (before versus after exercise) that was expected because of the loss of fluid due to sweat. However, no significant interactions of group \times trial were evident. It was hypothesized (a priori) that body weight before exercise in the Cr group would be greater before supplementation (PoS trial) than after supplementation (PrS trial) due to the increase in total body water found in previous studies [1,2,22,27–29]. The Cr group did have a significant increase in body weight of 1.4 kg from the PrS trial to the PoS trial ($P = 0.013$, Bonferroni's correction for two comparisons for $P \leq 0.05$ was $P \leq 0.025$).

Core temperature, mean skin temperature, and mean body temperature changes during exercise in the heat are listed in Table 3. Significant F ratios were found for trial for core temperature, with the overall core temperature being lower during the PoS trial. There was also a significant group \times time interaction. Post hoc analysis on this interaction was not done because it had no bearing on conclusions

Table 2
Weight changes before and after exercise testing and before and after supplementation*

Trial	Group	Before exercise (kg)	After exercise (kg)	Mean (kg)	P
PrS	Cr	84.0 ± 14.0	82.5 ± 13.8	83.3 ± 13.9	0.5842 for group 0.0375 for trial 0.1077 for group × trial
	Pl	81.3 ± 7.4	80.0 ± 7.4	80.7 ± 7.4	
	Mean	82.6 ± 10.9	81.2 ± 10.8		
PoS	Cr	85.4 ± 14.8	83.8 ± 14.6	84.6 ± 14.7	0.001 for time 0.5003 for group × time 0.1023 for trial × time
	Pl	81.4 ± 6.4	80.2 ± 6.2	80.8 ± 6.3	
	Mean	83.4 ± 11.2	81.9 ± 11.0		

Cr, creatine; Pl, placebo; PoS, after supplementation; PrS, before supplementation

* Values are mean ± standard deviation.

regarding the effect of Cr on heat tolerance. However, visual examination of the graphic data showed that there was little or no difference between groups for the PoS trials except that the difference between the Cr and placebo groups began to widen as exercise duration progressed. As expected, core temperature increased significantly over the 40-min exercise bouts. The three-way interaction (group × trial × time) was significant, potentially reflecting a treatment effect. A test of simple effects was performed to determine the source of the significant differences across the four tests at each time point. The results are shown in Fig.

1. The data are graphed for both groups (Fig. 1A) and for each group (Fig. 1B,C) to clarify within-group differences, which are difficult to grasp due to crossing over of lines in the combined graph. Figs. 1B and 1C show that both groups had a lower core temperature in the PoS trial than in the PrS trial over 40 min. This is reflected in the significant F ratio for trial (Table 3), with overall temperatures being 37.9°C for the PrS trial and 37.7°C for the PoS trial. The Cr group trials were significantly different from one another at every time point except for before exercise, whereas the placebo group trials differed at every time point (Figs. 1B and 1C,

