Review Article

Creatine Supplementation and Exercise Performance: An Update

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Creatine, a natural nutrient found in animal foods, is alleged to be an effective nutritional ergogenic aid to enhance sport or exercise performance. Research suggests that oral creatine monohydrate supplementation may increase total muscle creatine [TCr], including both free creatine [FCr] and phosphocreatine [PCr]. Some, but not all, studies suggest that creatine supplementation may enhance performance in high-intensity, short-term exercise tasks that are dependent primarily on PCr (i. e., <30 seconds), particularly laboratory tests involving repeated exercise bouts with limited recovery time between repetitions; additional corroborative research is needed regarding its ergogenic potential in actual field exercise performance tasks dependent on PCr.

Creatine supplementation has not consistently been shown to enhance performance in exercise tasks dependent on anaerobic glycolysis, but additional laboratory and field research is merited. Additionally, creatine supplementation has not been shown to enhance performance in exercise tasks dependent on aerobic glycolysis, but additional research is warranted, particularly on the effect of chronic supplementation as an aid to training for improvement in competitive performance.

Short-term creatine supplementation appears to increase body mass in males, although the initial increase is most likely water. Chronic creatine supplementation, in conjunction with physical training involving resistance exercise, may increase lean body mass. However, confirmatory research data are needed.

Creatine supplementation up to 8 weeks has not been associated with major health risks, but the safety of more prolonged creatine supplementation has not been established.

Creatine is currently legal and its use by athletes is not construed as doping.

Key teaching points:

- Phosphocreatine (PCr) is a major source of muscular energy during short-term, high-intensity exercise bouts lasting from approximately 2 to 30 seconds.
- Creatine supplementation, particularly with concomitant carbohydrate intake, may significantly increase intramuscular [TCr], [FCr], and [PCr], particularly in those consuming meat-free diets.
- In general, research supports the finding that creatine supplementation may enhance performance in certain repetitive, high-intensity, short-term exercise tasks.
- Research findings do not generally support an ergogenic effect of short-term creatine supplementation on exercise tasks dependent on anaerobic or aerobic glycolysis, but recommended research includes possible ergogenic effects associated with interaction effects of concomitant chronic physical training and creatine supplementation.
- Short-term creatine supplementation, up to 8 weeks, has not been associated with major health risks, but few safety data are available regarding chronic supplementation protocols.
- Creatine supplementation has not been prohibited by athletic governing bodies, so its use is currently regarded as legal.

INTRODUCTION

Athletes successful in strength/power/speed sports associated with high power production use intramuscular stores of adenosine triphosphate (ATP) and phosphocreatine (PCr) as the primary energy substrate. PCr is constituted in the muscle from creatine and phosphate, and although the role of creatine in human metabolism has been understood for over a half-century

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[1], only recently has its potential as a sport ergogenic been explored. Previous reviews [2–9] regarding the ergogenicity of creatine supplementation have been published, but coverage of its effect on exercise performance was limited because few studies were available. A considerable number of studies have been published subsequently, meriting an update. This review will highlight the theory of creatine supplementation and its effects on muscle concentration of PCr, various types of physical performance, body mass, health-related issues, and legal and ethical concerns.

THEORY UNDERLYING CREATINE SUPPLEMENTATION

Creatine is a nitrogenous amine. Normal daily dietary intake of creatine from an omnivorous diet approximates 1 g. Exogenous dietary sources of creatine include meat, fish, and other animal products, but it may also be formed endogenously in the liver, kidney, and pancreas from the amino acids glycine, arginine, and methionine. Harris et al [10] indicate the normal daily requirement from either exogenous or endogenous sources approximates 2 g to replace catabolized creatine, which is excreted from the kidneys as creatinine. One-half kg of fresh, uncooked steak contains about 2 g creatine.

Approximately 120 g of creatine is found in a 70 kg male, 95% in the skeletal muscle. Total creatine (TCr) exists in the muscle as both free creatine (FCr) and phosphocreatine (PCr). About 60% of the TCr is PCr, and the remainder is FCr. Creatine is an important source of chemical energy for muscle contraction because it can undergo phosphorylation that is both rapid, with the formation of PCr, and reversible, with donation of the phosphate group to adenosine diphosphate (ADP) to form adenosine triphosphate (ATP). This phosphorylation-dephosphorylation reaction, catalyzed by the enzyme creatine kinase, is a rapid source of high-energy phosphate for performing high-intensity, short-duration physical activity.

Intramuscular supplies of both high-energy phosphagens ATP and PCr are limited, with the combined total being estimated to sustain very high-intensity exercise for approximately 10 seconds [2]. Theoretically, creatine supplementation could increase [TCr], possibly facilitating the generation of intramuscular [PCr] and subsequent ATP formation, prolonging the duration of high-intensity physical activity [2].

CREATINE SUPPLEMENTATION: EFFECTS ON MUSCLE [TCr] AND [PCr]

For creatine supplementation to be effective, it must increase the amount of TCr or PCr within the muscle, and these increased stores must help rapidly replenish PCr and ATP during exercise. Various supplementation strategies have been used in attempts to increase [TCr], particularly [PCr]. The most commonly used protocol is to ingest a daily total of 20 to 30 g of creatine, usually creatine monohydrate, in four equal doses of 5 to 7 g dissolved in fluids over the course of the day, for 5 to 7 days, although some studies used lower doses or supplemented for fewer days.

Using 20 to 30 g of creatine monohydrate/day for 2 days, Harris et al [10] reported a significant increase in the [TCr] of the quadriceps femoris muscle, indicating that 20 to 40% of the increase in [TCr] was accounted for by [PCr]. They noted that muscle uptake of oral creatine supplementation was greatest in the first 2-day supplementation period, with smaller increases in subsequent days. Casey et al [11] also reported significant increases in muscle [TCr] (about 18%) and [PCr] (about 10%) following supplementation with 20 g creatine monohydrate for 5 days. Other studies have also reported increases in both [TCr] and [PCr], and the [PCr]/[ATP] ratio [12–18].

Hultman et al [19] employed several strategies, including a rapid protocol involving 6 days of creatine supplementation at a rate of 20 g/day, and a slower protocol with supplementation for 28 days at a rate of 3 g/day. Following the rapid protocol, they also studied a maintenance dose of 2 g/day for 28 days. Both the rapid and slow protocols produced similar findings, about a 20% increase in muscle [TCr]. The elevated [TCr] was maintained when supplementation was continued at a rate of 2 g/day. However, although [PCr] increased, the increase was not significant in each separate group studied, but was significant when the results from the groups were combined.

Greenhaff et al [20], using a 20 g dose for 5 days, noted a mean 25% increase in TCr, but no increase in [PCr]. However, PCr resynthesis after muscle contraction was increased by 35%. These are the first data that an increase in muscle FCr concentration, resulting from dietary creatine supplementation, can accelerate the rate of muscle PCr resynthesis during recovery from exercise.

Not all studies have shown positive effects. For example, one study [21], using only 2 g creatine monohydrate/day for 6 weeks showed no beneficial effects on either muscle TCr or PCr levels. Even in those studies [10,20] that have reported significant group increases in muscle [TCr], the investigators did note substantial individual differences. For example, Greenhaff et al [20] noted that five of their eight subjects increased muscle [TCr] following supplementation, while three subjects did not. Individuals who increased muscle [TCr] most were those who had subnormal levels before supplementation, about 120 mmol creatine/kg dry matter or less, such as vegetarians. Individuals who have somewhat higher levels of muscle creatine are less responsive to creatine supplementation.

However, studies by Green et al [22,23] have shown that combining the creatine with a simple carbohydrate, such as glucose, will increase creatine transport into the muscle even in subjects with near normal levels of muscle creatine, possibly via an insulin-mediated effect. The solution consisted of 5 g of creatine and about 90 g of simple carbohydrate, consumed 4

times per day. Both the creatine and the creatine-carbohydrate supplements increased [TCr] and [PCr], but the creatine-carbohydrate supplement increased [TCr] by 60% and [PCr] by 100% compared to the creatine supplement alone [23]. Even one subject with a high initial [TCr] experienced a 43 mmol/kg/dry muscle increase as a result of the creatine-carbohydrate supplement.

Normal muscle creatine content approximates 125 mmol/kg dry matter, and human muscle appears to have an upper limit of creatine storage of 150–160 mmol/kg dry matter [3]. Subjects who increase muscle [TCr] by 20 mmol/kg dry matter may increase the rate of PCr resynthesis during recovery from exercise [20]. Casey et al [11] suggest that any performance benefits may be related to increased creatine within the type II muscle fibers.

Most studies used absolute doses of creatine, not basing the amount supplemented on body weight. However, Hultman et al [19] recommend a loading dose of 0.3 g/kg body mass/day for a period of 5 to 6 days, followed by a maintenance dose of 0.03 g/kg body mass/day thereafter.

