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Creatine Supplementation and Exercise Performance

Recent Findings

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Abstract

Creatine monohydrate (Cr) is perhaps one of the most widely used supplements taken in an attempt to improve athletic performance. The aim of this review is to update, summarise and evaluate the findings associated with Cr ingestion and sport and exercise performance with the most recent research available. Because of the large volume of scientific literature dealing with Cr supplementation and the recent efforts to delineate sport-specific effects, this paper focuses on research articles that have been published since 1999.

Cr is produced endogenously by the liver or ingested from exogenous sources such as meat and fish. Almost all the Cr in the body is located in skeletal muscle in either the free (Cr: ~40%) or phosphorylated (PCr: ~60%) form and represents an average Cr pool of about 120–140g for an average 70kg person.

It is hypothesised that Cr can act though a number of possible mechanisms as a potential ergogenic aid but it appears to be most effective for activities that involve repeated short bouts of high-intensity physical activity. Additionally, investigators have studied a number of different Cr loading programmes; the most common programme involves an initial loading phase of 20 g/day for 5–7 days, followed by a maintenance phase of 3–5 g/day for differing periods of time (1 week to 6 months). When maximal force or strength (dynamic or isotonic contractions) is the outcome measure following Cr ingestion, it generally appears that Cr does significantly impact force production regardless of sport, sex or age. The evidence is much more equivocal when investigating isokinetic force production and little evidence exists to support the use of Cr for isometric muscular performance. There is little benefit from Cr ingestion for the prevention or suppression of muscle damage or soreness following muscular activity.

When performance is assessed based on intensity and duration of the exercises, there is contradictory evidence relative to both continuous and intermittent endurance activities. However, activities that involve jumping, sprinting or cycling generally show improved sport performance following Cr ingestion. With these concepts in mind, the focus of this paper is to summarise the effectiveness of Cr on specific performance outcomes rather than on proposed mechanisms of action.

The last brief section of this review deals with the potential adverse effects of Cr supplementation. There appears to be no strong scientific evidence to support

any adverse effects but it should be noted that there have been no studies to date that address the issue of long-term Cr usage.

1. Background

The lure of possible enhanced sport performance or improved exercise potential continues to make dietary supplement products a very lucrative industry. One of the most utilised oral dietary supplements is creatine monohydrate (Cr). Cr ingestion at supra-physiological doses has become widespread and is no longer only being used by professional athletes or elite collegiate athletes. Many recreational exercisers, high-school athletes,[1] the elderly[2-5] and children[6] of both sexes have been ingesting Cr with the hope of improved physical performance. This review will provide a summary and evaluation of the most recent scientific literature (1999 to present) as it pertains to Cr supplementation and exercise or sport performance.

1.1 What is Creatine?

Cr, a nonessential dietary compound, can either be ingested from exogenous sources such as fish or meat or can be produced endogenously by the body, primarily in the liver. Cr is synthesised by a two-step process involving three amino acids (arginine, glycine and methionine). Initially, arginine and glycine combine to form guanidinoacetate, then a methyl group from *S*-adenosylmethionine is added for the formation of Cr. Since Cr is produced primarily in the liver, it must therefore be released into the blood and then must enter the muscle cell, against a concentration gradient, with the aid of a sodium-dependent transporter, Cr transporter-1.[7,8]

Almost all of the Cr in the human body is located in skeletal muscle with approximately 40% of the Cr in the free form (Cr) and 60% in the phosphorylated form (PCr). In general, a 70kg person with an average Cr pool of 120–140g, would lose about 2 g/day as creatinine in the urine. This loss is replaced by both exogenous consumption of about 1 g/day from a normal mixed diet and the other 1g being synthesised endogenously.