Table 3
Temperature responses to exercise in the heat*

Variable	Trial	Group	Before	10 min	20 min	30 min	40 min	Mean	P
Core temperature (°C)	PrS	Cr	37.4 (0.3)	37.6 (0.3)	37.8 (0.3)	38.1 (0.4)	38.4 (0.4)	37.8 (0.49)	0.590 [†] 0.024 [‡]
		Pl	37.4 (0.2)	37.6 (0.3)	37.9 (0.3)	38.3 (0.4)	38.6 (0.4)	37.9 (0.54)	<0.001 [§]
		Mean	37.4 (0.2)	37.6 (0.3)	37.8 (0.3)	38.2 (0.4)	38.5 (0.4)		0.538
	PoS	Cr	37.3 (0.3)	37.4 (0.3)	37.7 (0.3)	37.9 (0.4)	38.1 (0.4)	37.7 (0.45)	0.001 [#]
		Pl	37.2 (0.3)	37.4 (0.2)	37.6 (0.2)	38.0 (0.2)	38.4 (0.3)	37.7 (0.51)	0.058 [¶]
		Mean	37.2 (0.3)	37.4 (0.3)	37.6 (0.3)	37.9 (0.3)	38.3 (0.4)		0.025 ^{**}
Mean Skin temperature (°C)	PrS	Cr	35.9 (0.9)	36.4 (0.7)	36.7 (0.5)	37.1 (0.5)	37.4 (0.6)	36.7 (0.82)	0.930 [†] 0.477 [‡]
		Pl	35.6 (1.0)	36.4 (0.7)	36.8 (0.6)	37.1 (0.6)	37.5 (0.5)	36.7 (0.93)	<0.001 [§]
		Mean	35.8 (0.9)	36.4 (0.7)	36.8 (0.5)	37.1 (0.5)	37.5 (0.5)		0.520
	PoS	Cr	35.7 (0.8)	36.4 (0.6)	36.7 (0.5)	37.0 (0.5)	37.1 (0.8)	36.6 (0.82)	0.490 [#]
		Pl	35.7 (0.4)	36.4 (0.3)	36.8 (0.5)	37.0 (0.7)	37.5 (0.6)	36.7 (0.77)	0.897 [¶]
		Mean	35.7 (0.6)	36.4 (0.5)	36.7 (0.5)	37.0 (0.6)	37.3 (0.7)		0.612 ^{**}
Mean body temperature (°C)	PrS	Cr	36.9 (0.3)	37.2 (0.3)	37.4 (0.3)	37.7 (0.3)	38.0 (0.4)	37.4 (0.50)	0.713 [†] 0.050 [‡]
		Pl	36.8 (0.4)	37.2 (0.4)	37.6 (0.3)	37.9 (0.4)	38.3 (0.4)	37.5 (0.62)	<0.001 [§]
		Mean	36.9 (0.3)	37.2 (0.3)	37.5 (0.3)	37.8 (0.4)	38.1 (0.4)		0.545
	PoS	Cr	36.8 (0.3)	37.1 (0.4)	37.3 (0.4)	37.6 (0.4)	37.8 (0.5)	37.3 (0.52)	0.069 [#]
		Pl	36.7 (0.2)	37.0 (0.2)	37.3 (0.2)	37.6 (0.3)	37.9 (0.5)	37.3 (0.53)	0.139 [¶]
		Mean	36.7 (0.3)	37.0 (0.3)	37.3 (0.3)	37.6 (0.4)	37.8 (0.5)		0.696 ^{**}

Cr, creatine; Pl, placebo; PoS, after supplementation; PrS, before supplementation

* Values are mean (standard deviation).

[†] For group.

[‡] For trial.

[§] For time.

^{||} For group × trial.

[¶] For trial × time.

[#] For group × time.

^{**} For group × trial × time.