CREATINE SUPPLEMENTATION: EFFECTS ON PHYSICAL PERFORMANCE

Creatine supplementation primarily has been studied in attempts to increase energy production in the ATP-PCr energy system. The ATP-PCr energy system has the greatest power potential. Muscle stores of PCr may split and release energy for the rapid resynthesis of ATP, although the supply of PCr, like ATP, is limited. The combined total of ATP and PCr might sustain energy production for approximately 5 to 10 seconds of maximal effort, and thus would be the primary energy source in track events ranging from 50 to 100 meters. Fatigue in such events may be attributed to the rapid decrease in PCr. Additionally, Stroud et al [24] cited anecdotal reports that creatine supplementation may influence the pattern of substrate utilization and improve performance during more prolonged, submaximal exercise. Over the past 5 to 6 years, investigators have used various approaches, including laboratory and field studies, in order to evaluate the effect of creatine supplementation not only on exercise tasks associated with the ATP-PCr energy system, but also on exercise tasks associated with the designated lactic acid (anaerobic glycolysis) and oxidative (particularly aerobic glycolysis) energy systems.

This review includes only those studies that have investigated the effect of pure creatine, primarily creatine monohydrate, on exercise performance in humans. Studies that have evaluated the ergogenic potential of commercial supplements containing not only creatine monohydrate, but other substances such as β-hydroxy-β-methylbutyrate (HMB), taurine, L-glutamate, and yeast-derived RNA, are not included [25–30]. Although animal models have been used to study biochemical adaptations and changes in performance associated with creatine supplementation [31], this review is limited to human studies. Published abstracts are included if adequate information is provided regarding subjects, supplementation dosage and protocol, and performance results. Personal contact with authors of published abstracts provided additional details.

ATP-PCR ENERGY SYSTEM

Anecdotal reports indicate that several British track athletes, including the gold medal winner in the 100 meter dash, used creatine supplements in conjunction with the 1992 Barcelona Olympic Games [32]. It is known that the generation of peak anaerobic power (highest force attainable) and anaerobic capacity (maintenance of peak muscular force production) in short-term, high-intensity exercise tasks may be dependent upon endogenous levels of ATP and PCr, particularly PCr as a means to rapidly regenerate the more limited intramuscular supply of ATP for anaerobic capacity. Theoretically, elevation of [FCr] through exogenous supplementation is a potential ergogenic mechanism for rapid replenishment of PCr, which in turn could provide a means of rapid ATP synthesis during intermittent, high-intensity, short duration activity. The key question addressed by the studies reviewed in this section is whether oral supplementation with creatine, and the possible increased muscle [FCr] and [PCr] can enhance performance in high-intensity, short-term (4 to 30 seconds) exercise.

Laboratory Studies

Several groups have investigated the efficacy of creatine supplementation as an ergogenic aid in the performance of high intensity short-term ($\leq$30-second) tasks in a laboratory-based setting. These studies, presented alphabetically by author's name in Table 1, are grouped and discussed below according to type of performance task.

Isotonic Strength and Endurance. Becque et al [33] studied the effect of creatine-supplemented strength training [(6-week periodized program beginning with 8-repetition maximum (RM) and ending with 2-RM)] on 1-RM performance. Twenty-three experienced male weight-lifters were assigned in a double-blind, non-randomized manner to either creatine supplementation (20 g/day for 7 days, followed by 2 g/day) or placebo (sucrose) groups. Strength training significantly increased 1-RM in both groups, but the creatine-supplemented group experienced greater increases in 1-RM compared to the placebo group.

Earnest et al [34] randomly assigned eight weight-trained males to either placebo-control or creatine supplementation (20 g/day for 14 days) in a double-blind manner. Significant increases in bench press 1-RM (6%) and bench press repetitions at 70% of 1-RM (35%) were observed in the creatine group.

Goldberg and Bechtel [35] randomly assigned 34 male

Table 1. Effect of Creatine Monohydrate Supplementation on Short-Term (≤30 Seconds) High-Intensity Performance—A Review of the Literature

Investigator	Year	N	Gender	Population	Design[a]	CM dose g/day	Days	Measured uptake?[b]	Mode[c]	Description	Ergogenic effect?	
Balsom et al [43]	1993	16	M	Active/well trained	RDBPC	25	6	N	CE	2 protocols (10×6-sec)	Y	Attenuated decline in power for bouts 7–10
Balsom et al [17]	1995	7	M	Physically active	SGRM	20	6	Y-B	CE	5×6-sec; 1×10-sec	Y	Increase in power during 10-s trial
Barnett et al [50]	1996	17	M	Recreationally active	RDBPC	20	4	N	CE	7×10-sec sprints	N	
Becque et al [33]	1997	23	M	Weight-lifters	DBPC	20	7	N	IT	Bicep curl 1-RM	Y	28% increase in bicep curl 1-RM
Birch et al [44]	1994	14	M	Healthy, not highly trained	RDBPC	20	5	N	CE	3×30-sec	Y	Increase in peak power, mean power and work for bouts 1 and 2
Burke et al [51]	1996	32	M/F	Elite swimmers	RDBPC	20	5	N	CE	2×10-sec	N	
									Swim	25-m/50-m swim	N	
Casey et al [11]	1996	9	M	Healthy	SGRM	20	5	Y-B	CE	2×30-sec	Y	4% increase in peak power ($p=0.052$); 1% increase in total work
Cooke et al [52]	1995	12	M	Untrained	RDBPC	20	5	N	CE	2×15-sec	N	
Dawson et al [45]	1995	18	M	Healthy active	RDBPC	20	5	N	CE	1×10-sec	N	
		22	M	Healthy active	RDBPC	20	5	N	CE	6×6-sec	Y	Increase in peak power and total work
Earnest et al [34]	1995	8	M	Weight trained	RDBPC	20	14	N	CE	Wingate test (×3)	Y	Increase in total work
									IT	1-RM; reps @ 70% 1-RM	Y	Increase in isotonic strength and endurance
Goldberg and Bechtel [35]	1997	34	M	Varsity football and track athletes	RDBPC	3	14	N	IT	1-RM Bench	N	
									Jump	Vertical Jump	Y	2.6% increase with %Δ BMI as a covariate
Gonzalez de Suso et al [53]	1995	19	M/F	Trained	RDBPCX	21	14	Y-NMR	CE	7×7-sec	N	Equivocal (7% increase in PL→CM group; no change in CM→PL group)
Greenhaff et al [41]	1993	12	M/F	Physically active	RDBPC	20	5	N	IK	30 reps×5 sets	Y	Greater absolute leg torque; attenuated decline in leg torque
Greenhaff et al [18]	1994	6	M	Healthy	SGRM	20	5	Y-B	CE	Isokinetic cycling (×2)	Y	Increased total work in 2nd test
Grindstaff et al [49]	1997	18	M/F	Junior competitive swimmers	RDBPC	21	9	N	AE	3×20-sec maximal swim bench	N	
Hamilton-Ward et al [38]	1997	20	F	Athletes	RDBPC	25	7	N	IK	Elbow flexion torque	N	
									IT	Elbow flexion 1-RM	N	
Johnson et al [36]	1997	18	M/F	Volunteers	RPC	20	6	N	IK	Bilateral muscle fatigue test of knee extensors	Y	6% increase in concentric power 9% increase in eccentric power
									IT		Y	25% increase in concentric work 15% increase in eccentric work
Kirksey et al [39]	1997	36	M/F	Track and field athletes	RDBPC	0.3 $g \cdot kg^{-1} \cdot d^{-1}$	42	N	CE	Wingate test (×5)	Y	13% increase in mean peak power
									IT	Vertical Jump performance	N	
Kurosawa et al [42]	1997	5	M/F	Healthy	SGRM	5	14	Y-NMR	IM	High intensity Grip Strength	Y	20%-untrained arm (35%-trained arm)
Lemon et al [12]	1995	7	M	Physically active	RDBPCX	20	5	Y-NMR	IM	Ankle (20×30-sec max)	Y	11% increase in total force; 12% increase in maximal force
Mujika et al [56]	1996	20	M/F	Swimmers	RDBPC	20	5	N	Swim	25-m/50-m swim	N	
Odland et al [54]	1997	9	M	Physically active	SGRM	20	3	Y-B	CE	Wingate test	N	
Prevost et al [46]	1997	18	M/F	Active college students	RPC	18.75	5	N	CE	Time to exhaustion at 150% VO_{2max}		
						2.25	7			30-s work/60-s rest	Y	61% increase
										20-s work/40-s rest	Y	62% increase
										10-s work/20-s rest	Y	100% increase

Table 1. *Continued*

Investigator	Year	N	Gender	Population	Design[a]	CM dose g/day	Days	Measured uptake?[b]	Mode[c]	Description	Ergogenic effect?
Redondo et al [57]	1995	22	M/F	Highly trained athletes	RDBPC	25	7	N	Run	60-m sprint velocity	N
Ruden et al [55]	1996	9	M/F	College aged	SGRM	20	4	Y-?	CE	Wingate test	N
Schneider et al [47]	1997	9	M	Untrained	RSBPC	25	7	N	CE	5 × 15-sec	Y 6.5% increase in total work (kJ)
Stout et al [40]	1997	24	M	College football players	RDBPC	21 10.5	5 51	N	IT	1-RM Bench	N
									Jump	Vertical jump	N
									Run	100-yard dash	N
Vandenberghe et al [15]	1996	20	F	Females	RDBPC	20	4	Y-NMR	IK	5 × 30 max arm	N
Vandenberghe et al [13]	1996	9	M	Healthy	RDBPCX	40	6	Y-NMR	IM	Maximal (×3)	N
									IK	3 × 30/4 × 20/5 × 10 @ 180°	Y 10–23% increase in torque production
Volek et al [37]	1996	14	M	Healthy active	RDBPC	25	7	N	IT	Jump squat; 10-RM (×5)	Y Increased jump power output; increased repetitions for combined 5 × 10-RM bench press
Ziegenfuss et al [48]	1997	33	M/F	High power athletes	RDBPC	20	3	N	CE	6 × 10-sec	Y Increased total work in sprint 1; increased peak power (sprints 2–6) ($p = 0.10$)

[a] RDBPC = randomized double blind placebo control, RPC = randomized placebo control, RSBPC = randomized single blind placebo control, SGRM = single group repeated measures, RDBPCX = randomized double blind placebo control crossover.