There seems to be basic agreement in the literature that PCr levels are slightly higher in type II glycolytic muscle fibres when compared with the more aerobic type I muscle fibres and there is little evidence to suggest any sex differences in PCr concentrations.[9,10] There might be a slight decline in PCr concentration with increased age but it is not clear if this is due to a decline in physical function or to aging itself.[11]

1.2 Brief Historical Perspective

Cr was initially discovered in the early 1830s by Chevreul and confirmed as a 'real' entity in meat by Liebeg in 1847. Liebeg was also the first to theorise that Cr was somehow linked to muscle performance; however, it was not until the early 1900s when the extraction of Cr from meat began to lead to the investigation of Cr as an oral supplement. The Soviet States and the Eastern block countries began to utilise Cr as a potential performance enhancer in the 1970s,[7,12] but the real push towards studying Cr supplementation did not occur until the early 1990s in the US and Great Britain.[12] Today, it is estimated that >2.5 million kilograms of Cr are used each year,[8] with Cr sales increasing to over $US200 million in 1998.[13]

In general, the majority of the scientific literature dealing with young, healthy males, agrees that exercise performance that involves short periods of extremely powerful activity (1–2 seconds) can be enhanced by Cr supplementation, especially if the activity is performed in repetitive bouts separated by short rest periods (30 seconds to 1 minute).

1.3 Proposed Mechanisms of Action

It has been suggested that Cr supplementation can act through a number of distinct mechanisms. First, if PCr concentrations are increased in skeletal muscle, PCr can then aid in the rapid rephosphorylation of adenosine diphosphate (ADP) back to adenosine triphosphate (ATP) by the Cr kinase reaction

during high-intensity, very short duration activities, especially if the bouts of intense activity are repeated with short rest periods between them.[7,8,14,15] Examples of this type of activity include sprints, jumping events and weight lifting. Secondly, it can enhance the capacity for high-energy phosphate diffusion between the mitochondria and myosin heads, thus, better enabling the heads to engage in cross-bridge cycling and tension maintenance.[7,9,16] Thirdly, Cr can act to buffer pH changes brought about by an increasing acidosis by utilising the hydrogen ions during the Cr kinase reaction and the rephosphorylation of ADP to ATP and improve cellular homeostasis.[7,9] Fourthly, declining levels of PCr in the cell due to the increased need to rephosphorylate ADP can stimulate phosphfructokinase, the rate-limiting enzyme for glycolysis, thus increasing the rate of glycolysis in order to increase the rapid production of ATP.[7,9] Once again, activities lasting between 10 seconds and 2 minutes would benefit from this mechanism, i.e. 200m, 400m and 800m sprints.

It has also been suggested that increased concentrations of PCr can be associated with muscle hypertrophy and increased protein synthesis. Cr may cause an osmotic loading effect resulting in the movement of extracellular water into the muscle cell, which is a stimulus for protein synthesis or by decreasing the rate of protein degradation.[17] Changes in body mass following Cr ingestion is somewhat controversial but often it is reported that significant increases occur.[18] Lastly, Cr has been suggested to shorten relaxation time during intermittent maximal isometric contraction by facilitating calcium uptake by the sarcoplasmic reticulum.[19,20]

1.4 Supplement Strategies

The typical Cr loading programme consists of 20 g/day (four doses of 5g each) for 5–7 days followed by a maintenance load of 3–5 g/day, although lower dosages (2–3 g/day) for a greater length of time (1 month) can be as equally effective in raising intracellular PCr levels. In general, the greatest increases in cellular levels of PCr following supplementation occur in those individuals that have the lowest initial values[11] and the greatest uptake of Cr into the muscle occurs during the initial stages of the loading regimen. Exercise seems to enhance the uptake of Cr, especially if the Cr is ingested after the exercise with a simple carbohydrate drink.[8] The use of a carbohydrate drink appears to be more important during the initial phases of the Cr loading and less important as intracellular Cr stores near saturation. Most researchers also agree, that as with most intervention protocols, there are responders and non-responders to Cr supplementation.[21]

2. Ergogenic Effects

Although Cr supplementation has been used in a number of clinical situations, such as congestive heart failure,[22,23] atherosclerosis, neuro-degenerative diseases[24] and neuromuscular diseases,[25] often with mixed results, this review will focus only on the proposed ergogenic effects relative to sport and exercise performance. Medline and Sport Discus were used as the primary databases for this topic of Cr and sport performance. Articles from 1999 onwards were used in this review and the rationale for this decision was based on the overwhelming volume of literature that dealt with Cr supplementation during the 1990s, the recent scientific advances in mechanisms related to the proposed actions of Cr, the recent use of specialised groups (elderly, diseased), and improved statistical analyses and interpretation (table I).