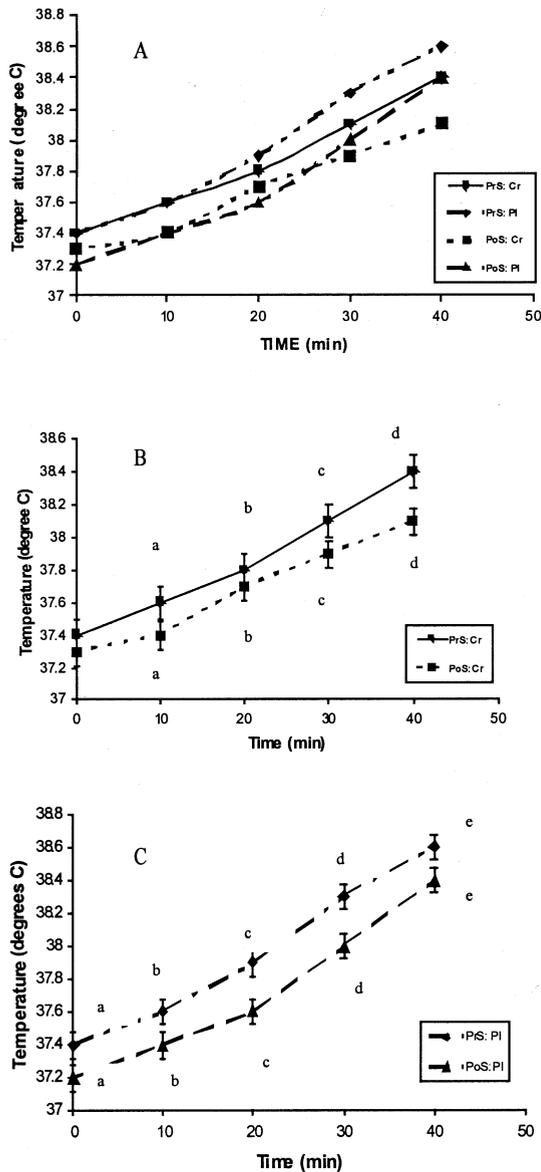


Fig. 1. Group \times trial \times time analysis (mean \pm standard error) of core (rectal) temperature responses to exercise in the heat for the Cr and PI groups combined (A), the Cr group only (B), and the PI group only (C). Like letters represent significant differences ($P \leq 0.05$). Cr, creatine; PI, placebo; PoS, after supplementation; PrS, before supplementation.

respectively). Between-group differences for the PoS trial showed that values in the placebo group were lower than those in the Cr group before exercise, whereas those in the Cr group were lower than those in the placebo group at the end of the 40-min exercise bout (Fig. 2).

Analysis of mean skin temperature responses is also presented in Table 3. A significant F ratio was found only for change over time for the combined groups and trials, with temperature increasing over the course of the trial. No other main effects or interactions were significant. Similar to mean skin temperature, mean body temperature showed a significant increase over time, with no interaction attribut-

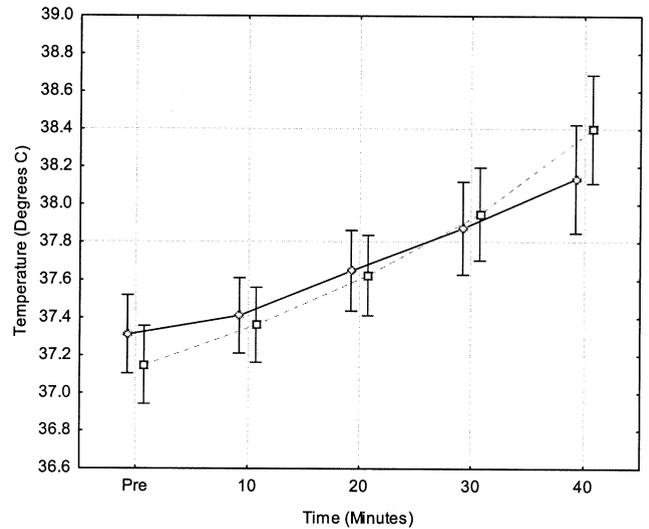


Fig. 2. Group \times time analysis (mean \pm standard error) of core temperature responses to exercise in the heat for the creatine (diamonds) and placebo (squares) groups after supplementation.

able to the treatment (Table 3). However, there was a significant trial effect, with the overall mean body temperature being significantly lower during the PoS trial. Thermal sensation, as described by the Gagge scale, showed a significant increase over time but no treatment effect (Table 4).

Discussion

This study investigated the effects of short-term supplementation of Cr monohydrate on thermoregulatory responses during exercise in a hot environment (39°C). It was hypothesized that Cr would negatively affect the body's ability to thermoregulate because its osmotic effect holds fluid within skeletal muscle cells, thereby decreasing the body's ability to release heat through the sweat mechanism. Results indicated that core temperature was significantly lower after supplementation for both groups combined (PrS at 37.85°C and PoS at 37.7°C), with no difference between groups. Further, both groups had significantly lower core temperatures after supplementation, but neither treatment showed an advantage over the other. Mean body and mean skin temperatures also showed no differences.