[b] Y-B = muscle biopsy, Y-NMR = ^{31}P-nuclear magnetic resonance spectroscopy.

[c] CE = cycle ergometer, IT = isotonic, IK = isokinetic, IM = isometric.

football and track athletes in a double-blind manner to either a placebo or creatine group in order to study the effects of a low-dose creatine supplementation regimen (3 g/day for 14 day) on vertical jump, lower body strength and 1-RM bench press performance. During the study, subjects were concurrently engaged in off-season resistive training and were tested at baseline, 7 days and 14 days of supplementation. Using ANCOVA with percent change in body mass index as a covariate, the investigators reported that creatine supplementation significantly improved vertical jump performance by 2.5%. No other performance measures were significantly improved following creatine supplementation.

Johnson et al [36] measured concentric and eccentric work in a bilateral knee extensor test to exhaustion prior to and following creatine supplementation (20 g/day for 6 days) in 18 males and females who were randomly assigned to either placebo or creatine groups. Following supplementation, increases of 25 and 15% were reported for concentric and eccentric work for the dominant (right) leg. The authors concluded that creatine supplementation was effective in improving muscular work.

Volek et al [37] assigned 14 healthy, active males in a double-blind manner to either placebo or creatine supplementation (25 g/day for 7 days). Dependent variables were bench press performance (5 sets to failure using a 10-RM resistance) and jump squat performance (5 sets of 10 repetitions using 30% of squat 1-RM). Creatine supplementation significantly increased power output in the number of 10-RM bench press repetitions and all five jump squat sets.

Using a double-blind design, Hamilton-Ward et al [38] randomly assigned 20 female athletes paired on body composition and age to either placebo or creatine supplementation (25 g/day for 7 days) groups. Dependent variables included isotonic elbow flexion 1-RM and muscle fatigue during elbow flexion, measured as the number of repetitions at 70% of 1-RM. For the creatine group, the number of post-supplementation elbow flexion repetitions (15.0 ± 1.3) was 16% greater than the number of pre-supplementation repetitions (12.9 ± 1.1). However, this change was not statistically significant. It was concluded that creatine supplementation did not affect muscle strength or endurance.

Kirksey et al [39] used a longer supplementation regimen (42 days) to study the effects of creatine on power output. In a double-blind manner, 36 male and female collegiate track and field athletes were randomly assigned to either placebo or creatine (0.3 g/kg/day [~20 g/day]) groups. Static and counter movement vertical jump (CMVJ) performance was measured using a force plate before and after the 6-week supplementation period. There was no apparent effect of creatine supplementation on vertical jump performance.

Stout et al [40] compared the effects of a creatine monohydrate and glucose supplement (CM) with a supplement containing creatine monohydrate, sodium and potassium phosphates and taurine (Phosphagen HP™) on 1-RM bench press,

and vertical jump performance in football players. Twenty-four athletes were randomly assigned to either CM, Phosphagen HP™ or placebo control for 8 weeks of supplementation, during which they also were engaged in speed drills and resistive training. Compared to the placebo, the CM supplementation regimen (21 g/day for 5 days, then 10.5 g/day for 51 days) did not significantly increase 1-RM bench press or vertical jump performance, due in part to large intra-group variance.

Overall, these studies suggest that a creatine monohydrate supplement of 20 to 25 g/day for 7 to 14 days may improve isotonic strength and endurance performance.

Isokinetic Torque. Greenhaff et al [41] investigated the influence of creatine monohydrate supplementation on muscle torque during repeated bouts of maximal voluntary exercise in 12 physically-active, but not highly-trained subjects randomly assigned to a placebo or treatment group. Subjects completed 5 bouts of 30 maximal voluntary isokinetic contractions, interspersed with 1-minute recovery periods, before and after 5 days of placebo or creatine monohydrate (20 g/day) supplementation. For their analysis, the 30 contractions were partitioned into three segments: 1–10, 11 to 20, and 21 to 30 contractions. No difference was seen in muscle torque production during exercise before and after placebo ingestion. However, muscle peak torque production after creatine supplementation was greater in all subjects during the final 10 contractions of exercise bout 1, throughout the whole of exercise bouts 2, 3, and 4, and during contractions 11 to 20 of the final exercise bout. An observed lower accumulation of plasma ammonia during exercise after creatine ingestion suggested that dietary creatine supplementation may accelerate skeletal muscle phosphocreatine resynthesis, and that the increased availability of phosphocreatine would maintain better the required rate of ATP demand during contraction.

Johnson et al [36] measured concentric and eccentric isokinetic power production of the knee extensors of the dominant leg at 60°/second prior to and following creatine supplementation (20 g/day for 6 days) in 18 males and females who were randomly assigned to either placebo or creatine groups. Concentric and eccentric power increased by 6 and 9%, respectively, in the creatine group with no change in the placebo group. The authors concluded that creatine supplementation can improve muscular power production.

In one of several cross-over designs in the literature, Vandenberghe et al [13] measured isokinetic torque production in nine males before and after creatine supplementation (40 g/day for 6 days). Muscle [PCr]/[ATP] increased as measured by ^{31}P-nuclear magnetic resonance spectroscopy (^{31}P-NMRS). Subjects performed maximal voluntary contractions in three interval series of 3 sets×30, 4 sets×20, and 5 sets×10 contractions separated by 2-minute rest. Isokinetic torque production increased by 10 to 23% following creatine supplementation, with the most noticeable improvement observed immediately after the 2-minute rest between sets.

In their study of female athletes, Hamilton-Ward et al [38] also measured peak shoulder internal rotation velocity (°/second), as well as concentric and eccentric torque prior to and following creatine supplementation (25 g/day for 7 days). Isokinetic performance remained unchanged following creatine supplementation.

Vandenberghe et al [15] randomly assigned 20 females to either a placebo or high-dose creatine supplementation phase (20 g/day for 4 days), followed by a low-dose supplementation phase (5 g/day for 10 weeks). Muscle [PCr]/[ATP], measured via ^{31}P-NMRS, was increased following the high dose phase, but elbow flexion power output at 70% 1-RM was unchanged. Muscle [PCr]/[ATP] remained elevated throughout the low-dose phase. However, elbow flexion power output increased in the creatine group following the low-dose phase.

Although the results are not unanimous with regard to the ergogenicity of creatine, there is evidence that supplementation with 20 to 40 g/day for 4 to 7 days may improve isokinetic torque force production and attenuate the decline in power during repetitive isokinetic exercise in a laboratory setting.

Isometric Force

In a single-group repeated measures study combining creatine supplementation with isometric training, Kurosawa et al [42] trained five subjects using a 2-week grip exercise protocol. Subjects trained the non-dominant forearm 6 sessions/day isometrically to exhaustion at a rate of 1/second at 30% of maximal voluntary contraction, during which they also consumed 5 g creatine monohydrate/day. Prior to and following training, high-intensity (measured in nm/second) and low-intensity grip performances (time to exhaustion using the training protocol) were measured in both dominant and non-dominant arms. Following supplementation, forearm muscle [PCr], measured by ^{31}P-NMRS, was significantly increased in both arms. In addition, significant increases of 20 and 35% in high-intensity grip strength were observed in the non-trained and trained arms, respectively. The authors concluded that 2 weeks of creatine supplementation increased muscle [PCr] and enhanced high-intensity exercise performance.

In a cross-over design, Lemon et al [12], using seven active men as subjects, studied the effect of creatine monohydrate supplementation (20 g/day for 5 days) on total integrated force in 20 30-second maximal isometric ankle extensions with a 16-second recovery between contractions. The washout period was 5 weeks. The supplement increased the pre-exercise muscle [PCr]/[ATP] ratio and significantly increased total integrated muscle force by 11%. The authors also noted that the effect of the supplement was somewhat prolonged, since the [PCr]/[ATP] ratio, as measured by ^{31}P-NMRS, was still elevated in one of the three subjects who received the creatine monohydrate supplement as the first treatment.

As part of their previously described study, Vandenberghe et al [13] also measured maximal static (isometric) quadriceps force production at 95°, 120°, and 145° in nine healthy males.