2.1 Peak Force

2.1.1 Isoinertial Strength and Rate of Force Development

A number of studies have examined the acute effects of Cr loading (20 g/day for 5 days) as well as the longer term effects of a maintenance regimen (3–5 g/day for 4–16 weeks) coupled with resistance training. The most commonly used method of isoinertial strength assessment is the one-repetition maximum (1RM) testing. The supine bench press and incline leg press are the most commonly cited tests within the Cr literature.

Rossouw et al.[34] investigated the acute effects of Cr loading on lifting performance. Thirteen subjects were randomly assigned to receive either Cr (n = 8;

Table I. Creatine supplementation and exercise and sport performance summary

Study	Year	Dosage	Population	Findings
Isotonic/dynamic peak force				
Wilder et al.[26,27]	2001, 2002	CR loading: Gr1: 3 g/d Gr2: 7 g/d for 7d Maintenance: 5 g/d for 12wk	Collegiate football players: Gr1 = 8; Gr2 = 8; Gr3 = 9 (PL); resistance training	↔ between groups
Bemben et al.[28]	2001	CR loading: 20 g/d for 5d Maintenance: 5 g/d for 8wk	Collegiate redshirt football players: CR = 9; PL = 8; con = 8; resistance training	↑ 1RM
Chrusch et al.[29]	2001	CR loading: 0.3 g/kg BW for 5d Maintenance: 0.07 g/kg BW for 11wk	30 older men: CR = 16; PL = 14; resistance training	↑ 1RM
Tarnopolsky et al.[30]	2001	Gr1: 10g CR + 75g CHO Gr2: 10g prot + 75g CHO for 8wk	Untrained males: Gr1 = 11; Gr2 = 8; resistance training	↔ between groups
Becque et al.[31]	2000	CR loading: 5g, 4 ×/d for 5d Maintenance: 2 g/d for 5wk	Weight-trained males: CR = 10; PL = 13	↑ strength 1RM and muscle hypertrophy
Brenner et al.[32]	2000	CR loading: 20 g/d for 7d Maintenance: 2 g/d for 5wk	Female collegiate lacrosse: CR = 7; PL = 9; resistance training	↑ 1RM
Larson-Meyer et al.[33]	2000	CR loading: 7.5g 2 ×/d for 5d Maintenance: 5 g/d for 12wk	Female collegiate soccer: CR = 7; PL = 7; resistance training	↑ 1RM
Rossouw et al.[34]	2000	CR loading: 9g 3 ×/d for 5d	Trained power lifters: CR = 8; PL = 5	↑ 1RM
Syrotuik et al.[35]	2000	Gr1: 0.3 g/kg for 5d Maintenance: PL 32d Gr2: 0.3 g/kg for 5d Maintenance: 0.03 g/kg for 32d Gr3: PL for 32d	Recreationally active men and women: Gr1 = 7; Gr2 = 7; Gr3 = 7; resistance training	↔ between groups
Isokinetic peak torque				
Stevenson and Dudley[36]	2001	CR loading: 20 g/d for 7d Maintenance: 5 g/d for 8wk	Male and female college students: CR = 12; PL = 6; resistance training	↑ peak torque
Chrusch et al.[29]	2001	CR loading: 0.3 g/kg BW/d for 5d Maintenance: 0.07 g/kg/d for 11wk	30 older men: CR = 16; PL = 14; resistance training	↑ power output
Tarnopolsky et al.[30]	2001	Gr1: CR 10g + 75g CHO Gr2: prot 10g + 75g CHO for 8wk	Young untrained men: CR = 11; prot = 8; resistance training	↔ between groups in peak torque
Gilliam et al.[37]	2000	CR loading: 5g, 4 ×/d for 5d	Active untrained men: CR = 11; PL = 12	↔ between groups in peak torque