The osmotic effect that was hypothesized to have a negative effect on thermoregulation apparently was not a factor. The body regulates blood and cellular osmolality within fine limits. Although not measured, there may have been extra fluid intake by the Cr group and that increased volume was dispersed so that blood osmotic homeostasis was maintained (Table 5). This suggests that this possible increase of fluid in the Cr group helped to maintain osmolality at its pretreatment level. This potential mechanism for increased extracellular fluid may have helped the body deal with the heat stress and may have played a role in the

Table 4
Thermal responses to exercise in the heat*

Variable	Trial	Group	Before	10 min	20 min	30 min	40 min	Mean	P
Thermal sensation scale	PrS	Cr	—	5.1 (0.5)	5.6 (0.8)	5.9 (0.9)	6.5 (1.1)	5.77 (0.98)	0.496 for group 0.483 for trial
		Pl	—	4.8 (0.6)	5.6 (0.6)	5.9 (1.2)	7.1 (1.1)	5.84 (1.19)	<0.001 for time
		Mean	—	4.9 (0.5)	5.6 (0.7)	5.9 (1.0)	6.8 (1.1)		0.171 for group × trial
	PoS	Cr	—	4.8 (0.3)	5.4 (0.5)	5.8 (0.9)	6.1 (1.0)	5.53 (0.85)	0.120 for group × time
		Pl	—	4.9 (0.2)	5.6 (0.6)	6.3 (0.9)	6.9 (1.1)	5.92 (1.06)	0.074 for trial × time
		Mean	—	4.9 (0.2)	5.5 (0.6)	6.0 (0.9)	6.5 (1.1)		0.749 for group × trial × time

Cr, creatine; Pl, placebo; PoS, after supplementation; PrS, before supplementation

* Values are mean (standard deviation).

increased body weight of the Cr group seen after supplementation.

Of primary interest was the response of core temperature, skin temperature, and overall mean body temperature to the stress of exercise in the heat after a loading period of Cr monohydrate. Core temperature was maintained at a lower level in the PoS trial than in the PrS trial in both groups, which does not support a treatment effect for Cr. One possible conclusion would be acclimatization by the subjects, but we do not support this idea. However, visual data of just the PoS trials suggested a potential benefit of Cr supplementation. Although not statistically significant, Fig. 2 shows that, at 40 min, the core temperature of the Cr group was lower than that of the placebo group, even though the Cr group started the trial at a slightly higher core temperature. If there truly was an increase in extracellular volume, it may have been such that the heat dissipation could occur to a greater extent, thereby keeping core temperature lower.

At the time of data collection, no studies had been published that compared or contrasted results; since then, one similar study has been published. Volek et al. [30] examined the influence of Cr supplementation on temperature responses and other system responses to exercise in the heat. As in our study, no differences in rectal response were seen in either group, and body mass was significantly increased in the Cr group. Both studies incorporated cycling as the mode of exercise. They cycled for 30 min but then included three 10-s sprints at the end of the trial. Our ambient tem-

perature was slightly higher (39°C versus 37°C) while they worked at a slightly greater intensity. Although these studies are somewhat similar, there are too many differences to say with any certainty what role Cr plays relative to thermoregulation in submaximal exercise in the heat.

Mean skin temperature showed no significant differences except over time (Table 3). Mean body temperature, like core temperature, showed a significant main effect for trial, with the PoS trial having an overall lower mean temperature than the PrS trial. No other measurements of core, mean skin, or mean body temperatures were found to be different between groups.