No improvement in isometric force production was observed at any of these joint angles following creatine supplementation (40 g/day for 6 days).

As evident, the literature is scant and somewhat equivocal regarding the effect of creatine monohydrate on isometric force production, although the majority of the studies report significant improvement in isometric exercise performance following creatine supplementation.

Arm and Cycle Ergometer Performance. Various short-term, high-intensity ergometer protocols have been used to investigate the possible ergogenic effect of creatine supplementation, with time frames ranging from 6 to 30 seconds.

Balsom et al [43] randomly assigned 16 highly motivated male physical education students to a placebo or creatine supplement (25 g/day) group and had them undergo two intermittent high-intensity cycle ergometer exercise protocols before and after 6 days of supplementation. The exercise task involved 10 6-second bouts of high-intensity cycling interspersed with 30-second of passive rest. One of the protocols was designed to induce fatigue so that subjects would be unable to maintain force output throughout each 6-second period over the 10 exercise bouts. The investigators partitioned the work output of each 6-second bout into three intervals: 0 to 2 seconds; 2 to 4 seconds; and 4 to 6 seconds. Theoretically, creatine supplementation would be most beneficial in the latter intervals, i.e., 4 to 6 seconds, and indeed the authors noted that significant differences in this time frame between the groups began after the 7th bout, with the creatine group experiencing a significantly lower decrease in performance compared to the placebo group. Examination of their data plots also indicated that although the performance of the placebo group declined from bout one through bout three, the performance of the creatine group actually increased during these first three bouts. However, the differences became increasingly greater following trial four and became significant after trial seven.

In a later study by Balsom et al [17], seven highly motivated, physically active male subjects performed repeated bouts of fixed-intensity cycle ergometer exercise (5×6 seconds with 30-second recovery periods), followed by a maximal 10-second bout to determine maximal power output, before and after 6 days of creatine supplementation (20 g/day). Following supplementation, subjects were able to maintain power output, as demonstrated by an attenuated rate of decline in pedal frequency at the end of the 10-second bout. They concluded that the enhanced fatigue resistance following creatine supplementation was associated with greater [PCr] and decreased muscle [lactate].

Birch et al [44] measured maximal isokinetic cycle performance (3 bouts×30 seconds at 80 rev/minute with 4-minute rest) in 14 healthy, but not highly trained males who were randomly assigned in a double-blind manner to either placebo or creatine supplementation (20 g/day for 5 days). Significant increases in peak power output (8% for bout 1), mean power output (6% for bouts 1 and 2) and total work (6% for bouts 1 and 2) were observed in the creatine group. The authors concluded that whole body performance can be improved in the first two of three maximal 30-second bouts. There were no effects of creatine supplementation on [lactic acid], but creatine ingestion did lead to a lower accumulation of plasma [NH_3], suggestive of an enhanced effect on muscle ATP turnover.

In a single group design, Casey et al [11] measured maximal isokinetic cycle ergometer performance (2 bouts×30-seconds at 80 rev/minute with 4-minute rest) in nine healthy males before and after 5 days of creatine supplementation (20 g/day). Creatine supplementation resulted in a significant 19% increase in muscle [TCr] as measured by biopsy. Total work increased significantly by about 4% in both bouts. The authors reported the increases in peak and total work to be positively correlated with the increases in muscle [TCr], specifically in Type II fibers. They concluded that the improvements in work output were related to enhanced ATP resynthesis secondary to increased [PCr] in Type II fibers.

In one of two studies presented in the same report, Dawson et al [45] measured cycle ergometer sprint performance (6 bouts×6 seconds with a 24-second recovery period between bouts) in 22 subjects who were randomly assigned to either placebo or creatine supplementation (20 g/day for 5 days) groups. Significantly greater increases in peak power output and total work were observed in the creatine group following supplementation. Additionally, the creatine group completed more work in sprint one (in isolation) compared to the placebo group, which is in contrast to the results for the 10-second performance test in the other study presented in this report [45], and described later.

Using three Wingate tests (30 seconds) interspersed with a 5-minute rest as their test protocol, Earnest et al [34] studied the effect of creatine monohydrate (20 g/day for 14 days) ingestion on peak anaerobic power (highest power output in a 5-second period) in eight weight-trained men who were matched according to mean anaerobic capacity and assigned to the placebo or treatment group. They also evaluated the effects of the creatine supplementation on anaerobic capacity (total work in 30 seconds). There were no significant differences between the groups relative to peak anaerobic power; however, the creatine group experienced a significant improvement in anaerobic capacity performance in all three trials, while the placebo group experienced no changes.

In a single-group ordered repeated measures design, Greenhaff et al [18] investigated the effect of creatine supplementation (20 g/day for 5 days) on isokinetic cycle ergometer exercise (2 bouts×30 seconds at 80 rev/minute with 4-minute rest interval) in six healthy male subjects. Creatine ingestion resulted in a 19% increase in muscle [TCr], as well as a significant increase in total work in the second bout. Following creatine supplementation, the authors noted a 50% reduction in ATP loss in the second exercise bout despite increased work

performance, suggesting that a possible consequence of increased [TCr] ([PCr]+[Cr]) is an attenuation of ATP degradation during intense work.

In their previously mentioned study of track and field athletes (n=36 males and females), Kirksey et al [39] measured cycle ergometer performance (5×10 seconds with 1-minute recovery) prior to and following creatine supplementation (0.3 g/kg/day [~20 g/day] for 6 weeks). They reported a significant group by trial interaction in mean peak power across all five Wingate trials with a 13% increase in the creatine group compared to a 5% increase in the placebo group. They concluded that creatine supplementation favorably increased power output in male and female track and field athletes.

Prevost et al [46] randomly assigned 18 college-aged, physically active males and females to placebo or creatine supplementation groups. Creatine supplementation consisted of 18.75 g/day for 5 days, followed by 2.25 g/day for 6 days. Subjects were administered three different cycle ergometer intermittent interval training regimens, each with a work component at 150% of $\dot{V}O_{2max}$. Creatine supplementation increased time to exhaustion by 61% for 30-second work/60-second rest; 62% for 20-second work/40-second rest; and 100% for 10-second work/20-second rest regimens. They concluded that the ability to maintain high-intensity, intermittent exercise is enhanced by creatine supplementation.

Using a single-blind placebo control design, Schneider et al [47] randomly assigned nine untrained males to either placebo or creatine (25 g/day for 7 days) supplementation groups. Total work performed in 5×15-second maximal cycle ergometer bouts was measured prior to and following supplementation. Creatine ingestion resulted in a significant 6.5% increase in total work (kJ) compared to the placebo treatment. They concluded that creatine supplementation may increase the rate of ATP resynthesis in untrained subjects.

Ziegenfuss et al [48] randomly assigned 33 high power male and female athletes to either creatine (0.35 g/kg fat free mass/day for 3 days) or placebo groups to investigate the effects of creatine supplementation on sprint cycle performance (6 bouts×10-second). They reported significant ($p=0.10$) increases in total work performed in bout 1 and peak power in bouts 2 to 6 in the creatine group.

Grindstaff et al [49] studied the effect of creatine supplementation (21 g/day for 9 days) on swim-bench sprint test performance (3×20-second maximal-effort interspersed with 60-second rest) in 18 male and female junior competitive swimmers. Although creatine supplementation did not result in improved peak power and total work, they reported a trend toward a significant group by test interaction ($p=0.06$) using the change in work (i.e., Δwork=post-supplementation work minus pre-supplementation work) as the dependent variable. They discuss evidence of a greater change in work in the first sprint for the creatine group compared to the placebo group. It is important to note, however, that there were large standard deviations around these mean changes in work, suggesting the presence of considerable inter-individual response with regard to repeated trials.

In a double-blind, placebo-control, matched-group design, Barnett et al [50] reported no effect of creatine supplementation (~20 g/day for 4 days) on peak power output or mean power output during sprint cycle performance (seven bouts×10 seconds) in 17 recreationally active males.

Using a single test protocol, Burke et al [51] subdivided 32 elite male and female swimmers from the Australian National Team into either a placebo or creatine monohydrate supplementation group (20 g/day for 5 days), evaluating their maximal cycle ergometry performance in a single 10-second test prior to and following the supplementation period. The investigators reported no significant effect of the creatine supplementation on either power or total work.

Cooke et al [52] reported no significant effect of creatine monohydrate supplementation (20 g/day for 5 days) on peak power, time to peak power, total work, and an index of fatigue in 12 untrained males assigned to either a placebo or supplement group. The cycle performance involved two 15-second power tests, with a recovery period of 20 minutes between tests.

In their second study in the same report, Dawson et al [45] randomly assigned 18 subjects in a double-blind manner to either placebo or creatine supplementation (20 g/day for 5 days) groups to investigate the effects on single bout (10-seconds) maximal cycle ergometer performance. They reported no differences between the groups in maximal cycle ergometer performance following supplementation.