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Table I. Contd

Study	Year	Dosage	Population	Findings
Rossouw et al.[34]	2000	CR: 5g, 3 ×/d for 5d	Trained power lifters: CR = 8; PL = 5	↑ peak torque
Rawson et al.[4]	1999	CR: 4 × 5 g/d for 5d	Older men: CR = 9; PL = 8	↔ between groups
Isometric force production				
Kilduff et al.[38]	2002	CR: 20 g/d for 5d	Resistance-trained men: CR = 21; PL = 11	↔
Jakobi et al.[39]	2001	CR: 5g, 4 ×/d for 5d	Older men: CR = 5; PL = 5	↔ for maximum force or endurance
Muscle soreness and damage				
Rawson et al.[4]	1999	CR: 5g, 4 ×/d for 5d	Young non-weight-trained men: CR = 12; PL = 11	↔ between groups
Jumping/Sprinting				
Izquierdo et al.[40]	2002	CR: 5g, 4 ×/d for 5d	Male handball athletes: CR = 9; PL = 10	↑ sprint and jump
Cox et al.[41]	2002	CR: 5g, 4 ×/d for 6d	Elite female soccer players: CR = 6; PL = 6	↑ sprint and agility
Skare et al.[42]	2001	CR: 5g, 4 ×/d for 1d	Male track sprinters: CR = 9; PL = 9	↑ sprint and jump
Romer et al.[43]	2001	CR: 0.075 g/kg, 4 ×/d for 5d	Male competitive squash players	↑ sprint
Haff et al.[44]	2000	CR: 0.3 g/kg BW for 6wk	Male and female track-and-field athletes: CR = 15; PL = 21	↑ vertical jump
Sprint power cycling				
Ziegenfuss et al.[45]	2002	CR: 0.35 g/kg FFM for 3d	Male and female collegiate athletes: CR = 10; PL = 10	↑ total work and peak power
Green et al.[46]	2001	CR: 5g, 4 ×/d for 6d	Physically active men: CR = 9; PL = 10	↑ peak power and ↓ in % decline for endurance
Wiroth et al.[47]	2001	CR: 5g, 3 ×/d for 5d	Sedentary elderly men: CR = 7; PL = 7 Trained elderly cyclists: CR = 7; PL = 7 Young sedentary men: CR = 7; PL = 7	↑ maximal power for CR sedentary groups only
Rockwell et al.[48]	2001	CR: 20 g/d for 4d during energy restriction	Active training young men: CR = 8; PL = 8	Nonsignificant ↑ for higher total sprint work (energy restriction)
Volek et al.[49]	2001	CR: 0.3 g/kg/d for 7d	Young men: CR = 10; PL = 10	Significantly better peak power and repeated sprint performances (high temperature and humidity)
Deutekom et al.[50]	2000	CR: 5g, 4 ×/d for 6d	Well trained rowers: CR = 11; PL = 12	↔ between groups, peak power, time to peak power and work
Vogel et al.[51]	2000	CR: 5g, 4 ×/d for 5d	Active young men: CR = 7; PL = 9	↔ supramaximal cycle performance (hypohydration)

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Table I. Contd

Study	Year	Dosage	Population	Findings
Continuous endurance cycling/rowing				
Jones et al.[52]	2002	CR: 20 g/d for 5d	Young men and women	↔ between groups
Syrotuik et al.[53]	2001	CR: 0.3 g/kg/d for 5d Maintenance: 0.03 g/kg/d for 5wk	Male and female rowers: CR = 11; PL = 12; resistance trained	↔ repeated interval rowing or 2000m row times
Rico-Sanz and Marco[54]	2000	CR: 20 g/d for 5d	Highly trained cyclists: CR = 7; PL = 7	Significant improvements for CR
Intermittent endurance cycling/running				
Yquel et al.[15]	2002	CR: 20 g/d for 6d	Young men; isometric contractions	Significant ↑ total power output
Cottrell et al.[55]	2002	CR: 0.3 g/kg/d for 7d	Highly trained male cyclists: CR = 15; PL = 15	Significant improvements for power outputs when rest intervals ≤3 min
Preen et al.[56]	2002	CR: 2 × 15g, 1h apart	Eight active young men	↔ between groups for cycling
Finn et al.[57]	2001	CR: 20 g/d for 20d	Active triathletes: CR = 8; PL = 8	↔ between groups for cycling
Edwards et al.[58]	2000	CR: 20 g/d for 6d	Moderately active men: CR = 11; PL = 10	↔ treadmill running

