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Creatine supplementation *per se* does not enhance endurance exercise performance

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Creatine supplementation has been shown to increase total creatine content in skeletal muscle (Harris *et al.* 1992). The resulting enhancement of performance and effect on anaerobic energy metabolism observed during high-intensity intermittent exercise (Balsom *et al.* 1993, Greenhaff *et al.* 1993b) have been attributed to both a higher pre-exercise phosphocreatine (PCr) concentration and an increased rate of PCr resynthesis during rest periods (Greenhaff *et al.* 1993a). During prolonged continuous exercise, energy is produced primarily via aerobic pathways; however, contribution from anaerobic pathways is necessary in certain circumstances, such as, at the onset of exercise, at exercise intensities exceeding Vo_{2max} and where the exercise intensity is continuously fluctuating as in terrain running. It is currently not clear whether creatine supplementation influences performance and energy metabolism with these types of continuous exercise. This study investigated the influence of creatine supplementation on performance during a supramaximal run on a motor-driven treadmill until exhaustion and a ~ 6-km terrain run. The anaerobic energy demands of the two runs were high as indicated by the mean blood lactate accumulations (Table 1). Directly before, and at 30-s intervals during the treadmill run, oxygen uptake was measured using the Douglas bag technique with a Tissot spirometer (W. E. Collins Inc., MA, USA) and Beckman (Palo Alto, CA, USA) S-3A and LB-2 oxygen and carbon dioxide analysers. In both runs blood lactate was measured enzymatically (YSI 2300GL), from a finger-tip blood sample (25 μl) after the warm-up and 3 min post-exercise and heart rate (HR) was monitored continuously using a Polar 4000 Sport Tester (Polar Electro, Kempele, Finland). In the terrain run venous blood samples were taken from a forearm vein, pre- and 15 min post-exercise, to measure peak plasma concentration of hypoxanthine, an adenine nucleotide degradation product (cf. Balsom *et al.* 1993). Body mass was measured at each visit to the laboratory.

The study was performed as a double-blind design with 18 habitually active to well-trained male subjects divided into a creatine ($n = 9$) and placebo ($n = 9$) group. For these two groups the mean (range) age was 25.6 (21–32) and 27.3 (19–37) years, pre-experimental body mass was 73.6 (63–82.8) and 73.6 (58.4–92.6) kg, and Vo_{2max} was 4.7 (4.1–5.3) and 4.6 (4.0–5.5) 1 min^{-1}, respectively. Informed consent was received from each subject. Procedures used in the study were approved by the ethical committee of the Karolinska Institute. After completing a Vo_{2max} test subjects were habituated to the test procedures, they then returned on two consecutive days to perform a treadmill run to exhaustion at ~ 120% of Vo_{2max} (chosen to give a run time of between 3 and 6 min) and a ~ 6 km terrain run on a forest track with an undulating terrain. The two runs were repeated under standardized conditions after a 6-day administration period during which four 6-g doses, of either 5 g creatine monohydrate + 1 g glucose (creatine group) or 6-g glucose (placebo group), were administered per day (see Balsom *et al.* 1993). One subject (creatine group) did not complete the terrain run due to illness whereas seven subjects from each group completed the treadmill run. Statistical analysis was performed using a two-way ANOVA with repeated measures on one factor. When a significant F-value was observed *post hoc* Student's *t*-tests were performed. The level of significance was set at $P < 0.05$. Results are presented as mean and SEM.