Gonzalez de Suso et al [53] used a randomized double-blind placebo-control cross-over design to investigate the effect of creatine supplementation (21 g/day for 14 days) on cycle sprint performance (seven bouts×7 seconds) in 19 trained males and females. Creatine supplementation increased the [PCr]/[β-ATP] ratio in both groups, as determined by ^{31}P-NMRS. However, performance findings were equivocal, with a 7% increase in peak power output observed in the group that consumed the placebo followed by creatine, but no change in the group that consumed the creatine followed by the placebo. Although this study is one of few to employ a cross-over design, the length of the washout period was not clearly indicated and may have been short. Consequently, a short washout might mask a meaningful treatment effect if there was a residual effect in the group that consumed creatine in the first trial.

Odland et al [54] studied the effect of creatine supplementation on power output during the 30-second Wingate test. In a crossover design, nine males underwent three randomly ordered trials—control, placebo, and creatine monophosphate (20 g/day for 3 days). Using W/kg as the measure of power, these investigators reported no significant differences between the trials in peak power, mean 10-second power, or mean 30-second power. Moreover, although biopsies of the vastus lateralis revealed significantly higher [FCr] in the muscle following creatine supplementation, there were no differences in

[TCr] or [PCr], which may have been the basis for their insignificant findings in performance.

Ruden et al [55] investigated the effect of creatine supplementation (20 g/day for 4 days) vs. placebo on Wingate test performance (1×30 seconds) in nine college-aged subjects (five females, four males) using a single group repeated measures cross-over design. Treatment order was counter-balanced with a 14-day washout between treatments. Peak power, mean power and total work were unaffected by creatine supplementation. However, as previously discussed, 14 days may not be sufficient for a complete washout of supplemented increases in [TCr]. As a result, an order effect, if present, could mask an ergogenic effect of creatine supplementation.

Of the 17 studies reviewed in this section which employed cycle ergometer performance in a laboratory setting, 11 reported an ergogenic effect of creatine supplementation (25 ± 29% improvement). The results of one study are considered equivocal, while the remaining studies failed to support the ergogenic efficacy of creatine supplementation.

Field Studies

Five studies have investigated the effect of creatine supplementation on actual sport performance, i.e., sprint running and swimming, in a field setting. Since the performance of high-intensity, short-duration repetitive activities is at a premium in the field setting (e.g., the sports arena), it is important that the ergogenicity of creatine be documented in such settings.

Using a double-blind, placebo-control design involving 32 elite male and female swimmers from the Australian National Team, Burke et al [51] reported that oral creatine monohydrate (20 g/day for 5 days) did not enhance performance in maximal single effort swim sprints of 25 m and 50 m, each interspersed with approximately 10-minute recovery period. In a similar study, Mujika et al [56] assigned 20 male and female swimmers in a randomized, double-blind manner to either creatine supplementation (20 g/day for 5 days) or placebo groups in order to investigate the effect on 50-m swim sprint performance. They also reported no performance differences between the groups.

In their double-blind placebo controlled study of the effects of low-dose creatine supplementation (3 g/day for 14 days) on football and track athletes engaged in off-season conditioning, Goldberg and Bechtel [35] also measured 40 yard dash sprint speed. Compared to placebo, creatine supplementation failed to significantly improve 40 yard sprint speed.

Based on gender and 60-m sprint speed, Redondo et al [57] matched 24 highly trained male soccer and female field hockey athletes actively involved in training and randomly assigned them, in pairs, to either a treatment or placebo group. The treatment involved the effect of creatine monohydrate supplementation (25 g/day for 7 days) on sprint velocity during various zones (20 to 30 m; 40 to 50 m; 50 to 60 m) of three successive 60 m dash trials, each interspersed with a 2-minute recovery period. Subjects were videotaped with three high speed cameras, and velocities were determined from the videotape. Two sessions were conducted, one prior to and one following the treatment protocol. A four factor MANOVA (group, session, trial, zone) revealed no main or interaction effects for the groups, indicating that the creatine supplement did not enhance sprint performance with this particular protocol.

In their study of college football players, Stout et al [40] also compared the effects of 8 weeks of supplementation with either creatine and glucose (21 g creatine monohydrate/day for 5 days, followed by 10.5 g/day for 51 days), Phosphagen HP™, or placebo on 100 yard dash performance. Subjects were also engaged in resistive training and speed drills (4 sessions/week). Creatine monohydrate supplementation failed to significantly improve running speed.

Although these field studies are unanimous with regard to their null findings, the existence of only five studies of the effect of creatine on actual athletic performance clearly represents a dearth in the applied literature. More field investigations are needed concerning the use of creatine in sports events involving multiple high-intensity, intermittent exercise tasks, such as soccer.

LACTIC ACID ENERGY SYSTEM (ANAEROBIC GLYCOLYSIS)

Conceivably, increased levels of PCr could reduce reliance on anaerobic glycolysis as a replenishment source of ATP, and possibly mitigate the formation of lactic acid and enhance performance in high-intensity, more prolonged exercise tasks approximating 30 to 150 seconds. Some studies have investigated the effect of creatine supplementation on such exercise tasks. A summary of the literature pertaining to the effects of creatine supplementation on more prolonged, predominantly anaerobic performance tasks is provided in Table 2.

Laboratory Studies

Bosco et al [58] reported a 13% increase in treadmill running (20 km/hr at 5% incline) time to exhaustion (~60 seconds) in sprinters and jumpers following creatine supplementation (25 g/day for 7 days). In addition, compared to placebo, creatine supplementation resulted in performance improvements during 0 to 15 seconds (7%) and 15 to 30 seconds (12%) of a 45-second maximal continuous jumping test.

Jacobs et al [59] reported an ergogenic effect of creatine supplementation on moderately prolonged anaerobic exercise tasks. In a double-blind placebo study, 26 male and female subjects were randomly assigned to either a placebo or creatine monohydrate supplementation (20 g/day for 5 days) group. Subjects were tested on a cycle ergometer, riding to exhaustion at 125% of $\dot{V}O_{2max}$. These investigators reported that ride time to exhaustion was increased significantly following creatine

Table 2. Effect of Creatine Monohydrate Supplementation on High-Intensity, More Prolonged (>30 to ≤150 Seconds) Performance—A Review of the Literature

Investigator	Year	N	Gender	Population	Design[a]	CM dose g/day	Days	Measured uptake?[b]	Mode[c]	Description	Ergogenic effect?	
Balsom et al [64]	1993	18	M	Well trained	RDBPC	20	6	N	Run	TM time @ 125% $\dot{V}O_{2max}$	N	
Bosco et al [58]	1997	14	M	Sprinters/jumpers	RBDPC	20	5	N	Run	Treadmill 20-km · hr^{-1} 5% incline (~60-sec)	Y	13% increase in time to exhaustion
									Jump	45-sec continuous	Y	7% increase 0–15 s 12% increase 15–30 s
Burke et al [51]	1996	32	M/F	Elite swimmers	RDBPC	20	5	N	Swim	100-m swim time	N	
Earnest et al [60]	1995	11	M	Males	RDBPC	20	4	N	Run	90-sec TM test (×2)	N	
Febbraio et al [61]	1995	6	M	Untrained	SGRM	20	5	Y-B	CE	4×60-s; 115–125% $\dot{V}O_{2max}$ 5th bout to fatigue	N	
Grindstaff et al [49]	1997	18	M/F	Junior competitive swimmers	RDBPC	21	9	N	Swim	3×50-m freestyle cumulative time	N	
										3×100-m freestyle cumulative time	N	
Harris et al [63]	1993	10	M	Middle distance runners	RSBPC	30	6	N	Run	4×300-m sprint time	Y	0.3-sec decrease in best 300-m sprint time
Jacobs et al [59]	1997	26	M/F	Physically active	RDBPC	20	5	N	CE	125% of $\dot{V}O_{2max}$	Y	8.5% increase in time to exhaustion; 9% increase in max accumulated O_2 debt
Kurosawa et al [42]	1997	5	M/F	Healthy	SGRM	5	14	Y-NMR	IM	Low intensity Grip performance Time to exhaustion	N	
Mujika et al [56]	1996	20	M/F	Swimmers	RDBPC	20	5	N	Swim	100-m swim time	N	
Prevost et al [46]	1997	18	M/F	Active college students	RPC	18.75 2.25	5 7	N	CE	Time to exhaustion at 150% $\dot{V}O_{2max}$	Y	24% increase
Schneider et al [47]	1997	9	M	Untrained	RSBPC	25	7	N	CE	5×60 sec	N	
Terrillion et al [62]	1997	12	F	Runners	RDBPC	20	5	N	Run	700-m run time (×2)	N	
Thompson et al [21]	1996	10	F	Competitive swimmers	RBDPC	2	42	Y-NMR	Swim	100-m swim time	N	

[a] RDBPC=randomized double blind placebo control, RPC=randomized placebo control, SGRM=single group repeated measures, RSBPC=randomized single blind placebo control, RDBPCX=randomized double blind placebo control crossover.

[b] Y-B=muscle biopsy, Y-NMR=^{31}P-nuclear magnetic resonance spectroscopy.