1RM = one-repetition maximum; **BW** = bodyweight; **CHO** = carbohydrate; **con** = control; **CR** = creatine group; **FFM** = fat-free mass; **Gr** = group; **PL** = placebo group; **prot** = protein; ↓ indicates decrease; ↑ indicates increase; ↔ indicates no difference.

seven males and one female; 9 g/day for 5 days) or a placebo treatment (n = 5; four males and one female; 9g sucrose/day for 5 days). Deadlift 1RM (performed in a style conforming to national powerlifting sanctioned rules) significantly improved after only 5 days of supplementation for the Cr group, suggesting that acute Cr loading may be a practical pre-competition dietary strategy to improve powerlifting competition performance.[34] The results from this study, therefore, have practical applications for other well trained athletes engaged in high-intensity anaerobic exercise. However, one limitation of this study was the use of paired t-tests to explore only within group change and the failure to evaluate a possible statistical interaction term, thus losing, or at least minimising, the scientific advantage of using a placebo group.

More commonly, Cr supplementation involves an initial acute loading period followed by a longer term, chronic maintenance phase. Becque et al.[31] examined the effects of Cr supplementation and a periodised resistance programme on arm flexor 1RM strength. Twenty-three male subjects with weight-training experience were randomly assigned to either a Cr group (n = 10) or a placebo group (n = 13). Cr loading consisted of ingesting 5g Cr, four times daily for 5 days, then supplementation was reduced to 2 g/day while the placebo group received a 500mL flavoured sucrose drink containing 32g of sucrose. Loads utilised during twice-weekly training sessions started out at a 6RM and were then reduced to a 2RM during week six. Following analyses with a repeated measures analysis of variance (ANOVA), results indicated that both the Cr and placebo groups had significant increases in 1RM strength, while only the Cr group demonstrated a significant increase in upper arm muscle area (measured anthropometrically) and total fat-free mass (measured by underwater weighing). One limitation of the study was the use of anthropometry to estimate muscle cross-sectional area and the increased error associated with this technique. Chronic Cr administration during this study had a significant ergogenic effect upon 1RM strength and fat-free mass when compared with periodised resistance training alone.

Brenner et al.[32] reported similar findings as those presented by Becque et al.,[31] using 16 female collegiate lacrosse players. A similar loading and maintenance programme to that used by Becque et al.[31] resulted in a greater increase in 1RM measures for the Cr group (significant group × time interaction) and reduced skinfold measures when compared with the placebo group.

The influence of Cr on measures of performance are more controversial when collegiate football players are used as the experimental group. Wilder et al.[26,27] reported that neither low-dose (3 g/day) nor high-dose (20 g/day for 7 days followed by 5 g/day) Cr supplementation during a 10-week periodised strength training programme for collegiate football players had any additional effect on strength gains when compared with a control group. Both groups had significant strength increases over time but there was no significant group by time interaction. However, utilising a similar study group, Bemben et al.[28] found that a 9-week periodised strength training programme combined with Cr supplementation (20 g/day for 5 days followed by 5 g/day for the rest of the study) with red-shirt collegiate football players resulted in significantly greater improvements in strength, peak torque, and anaerobic power and capacity as assessed by the Wingate protocol when compared with both a placebo and control groups.[28] The higher maintenance dose used in the Bemben et al.[28] study may have been a contributing factor to the significant differences observed post-supplementation. Another possible explanation for the different findings of these two research groups may be linked to the college experience of the two groups of subjects. In the two Wilder et al.[26,27] studies, National Collegiate Athletic Association division I players had at least 1 year of college football experience, whereas the Bemben et al.[28] study utilised red-shirt freshmen (no college experience). The red-shirt freshmen had indicated no previous Cr use while the subjects from the Wilder et al.[26,27] studies reported no usage for the 4 weeks prior to the research. Additionally, the lower dose used in the Wilder et al.[26,27] studies (3 g/day) may not have provided adequate supplementation, especially for the players with larger body mass.