An acknowledged methodologic limitation of this study that may have affected the results was the measurement of $\dot{V}O_{2\max}$ and subsequent workload for each trial. The use of a standard relative percentage of $\dot{V}O_{2\max}$ may have resulted in different levels of perceived or physiologic exertion for the subjects. This could have been avoided had some specific point of ventilatory threshold been used instead of a percentage of $\dot{V}O_2$. In addition, the incremental, discontinuous protocol of 3-min stages for $\dot{V}O_{2\max}$ determination may have been insufficient to determine steady-state $\dot{V}O_2$ versus workload relationships. This would have resulted in a flawed $\dot{V}O_2$ to workload slope, thereby influencing the intensity of each subject's trial such that subjects were not working at relatively equal intensities. This is particularly important when testing two different groups.

Future recommendations should consider these limitations and use a longer protocol, a lower temperature, or

Table 5
Changes in osmolality during exercise in the heat*

Trial	Group	Pre	Post	Mean	P ≤ 0.05
PrS	Cr	287.6 (5.4)	293.6 (5.7)	290.6 (4.5)	0.645 for group 0.092 for trial
	Pl	289.4 (3.1)	294.4 (4.2)	291.9 (4.5)	0.001 for time 0.741 for group × trial
	Mean	288.5 (4.4)	294.0 (4.9)		0.951 for group × time 0.837 for trial × time
PoS	Cr	286.8 (5.0)	291.5 (3.9)	289.1 (4.2)	
	Pl	286.8 (3.1)	292.6 (5.2)	289.7 (4.2)	0.254 for group × trial × time
	Mean	286.8 (4.0)	292.1 (4.4)		

Cr, creatine; Pl, placebo; PoS, after supplementation; PrS, before supplementation

* Values are mean (standard deviation).

some combination. Perhaps a 60-min bout would have been enough to exhibit a statistically significant difference between Cr supplementation and placebo. This was not possible in our study because the pilot work had only one subject who completed the original duration of 60 min. Perhaps a slight decrease in the ambient temperature would have allowed the subjects to exercise longer.