[c] CE=cycle ergometer.

monohydrate supplementation from 131 to 143 seconds (8.5%), while the placebo group's time remained unchanged at 128 seconds. Additionally, creatine monohydrate supplementation significantly increased by 9% the maximal accumulated oxygen deficit (difference between the oxygen demand of the work from the $\dot{V}O_2$/PO relationship and the cumulative $\dot{V}O_2$).

In physically active college students, Prevost et al [46] reported a 24% increase (approximately 49 to 60 seconds) in continuous cycle ergometer time to exhaustion at 150% of $\dot{V}O_{2max}$ following creatine supplementation (18.75 g/day for 5 days, then 2.25 g/day for 6 days).

Earnest et al [60] used a treadmill run test to exhaustion (approximately 90 seconds) to investigate the effect of creatine monohydrate supplementation (20 g/day for 4 days and 10 g/day for 6 days) on intermediate length anaerobic performance. Eleven male subjects assigned to either the supplement or placebo group trained specifically for the treadmill tests for 2 weeks, and were administered both pre- and post-supplementation trials. Subjects were tested twice each trial, each test being separated by an 8-minute recovery period. The investigators concluded that creatine monohydrate supplementation had no significant effect on this type of exercise performance.

Using a single group repeated measures design, Febbraio et al [61] examined the effects of creatine supplementation (20 g/day for 5 days) on cycle ergometer performance (4×60-second sprints followed by a 5th bout to exhaustion, all at 115 to 125% of $\dot{V}O_{2max}$) in six active, but untrained male subjects. Subjects were retested following a 28-day washout, during which a placebo was consumed for the last 5 days. An increase in intramuscular [TCr] was observed following creatine supplementation, but there were no differences in duration of the 5th exercise bout between baseline, post-supplementation and post-washout trials. Although the supplementation dose was sufficient to increase muscle [TCr], 28 days without supplementation was considered to be a sufficient time for muscle [TCr] to return to baseline. Furthermore, these investigators concluded that creatine supplementation has no ergogenic effect on exercise performance when the ATP-PCr energy system is not the principal energy source.

Following two weeks of isometric grip exercise training of the non-dominant arm concurrent with creatine supplementation (5 g/day), Kurosawa et al [42] reported non-significant increases of 23% (81.3±6.6 to 99.8±15.9 seconds) and 95 (73.8±5.8 to 144.3±60.6 seconds) in time to exhaustion (30% of maximal voluntary contraction at a rate of one contraction/second) in the non-trained and trained arms, respectively. Presumably, these changes were not significant due to large variances and the small sample size.

Schneider et al [47] reported no improvement in cycle ergometer performance (5×60 seconds) in nine untrained males following creatine supplementation (25 g/day for 7 days).

Although more research is needed in this area, the available literature suggests that, in contrast to the findings for repetitive, short-term (≤30 seconds) high-intensity activity, creatine supplementation is less likely to enhance performance of high-intensity more prolonged (30 to 150 seconds) tasks in a laboratory setting. These predominantly null findings are probably explained by energy system specificity with regard to performance of high-intensity tasks of short (≤30 seconds) vs. more prolonged (30 to 150 seconds) duration. In tasks that rely primarily on fast glycolysis for ATP synthesis, the ergogenic potential of creatine supplementation appears to be limited.

Field Studies

Four studies have examined the effects of creatine supplementation on swim performance. Burke et al [51] examined the effect of creatine supplementation (20 g/day for 5 days) on 100-m swim time in 32 elite male and female swimmers. Subjects were randomly assigned to either placebo or creatine groups in a double-blind manner. Creatine supplementation failed to improve 100-m sprint swim time. In a similar study, Mujika et al [56] assigned 20 male and female elite swimmers to either placebo or creatine supplementation (20 g/day for 5 days) groups in a randomized double-blind manner. They also concluded that creatine supplementation failed to improve 100-m swim time.

In their study of male and female junior competitive swimmers, Grindstaff et al [49] randomly assigned subjects by matched pairs in a double-blind manner to either a placebo or creatine supplementation (21 g/day for 9 days) groups. Times for three heats of both 50-m and 100-m freestyle swim distance were measured prior to and following supplementation. Significant group (placebo, creatine) by time (pre-heats 1, 2, and 3; and post-heats 1, 2, and 3) interactions were reported for both 50-m ($p=0.04$) and 100-m ($p=0.04$) swim time, which were largely explained by slower post-supplementation swim times in the placebo group. Although it was concluded that their study provided some evidence of the efficacy of creatine in enhancing repetitive swim sprint performance, supplementation had no effect on cumulative 50-m or 100-m swim time.

Thompson et al [21] randomly assigned 10 college-aged female competitive swimmers in a double-blind manner to either placebo or creatine groups in order to study the effects of a low-dose creatine supplementation regimen (2 g/day for 56 days) on 100-m swim performance. Using ^{31}P-NMRS and near-infrared spectroscopy, they measured [PCr], [PCr]/[β-ATP] ratio and [ADP] at rest and during exercise (plantar flexion) both prior to and following supplementation. Creatine supplementation had no effect on muscle metabolites. Compared to the placebo group, creatine supplementation was also ineffective in improving 100-m swim time.

In one of two studies of running performance, Terrillion et al [62] randomly assigned 12 female runners to either placebo or creatine supplementation (20 g/day for 5 days) groups. Subjects were timed in a 2×700-m interval workout prior to

Table 3. Effect of Creatine Monohydrate Supplementation on Aerobic (>150 Seconds) Exercise Performance—A Review of the Literature

Investigator	Year	N	Gender	Population	Design[a]	CM dose g/day	Days	Measured uptake?[b]	Mode[c]	Description	Ergogenic effect?
Balsom et al [64]	1993	18	M	Well-trained	RDBPC	20	6	N	Run	6-km terrain run time	N
Barnett et al [50]	1996	17	M	Recreationally active	RSBPC	20	4	N	CE	$\dot{V}O_{2peak}$	N
Godly and Yates [65]	1997	16	M/F	Well-trained cyclists	RDBPC	20	5	N	CE	25-km simulated road race with 6×15-sec sprint every 4-km	N
Harris et al [63]	1993	10	M	Middle distance runners	RSBPC	30	6	N	Run	1000-m run time (×4)	Y 2.1-sec decrease in best 1000-m time
Myburgh et al [16]	1996	13	M	Cyclists	RDBPC	20	7	Y-B	Cycle	Cycle distance in 1 hr	N
Rossiter et al [66]	1996	38	M/F	Rowers	RDBPC	20	5	Y-Est	Row	1000-m rowing time	Y 2.3-sec decrease in 1000-m rowing time
Stroud et al [24]	1994	8	M	Physically active	SGRM	20	5	N	Run	Metabolic response to steady state exercise at 50–90% $\dot{V}O_{2max}$	N
Thompson et al [21]	1996	10	F	Competitive swimmers	RBDPC	2	42	Y-NMR	Swim	400-m swim time	N

[a] RDBPC=randomized double blind placebo control, RSBPC=randomized single blind placebo control, SGRM=single group repeated measures.

[b] Y-B=muscle biopsy, Y-Est=estimated from urinary [creatine] and [creatinine].

[c] CE=cycle ergometer.

and following the supplementation period. Creatine supplementation failed to improve 700-m run time. However, Harris et al [63] tested 10 trained middle distance runners, equally assigned to either a placebo or treatment group, on separate days prior to and following creatine supplementation. The test involved 4×300 m runs with 4-minute recovery between repetitions on separate days and the creatine monohydrate dose was 30 g/day for 6 days. They reported an enhanced performance in the final 300-m run and the best 300-m time decreased significantly by 0.3 seconds with creatine supplementation. The authors suggested the increased use of PCr during exercise may contribute to the buffering of H^+.

Similar to laboratory studies, creatine supplementation does not appear to enhance performance in field studies involving more prolonged high-intensity tasks. Four of the five field studies involving swimming and running performance, all using a double-blind placebo design, report null findings concerning the efficacy of creatine supplementation.

OXIDATIVE ENERGY SYSTEM (AEROBIC GLYCOLYSIS)

As mentioned previously, Stroud et al [24] suggested that creatine supplementation may modify substrate utilization and possibly improve performance during prolonged, submaximal exercise. However, only limited research has been conducted in this area. A summary of the literature pertaining to the effect of creatine supplementation on aerobic exercise performance tests (>150 seconds) is provided in Table 3.

Laboratory Studies

To our knowledge, only five groups have investigated the effects of creatine supplementation on aerobic performance in a laboratory setting. Balsom et al [64] randomly assigned 18 well-trained habitually active male subjects equally into a creatine supplementation (20 g/day for 6 days) and placebo group. Subjects performed a treadmill run to exhaustion at about 120% of $\dot{V}O_{2max}$ both before and after the supplementation period. Although it is reasonable to expect anaerobic glycolysis to be the predominant energy source for such a supramaximal bout, the average time to exhaustion following supplementation was 3.97 ± 0.25 minutes, a performance time that appears to be somewhat more dependent on aerobic glycolysis. There were no significant differences between the groups. The investigators indicated the lack of an ergogenic effect might be expected because the energy system used would not be theorized to benefit from creatine supplementation.