Using a different sport in their research design, Larson-Meyer et al.[33] conducted a double-blind, placebo-controlled study, which involved 14 division I female soccer players during their 13-week off-season resistance training programme. Seven of the women were Cr loaded with approximately 7.5g twice daily for 5 days, then maintained their Cr intake at 5 g/day for the remainder of the study. Following a repeated measures analyses to establish trial by group interactions, it was determined that bench-press and squat 1RM strength improved more for the Cr group compared with the placebo group. There was, however, no difference between the two groups concerning overall gains in lean tissue as determined by dual energy x-ray absorptiometry (DXA).[33]

Supportive findings have also been documented with healthy older men. Chrusch et al.[29] examined the effects of combined Cr ingestion and resistance training (36 total training sessions) on changes in body composition and muscle performance in men aged 60–84 years. A total of 30 subjects were randomly assigned to either a Cr group (n = 16; mean age 70.4 ± 1.6 years) or a placebo group (n = 14; mean age 71.1 ± 1.8 years). The Cr loading phase consisted of 0.3 g/kg bodyweight (BW) for the first 5 days, followed by a maintenance dose of 0.07 g/kg BW. Repeated measures ANOVA analysis regarding both main effects and interaction terms indicated that the Cr group had significantly greater increases in 1RM leg press (Cr: +50.1kg vs placebo: +31.3kg) and leg extension (Cr: +14.9kg vs placebo: +10.7kg) and had concomitantly greater increases in body mass and lean tissue mass as measured by DXA. The lack of a Cr effect for bench-press strength may have been the result of a lower training volume since only one exercise during the training programme targeted the upper. The results of this study also could have been influenced by the group differences in baseline strength (Cr group was significantly stronger than the placebo group).

There are also a number of studies that have not been able to detect a significant Cr effect following

supplementation. Syrotuik et al.[35] randomly assigned 21 men to one of three resistance training groups in which the volume and intensity of training were equated. The first group ingested Cr (0.3 g/kg BW for 5 days) and then a maintenance placebo, the second group followed the same loading programme followed by a maintenance phase (0.03 g/kg BW for 32 days). The final group consumed the placebo for the total 37-day period. Resistance training consisted of a periodised programme and strength was assessed by 1RM incline leg press and bench press. These measures were also expressed relative to body mass by dividing 1RM (kg) measures by each subjects body mass (kg). 1RM measures were taken before loading phase, after the 5-day loading phase and finally after the 32-day maintenance phase. Two-way ANOVA with repeated measures and Newman-Keuls *post hoc* analyses determined that each group significantly increased all 1RM measurements. There were significant main effects for all groups over time for 1RM measures of bench press and leg press, total lifting volume and strength-to-mass ratio, but no significant group or interaction effects between the groups.[35] The results of this study indicated that neither Cr loading or Cr loading plus a maintenance programme, in combination with resistance training controlled for training volume and intensity, were any more effective than resistance training alone. These findings suggest that Cr does not produce an anabolic effect on skeletal muscle that is independent of the quality and quantity of the exercise stimulus.

Another study that failed to support the use of Cr was conducted by Tarnopolsky et al.[30] who randomised 19 male subjects into either a Cr + carbohydrate group (n = 11; 10g Cr + 75g glucose) or protein + carbohydrate group (n = 8; 10g casein + 75g glucose) in a double-blind design. Prior to treatments, subjects were tested using 16 separate 1RM tests to assess isoinertial strength. Resistance training focused on training the whole body over a 6-day week in a split routine design. Training sessions lasted 1 hour for a total of 8 weeks. The results indicated that 1RM strength, in all 16 exercises, increased post-training (ranging from 14.2% to 39.9%) but there were no significant differences between the two groups.[30] Strength gains may have been similar for both conditions due to increased protein synthesis (resistance training plus Cr) or increased protein availability post-exercise (resistance training plus protein). It should be noted that this study used great care to ensure that both supplements provided the same energy content, a criticism of many Cr supplementation studies.