References

- [1] Balsom PD, Ekblom B, Soderlund K, Sjodin B, Hultman E. Creatine supplementation and dynamic high-intensity intermittent exercise. *Scand J Med Sci Sports* 1993;3:143–9.
- [2] Earnest CP, Snell PG, Rodriguez R, Almada AL, Mitchell TL. The effect of creatine monohydrate ingestion on anaerobic power indices, muscular strength and body composition. *Acta Physiol Scand* 1995;153:207–9.
- [3] Greenhaff PL, Casey A, Short AH, Harris R, Soderlund K, Hultman E. Influence of oral creatine supplementation of muscle torque during repeated bouts of maximal voluntary exercise in man. *Clin Sci* 1993;84:565–71.
- [4] Harris RC, Viru M, Greenhaff PL, Hultman E. The effect of oral creatine supplementation on running performance during maximal short term exercise in man. *J Physiol* 1993;467:74P.
- [5] Hultman E, Greenhaff PL. Skeletal muscle energy metabolism and fatigue during intense exercise in man. *Sci Prog* 1991;75:361–70.
- [6] Hultman E, Bergstrom M, McLennan Anderson N. Breakdown and resynthesis of adenosine triphosphate in connection with muscular work in man. *Scand J Clin Lab Invest* 1967;19:56–66.
- [7] Harris RC, Soderlund K, Hultman E. Elevation of creatine in resting and exercised muscle of normal subjects by creatine supplementation. *Clin Sci* 1992;83:367–74.
- [8] Greenhaff PL, Bodin K, Harris RC, Hultman E, Jones DA, McIntyre DB, et al. The influence of oral creatine supplementation on muscle phosphocreatine resynthesis following intense contraction in man. *J Physiol* 1993;467:75P.
- [9] Ziegenfuss TN, Lowery LM, Lemon PWR. Acute fluid volume changes in men during three days of creatine supplementation. *J Exerc Physiol Online* 1998;1(3).
- [10] Engelhardt M, Neumann G, Berbalk A, Reuter I. Creatine supplementation in endurance sports. *Med Sci Sports Exerc* 1998;30:1123–9.
- [11] Greenhaff PL. Creatine and its application as an ergogenic aid. *Int J Sports Nutr* 1995;5:S100–10.
- [12] American College of Sports Medicine. Guidelines for exercise testing and prescription. Baltimore: Lippincott Williams & Wilkins; 2000, p. 50–1.
- [13] McArdle WD, Katch FI, Katch VL. Individual differences and measurement of energy capacities. In: Balado D, editor. *Exercise physiology: energy, nutrition, and human performance*. Baltimore: Williams & Wilkins; 1996, p. 198–200.
- [14] Convertino VA, Keil LC, Bernauer EM, Greenleaf JE. Plasma volume, osmolality, vasopressin, and renin activity during graded exercise in man. *J Appl Physiol* 1981;50:123–8.
- [15] Convertino VA, Keil LC, Greenleaf JE. Plasma volume, renin and vasopressin responses to graded exercise after training. *J Appl Physiol* 1983;54:508–14.
- [16] Harrison MH. Effects of thermal stress and exercise on blood volume in humans. *Physiol Rev* 1985;65:149–209.
- [17] Harrison MH, Edwards RJ, Fennessy PA. Intravascular volume and tonicity as factors in the regulation of body temperature. *J Appl Physiol* 1978;44:69–75.
- [18] Miles DS, Sawka MN, Glaser RM, Petrofsky JS. Plasma volume shifts during progressive arm and leg exercise. *J Appl Physiol* 1983;54:491–5.
- [19] Ramanathan NL. A new weighting system for mean surface temperature of the human body. *J Appl Physiol* 1964;19:531–3.
- [20] Brooks GA, Fahey TD, White TP, Baldwin KM. Exercise in the heat and cold. In: Sordi M, editor. *Exercise physiology: human bioenergetics and its applications*. Mountain View, CA: Mayfield Publishing; 2000, p. 478–9.
- [21] Maron MB, Wagner JA, Horvath SM. Thermoregulatory responses during competitive marathon running. *J Appl Physiol Respir Environ Exerc Physiol* 1977;42:909–14.
- [22] Greenhaff PL, Constatin-Teodosiu D, Casey A, Hultman E. The effect of oral creatine supplementation on skeletal muscle ATP degradation during repeated bouts of maximal voluntary exercise in man. *J Physiol* 1994;476:84P.
- [23] Green AL, Simpson E, Littlewood J, MacDonald I, Greenhaff P. Carbohydrate ingestion augments creatine retention during creatine feedings in humans. *Acta Physiol Scand* 1996;158:195–202.
- [24] Gagge AP, Stolwijk AJ, Hardy JD. Comfort and thermal sensations associated with physiological responses at various ambient temperatures. *Environ Res* 1967;1:1–20.
- [25] Glickman-Weiss EL, Heaton CM, Nelson AG. A thermal perception scale for use during resting exposure to cold air. *Percept Motor Skills* 1994;79:547–60.
- [26] Bruning JL. *Computational handbook of statistics*. Glenview, IL: Scott, Foresman and Co; 1968.
- [27] Balsom PD, Harridge SDR, Soderlund K, Sjodin B, Ekblom B. Creatine supplementation per se does not enhance endurance exercise performance. *Acta Physiol Scand* 1993;149:521–3.
- [28] Chanutin A, Guy LP. The fate of creatine when administered to man. *J Biol Chem* 1926;67:29–41.
- [29] Soderlund K, Balsom PD, Ekblom B. Creatine supplementation and high-intensity exercise: influence on performance and muscle metabolism. *Clin Sci* 1994;87(suppl):120–1.
- [30] Volek JS, Mazzetti SA, Farquhar WB, Barnes BR, Gomez AL, Kraemer WJ. Physiological responses to short-term exercise in the heat after creatine loading. *Med Sci Sports Exerc* 2001;33:1101–8.