As part of a previously described study of the effect of creatine on repetitive cycle sprint performance, Barnett et al [50] measured cycle ergometer $\dot{V}O_{2peak}$ in 17 recreationally active subjects before and after creatine supplementation (20 g/day for 4 days). Subjects were randomly assigned to either a

placebo or creatine group in a double-blind manner. Creatine supplementation failed to increase $\dot{V}O_{2peak}$.

Godly and Yates [65] measured time to completion in a simulated 25-km cycling race in which 16 well-trained male and female cyclists sprinted for 15 seconds every 4 km. Subjects were randomly assigned in a double-blind manner to either placebo or creatine supplementation (20 g/day for 5 days). There was no significant decrease in time to completion following creatine supplementation. They concluded that creatine supplementation has no effect on endurance activity combined with short-duration, high-intensity bouts in well-trained subjects.

In order to investigate anecdotal reports of improved substrate utilization, Stroud et al [24] had eight men perform a continuous incremental exercise treadmill running test at various predetermined workloads approximating 50 to 90% of their $\dot{V}O_{2max}$ before and after creatine supplementation (20 g/day for 5 days). Subjects achieved a steady state in each protocol, and both respiratory and blood analyses revealed creatine supplementation did not affect energy substrate metabolism during these tests. Additionally, there were no significant effects on substrate utilization during a 15-minute recovery period after the exercise bout.

Rossiter et al [66] randomly assigned 38 male and female competitive rowers to either placebo or creatine supplementation (20 g/day for 5 days) groups in a double-blind manner. Simulated rowing time over 1,000 m was measured before and after supplementation. Total creatine uptake was estimated as the difference between creatine consumed and urinary [creatine] and [creatinine]. Muscle creatine uptake was estimated as 38 ± 10 mmol/kg dry muscle. A significant 2.3-second decrease in 1,000 m rowing time (211.0 to 208.7 seconds) was observed in the creatine group with no change in the placebo group. The authors also reported a trend toward significance in the association between estimated creatine uptake and percent change in rowing performance ($r = 0.43$; $p = 0.09$).

Field Studies

Several groups have investigated the efficacy of creatine supplementation to enhance performance in running and cycling endurance tasks. In an extension of their study reported above, Balsom et al [64] also had their subjects perform a 6-km terrain run on a forest trail. The authors speculated that although this type of exercise task is primarily aerobic in nature, certain segments of the trail might stress the ATP-PCr energy system. However, creatine monohydrate supplementation did not enhance performance, but, on the contrary, impaired performance. The authors suggested the impairment may have been caused by the significant weight gain experienced by the subjects following creatine supplementation, a finding which has been reported in other studies as noted below.

In a study on cycling performance, Myburgh et al [16] assigned 13 cyclists to either placebo or creatine (20 g/day for 7 days) groups in a randomized double-blind manner. Creatine supplementation increased muscle [TCr], but did not increase the distance cycled in one hour.

As part of their study of interval training performance in middle distance runners, Harris et al [63] also tested 10 trained male middle distance runners, equally assigned to either a placebo or creatine group (30 g/day for 6 days), on separate days prior to and following creatine supplementation. The tests involved 4×1000-m runs with 3-minute recovery on separate days. They reported an enhanced performance in the final 1000-meter run and the total time for all 1000 m runs. The best 1000-m run time decreased significantly by 2.1 sec with creatine supplementation but was unchanged by the placebo. In their study on competitive female college swimmers, Thompson et al [21] reported that creatine supplementation (2 g/day for 56 days) failed to improve 400-m swim time.

Overall, there appears to be little scientific support for the concept that creatine supplementation will enhance performance in exercise tasks dependent primarily on oxidative metabolism of endogenous carbohydrate and fat.

CAFFEINE AND CREATINE SUPPLEMENTATION

Caffeine consumption has been reported to adversely affect the efficacy of creatine supplementation. Since creatine uptake is dependent upon extracellular Na^+, Vandenberghe et al [13] hypothesized that adrenergic stimulation of the sarcolemma might enhance muscle creatine uptake via increased Na^+-K^+-ATPase pump activity. In a double-blind, repeated-measures, crossover study, they compared creatine uptake, isometric force and isokinetic knee-extension torque production in nine healthy males following 6 days of both creatine supplementation (0.5 g/kg/day) and creatine (0.5 g/kg/day) in combination with caffeine (5 g/kg/day). A 3-week washout period intervened between treatments. While muscle [PCr] was increased following both treatments, torque production was increased only following creatine supplementation. They concluded that the ergogenic effect of creatine is completely eliminated by caffeine consumption. In a follow-up study using the same protocol, Vandenberghe et al [14] reported that caffeine inhibits PCr resynthesis during recovery. These data suggest that, in contrast to potentiating the ergogenic effects of creatine, caffeine ingested in combination with creatine nullifies any ergogenic effect. However, additional research is needed to confirm these preliminary findings.

EFFECTS OF CREATINE ON BODY MASS

Not all studies presented data on body mass changes or showed significant changes following creatine supplementation, but as presented in Table 4, creatine supplementation

Table 4. Effect of Creatine Monohydrate Supplementation on Body Composition/Body Mass—A Review of the Literature

Investigator	Year	N	Gender	Population	Design[a]	CM dose g/day	Days	Measured uptake?[b]	Outcome measure		Ergogenic effect?
Balsom et al [43]	1993	16	M	Active/well trained	RDBPC	25	6	N	Body mass	Y	1.1 kg increase
Balsom et al [64]	1993	18	M	Well trained	RDBPC	20	6	N	Body mass	Y	0.9 kg increase
Balsom et al [17]	1995	7	M	Physically active	SGRM	20	6	Y-B	Body mass	Y	1.1 kg increase
Becque et al [33]	1997	23	M	Weight-lifters	RDBPC	20	7	N	Body mass	Y	2.0 kg increase; 1.6 kg increase in Fat Free Mass [sic]
Dawson et al [45]	1995	18	M	Healthy active	RDBPC	20	5	N	Body mass	Y	0.7 kg increase
		22	M	Healthy active	RDBPC	20	5	N	Body mass	N	
Earnest et al [34]	1995	8	M	Weight trained	RDBPC	20	14	N	Body mass	Y	1.7 kg increase
Godly et al [65]	1997	16	M/F	Well-trained cyclists	RDBPC	20	5	N	Body mass	N	
Goldberg and Bechtel [35]	1997	34	M	Varsity football and track athletes	RDBPC	3	14	N	Body mass	Y	0.9 kg increase
Green et al [23]	1996	12	M	Healthy	SGRM	20	5	Y-B	Body mass	Y	0.9 kg increase
		12	M	Healthy	SGRM	20 +370 g of carbo-hydrates	5	Y-B	Body mass	Y	1.6 kg increase
Greenhaff et al [18]	1994	6	M	Recreational athletes	SGRM	20	5	Y-B	Body mass	Y	1.6 kg increase
Grindstaff et al [49]	1997	18	M/F	Junior competitive swimmers	RDBPC	21	9	N	Body mass	N	
Hamilton-Ward et al [38]	1997	20	F	Athletes	RDBPC	25	7	N	Body mass	N	
Kirksey et al [39]	1997	36	M/F	Track and field athletes	RDBPC	0.3 g/kg/day	42	N	Lean body mass (estimated from 7-site skinfolds)	Y	4.8 kg increase (3.5 kg increase in placebo group)
Prevost et al [46]	1997	18	M/F	Active college students	RPC	18.75	5	N	Body mass	N	
						2.25	7				
Stout et al [40]	1997	24	M	College football players	RDBPC	21	5	N	Fat free mass (DEXA)	N	
						10.5	51				
Stroud et al [24]	1994	8	M	Physically active	SGRM	20	5	N	Body mass	7	1.0 kg increase
Thompson et al [21]	1996	10	F	Competitive swimmers	RBDPC	2	42	Y-NMR	Body mass	N	
Terrillion et al [62]	1997	12	F	Runners	RDBPC	20	5	N	Body mass	N	
Volek et al [37]	1996	14	M	Healthy active	RDBPC	25	7	N	Body mass	Y	1.4 kg increase

[a] RDBPC=randomized double blind placebo control, RPC=randomized placebo control, SGRM=single group repeated measures.

[b] Y-B=Muscle biopsy.

significantly increased body mass in numerous studies [17,18,23,24,33–35,37,39,43,45,64]. Increases in body mass ranging from 0.7 to 2.0 kg have been reported following short-term creatine supplementation (20 to 25 g/day for 5 to 14 days). However, Hultman et al [19] reported that creatine ingestion markedly reduced urinary volume during the initial days of supplementation, suggesting that the increased body mass was primarily water retention. In support of this finding, Ziegenfuss et al [48] reported increases of 6.6% in thigh skeletal muscle volume (measured by magnetic resonance imaging) and 2 to 3% in total body and intracellular fluid volumes (measured by multifrequency bioimpedance) in aerobic and cross-trained males following short-term creatine supplementation. In addition, Ziegenfuss et al [48] reported evidence of improved nitrogen status (decreased degradation and/or increased synthesis as measured by ^{15}N-glycine tracer) in experienced weight lifters.