In agreement with previous studies (Balsom *et al.* 1993) body mass increased significantly as a result of creatine supplementation from 73.5 (2.3) to 74.4 (2.3) kg. No significant changes were found in the placebo group [73.6 (3.3) to 73.5 (3.2) kg]. The possibility that part of the increase in body mass could be attributed to morphological changes in skeletal muscle is currently being investigated in our laboratory. With the treadmill run [mean speed and

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Table 1. Performance and physiological measurements (mean and SEM) for the creatine and placebo groups for the pre- and post-administration runs

	Creatine		Placebo	
	Pre-admin.	Post-admin.	Pre-admin.	Post-admin.
Performance (min)				
Treadmill	3.72 (0.24)	3.97 (0.25)	3.33 (0.20)	3.54 (0.30)
Terrain	23.36 (0.82)	23.79 (0.85)*	23.92 (0.79)	23.76 (0.80)
Oxygen uptake (ml kg^{-1} min^{-1})				
30 s	30.4 (1.4)	27.6 (1.0)	28.5 (2.2)	27.1 (1.9)
60 s	52.7 (1.2)	52.7 (1.2)	53.9 (2.4)	53.8 (2.4)
Peak	62.4 (1.4)	62.1 (1.4)	61.8 (2.8)	61.8 (2.7)
Heart rate (beats min^{-1})				
Treadmill (peak)	186.1 (2.7)	188.3 (2.7)	181.8 (3.0)	180.9 (3.0)
Terrain (mean)	177.1 (1.4)	178.9 (0.8)	177.6 (3.4)	177.9 (3.4)
Blood lactate (mmol l^{-1})				
Treadmill	15.3 (1.2)	17.2 (1.4)*	14.6 (0.8)	13.8 (0.6)
Terrain	9.0 (0.5)	10.2 (1.1)	10.6 (0.8)	11.3 (1.0)
Plasma hypoxanthine (μmol l^{-1})	15.4 (2.9)	13.8 (1.8)	15.0 (0.9)	16.8 (1.5)

* Post-administration significantly different from pre-administration ($P < 0.05$).

gradient 16.7 (0.3) and 17.3 (0.6) km h^{-1} and 3.1 (0.2) and 3.0 (0.2)°, for the creatine and placebo group, respectively] no significant changes in performance were observed between the two groups (Table 1). With the terrain run, however, whereas there was no change for the placebo group comparing performance before to after administration, a significant increase in run time was observed in the creatine group (Table 1). The reason for this impairment of physical performance is not clear. Although it is feasible that it could have been due to the increase in body mass, no relationship was found between change in body mass and change in run time ($P > 0.05$). Oxygen uptakes measured at rest and during the treadmill run did not differ following the administration period (Table 1). Creatine has been shown to stimulate mitochondrial respiration *in vitro* (Bessman *et al.* 1988); however, the observation that peak oxygen uptake did not change following creatine supplementation was not unexpected as it is generally accepted that, in man, limitations in maximal aerobic power are with oxygen delivery to the muscle and not with peripheral factors (cf. Saltin & Strange 1992). Neither peak HR measured during the treadmill run nor mean HR during the terrain run changed significantly as a result of the administration period (Table 1). The observation that with the treadmill run blood lactate accumulation (post-exercise minus pre-exercise concentration) was significantly higher following creatine supplementation (Table 1) is not readily explainable. If muscle buffer capacity had increased following creatine supplementation as suggested by Harris *et al.* (1992), the expected smaller change in pH could have allowed for both greater anaerobic energy production (extra work was performed due to the $\sim 1\%$ increase in body mass) and a higher rate of lactate efflux in line with the finding that active lactate transport from the muscle *in vitro* is pH dependent (Juel & Wibrand 1989). With long-term creatine supplementation an increase in the diameter of type II fibres has been reported (Sipilä *et al.* 1981). If in the current study a similar adaptation had occurred, this might also partly explain the observed increase in blood lactate accumulation due to the high glycolytic activity of these fibres. No changes in blood lactate accumulation or peak plasma hypoxanthine concentration were observed for the terrain run (Table 1).

In summary, our data show clearly that creatine supplementation *per se* does not enhance performance or increase peak oxygen uptake during prolonged continuous exercise. It is not possible to explain with certainty the decrease in performance observed during the terrain run; however, the increase in body mass is a likely explanation.These findings are contrary to the enhancement of performance previously observed following creatine supplementation with short duration high-intensity intermittent exercise and suggest that, in line with theoretical reasoning, the ergogenic effects of creatine supplementation are restricted mainly to short duration high-intensity exercise.

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