Three studies [21,38,62] involving female subjects reported no significant increase in body mass following creatine supplementation. Thus, there may be an operational gender effect. However, it should be noted that the subjects in the study of Terrillion et al [62] were female distance runners, a population with a low potential for increased body mass.

When combined with physical training, chronic creatine supplementation may lead to increases in lean body mass. In both male and female track and field athletes undergoing preseason conditioning, Kirksey et al [39] reported a 4.8 kg increase in lean body mass (LBM), as estimated by skinfold measurements, following 6 weeks of creatine supplementation (0.3 g/kg/day [e.g., ~20 g/day]. However, an increase of 3.5 kg in LBM attributed to physical training was also observed in the placebo group. Significant increases in body mass and fat free mass [sic] were also reported by Becque et al [33] following a creatine-supplemented 6-week strength training regimen (20 g/day for the first week, 2 g/day thereafter).

Overall, it would appear that short-term creatine supplementation may contribute to increased total body and lean body mass, at least in males, although much of the increase in body mass may be attributed to water retention rather than increased contractile protein. Chronic creatine supplementation, combined with resistance training, may increase lean body mass, but more supportive research is desirable.

HEALTH-RELATED ISSUES

Other than the gain in body weight, presumably body water, no deleterious effects have been associated with creatine supplementation in amounts of 20 to 30 g for up to 7 days [2], nor have any adverse effects been reported with longer term studies, up to 6 weeks, using smaller dosages, 2 to 3 g/day. In addition, other than a proportionally greater change in lean body mass, no adverse changes were reported in the one study in this review which supplemented subjects with approximately 20 g of creatine/day for 6 weeks [39].

The breakdown product of creatine is creatinine, which is excreted by the kidney. Individuals with impaired kidney function may be at risk, but the healthy kidney should be able to excrete the excess creatinine provided daily hydration is adequate. Two brief reports [67,68] of the same study provided some data on the effect of chronic creatine monohydrate supplementation on markers of renal and hepatic function. In a double-blind, placebo-controlled, 12-week study involving 34 subjects, 20 males and females received 20 g creatine monohydrate/day for 5 days and 10 g/day for 51 days, followed by a 4-week withdrawal period. Blood was tested at baseline, week 4 and week 8 after supplementation, and week 12, 4 weeks after withdrawal. When the pooled data for males and females were analyzed, there were no significant changes in total protein, serum creatinine, bilirubin and BUN, or in serum enzymes AST, ALP, GGT, LDH, and CPK. However, when analyzed by gender, there was a significant increase in serum CPK in the males at week 8, which returned to normal at week 12 following withdrawal, and a significant increase in serum BUN in females at week 8, also returning to normal following withdrawal. Based on these data, the authors concluded that chronic high dose creatine monohydrate supplementation elicited minimal changes in markers of renal and hepatic function.

Some undocumented anecdotal reports indicate creatine supplementation may lead to muscle cramps and possible muscle strains. An increased intramuscular water content could dilute electrolytes, possibly leading to cramps, and a tightened musculature associated with intracellular swelling could predispose to muscle strains. However, no scientific data have been uncovered to substantiate these anecdotal accounts.

Some preliminary data suggest that creatine supplementation may confer some health benefits to hyperlipidemic patients. Individuals with total serum cholesterol concentrations exceeding 200 mg/dl experienced significant reductions in total cholesterol, triacylglycerols, and very low-density lipoprotein cholesterol following 56 days of supplementation with 20 g pure creatine monohydrate [69]. However, creatine supplementation had no effect on low-density or high-density lipoprotein cholesterol. These investigators noted that the mechanism of creatine's hypolipidemic effects remain enigmatic, but suggest that creatine may promote acute increases in hepatic insulin sensitivity, with resultant decreases in de novo triglyceride production [69].

One week of creatine supplementation also benefited patients with chronic heart failure, not by any direct effect on the heart but by increasing skeletal muscle strength and endurance [70]. The investigators involved in these studies emphasized that these data are preliminary and need replication.

Nevertheless, the Food and Drug Administration (FDA) recently warned consumers to consult a physician before using creatine. The FDA is investigating possible health risks of creatine, including its possible involvement in the deaths of three collegiate wrestlers. Speculatively, intracellular binding of water by creatine could impede dehydration techniques for

rapid weight loss, coercing wrestlers to use more dramatic approaches such as diuretics or increased heat stress that could induce heart attacks or heat stroke. Unfortunately, very little information is available to physicians regarding the adverse health effects of creatine supplementation.

LEGAL AND ETHICAL ASPECTS

Creatine is a natural dietary constituent; its use as a supplement to enhance sport performance has not been prohibited by the International Olympic Committee. Even if its use was prohibited, detection of ingested creatine would be problematic with current drug testing procedures [2]. Some might consider the use of creatine supplementation unethical, given the provision in the International Olympic Committee anti-doping legislation that consuming a substance in abnormal quantities with the intent of artificially and unfairly enhancing sports performance may be construed as doping.

SUMMARY

Although creatine has been available for supplementation for over a half-century, it is only recently that a concerted effort has been undertaken to investigate its potential ergogenic effect relative to sport or exercise performance. It does appear that oral creatine monohydrate supplementation may increase muscle [TCr], including both [FCr] and [PCr]. Many, but not all, studies suggest that creatine supplementation may enhance performance in high-intensity, short-term exercise tasks that are dependent primarily on the ATP-PCr energy system, particularly in laboratory tests involving repeated exercise bouts with limited recovery time between repetitions. In this regard, a summary of the literature supporting the efficacy of creatine supplementation on short-term, high-intensity exercise tasks $<$30 seconds is presented in Fig. 1. Percent change in performance for creatine supplemented subjects was obtained (or calculated in studies where data were available) as [(Post-Pre)$\div$Pre]$\times$100. In general, and as one might expect, creatine supplementation appears to be most effective in enhancing repetitive short-duration ($\leq$30 seconds), high-intensity tasks such as cycle ergometry; strength, torque and force production; and jump performance in a laboratory setting.

However, additional corroborative research is needed regarding the ergogenic potential of creatine monohydrate, particularly in actual field performance tests of the ATP-PCr energy system. Several research design issues should be considered. First, although most studies have used creatine monohydrate supplements, some have used creatine monophosphate. To our knowledge, there is no comparative study of the efficacy of these different forms of creatine to increase [TCr]. Second, carbohydrate appears to enhance intramuscular creatine uptake, so adequate carbohydrate should be consumed with the creatine. Third, an appropriate washout period, at least a month or more, should be used in studies with crossover designs. Any carryover effect could confound the results. Fourth, if possible, intramuscular [TCr], [FCr], and [PCr] should be measured. The interested reader is referred to the brief review by Sherman and Lamb [71] regarding other methodological considerations relative to research with purported nutritional ergogenic aids.

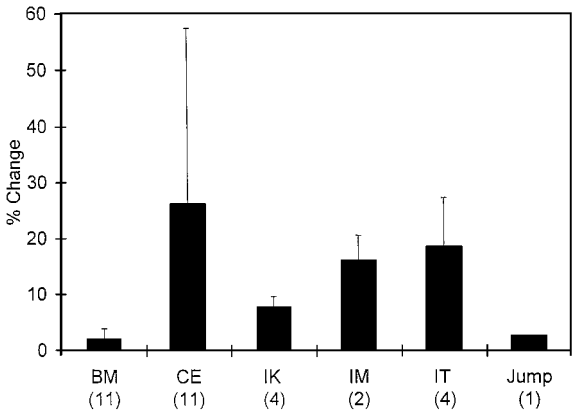

Fig. 1. Summary of the literature supporting the efficacy of creatine monohydrate. Numbers in parentheses are the number of studies reporting ergonegic effects. % Change is that observed in the creatine supplemented group and is calculated as (Post-Pre) $\div$ Pre $\times$ 100. Values are $\times$ %Δ $\pm$ SD.

BM=Body Mass; CE=Cycle Ergometry; IK=Isokinetic Force Production; IM=Isometric Force Production; IT=Isotonic Force Production; Jump=Jump Performance (vertical or continuous); Row=Rowing Performance; Run=Running Performance

In general, creatine supplementation has not consistently been shown to enhance performance in exercise tasks dependent on the lactic acid energy system (anaerobic glycolysis), but additional laboratory and field research is merited. Additionally, creatine supplementation has not been shown to enhance performance in aerobic endurance exercise tasks, but additional research is warranted, particularly on the effect of chronic supplementation as an aid to training for improvement in competitive performance.

Short-term creatine supplementation appears to increase body mass, although the initial increase is most likely water associated with the oncotic effect of increased intramuscular [TCr]. This effect has been observed mainly in males, although there are limited research data with females. Chronic creatine supplementation, in conjunction with physical training involving resistance exercise, may increase lean body mass. However, confirmatory research data are needed.

Short-term creatine supplementation, and somewhat more long-term supplementation up to 8 weeks, has not been associated with major health risks. However, the safety of more prolonged creatine supplementation has not been established.

Creatine, a nutrient found naturally in foods, is currently a legal supplement for use in athletic training and competition. The decision to use creatine as a means to enhance sport performance is left to the discretion of the individual athlete.

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