2.1.2 Isokinetic Peak Torque

The effect of Cr loading on measures of isokinetic performance are more controversial than for measures of dynamic or isoinertial maximal force. Rossouw et al.[34] conducted a study using 13 highly trained strength athletes to examine the effects of acute Cr supplementation on isokinetic peak torque. Subjects were randomly assigned to either a Cr group (n = 8; 9g, three times daily) or a placebo group (n = 5) for 5 days of treatment. Subjects were required to perform three sets of 25 consecutive, maximal concentric knee extensions at 180 degrees/second with 60 seconds recovery between sets. Paired t-tests indicated mixed results, with both groups having significant increases in peak torque for exercise bout two, but only the Cr group had a significant increase in bout three. The improvement in more of the repeated bouts of exercise for the Cr group was attributed to the fact that each exercise bout began with higher concentrations of PCr compared with the placebo group. However, the inappropriate use of paired t-tests without any adjustment in the p-values or the inability to evaluate any possible interaction terms makes direct comparisons between the two groups impossible.

An 8-week resistance training programme, coupled with electrical muscle stimulation (EMS) applied to isokinetic force production at 70 degrees/second, was designed by Stevenson and Dudley[36] in conjunction with or without Cr supplementation. Eighteen previously resistance-trained subjects were randomly assigned to a Cr group or placebo group. Cr loading consisted of 20 g/day for 7 days, then reverted to a maintenance dose of 5 g/day for 8 weeks. EMS, which elicited maximal coupled eccentric and concentric actions, was applied to the

left quadricep fermoris twice weekly (three to five sets) while subjects continued with their own individual lower-body workouts. Measures of muscle CSA were obtained by way of magnetic resonance imaging (MRI). Repeated measures ANOVA analyses revealed that the addition of electrical stimulation to the left quadricep increased CSA by 11%, independent of Cr supplementation, probably due to increased intracellular water.[36] Since both groups exhibited similar improvements in force production, fatigue resistance and muscle hypertrophy, the authors concluded that Cr supplementation does not augment mechanical or hypertrophic responses of trained individuals.[36]

Another study that was unable to detect the efficacy of Cr supplementation for isokinetic force parameters was conducted by Gilliam et al.[37] They examined the acute effects of Cr supplementation on isokinetic peak torque at 180 degrees/second in 23 active but untrained men. Subjects were randomly assigned to either a Cr group (n = 11) or a placebo group (n = 12). Treatment consisted of four doses of 5g of Cr + 1g of glucose for the Cr group and four doses of 6g glucose for placebo condition. Testing consisted of five sets of 30 maximal volitional contractions with a 1-minute rest period between sets. Peak torque measurements were taken during each of the 30 contractions, with the average value being used in the analyses. Peak torque declined from sets one to four, with no difference seen between sets four and five. A three-way ANOVA determined that there were no significant group, time or interaction effects, suggesting that acute Cr supplementation did not significantly affect indices of isokinetic torque production at a constant velocity of 180 degrees/second.[37]

Isokinetic studies with Cr supplementation in older populations have produced differing results from younger or athletic populations. Rawson and Clarkson[3] randomly assigned 17 men between the ages of 60 and 78 years to either a Cr group (5g + 1g sucrose four times daily for 5 days) or a placebo group (6g sucrose four times daily for 5 days). Prior to testing and following 5 days of Cr loading, subjects performed an intermittent isokinetic fatigue test of the knee extensors, which involved three sets of 30 maximal volitional actions at 180 degrees/second interspaced with 60 seconds of recovery. Each group was analysed separately with a two-way ANOVA. There was no significant interaction term for isokinetic performance for either group indicating that Cr did not exhibit a performance-enhancing effect for older men perhaps due to poorer Cr absorption, transportation or uptake by the muscle.[3]

Chrusch et al.[29] examined the effects of combined Cr ingestion and resistance training (36 total training sessions) on isokinetic muscle performance in older men. Thirty subjects were randomly assigned to either a Cr group (n = 6; mean age 70.4 ± 1.6 years) or a placebo group (n = 14; mean age 71.1 ± 1.8 years). The Cr loading phase consisted of 0.3 g/kg BW for the first 5 days, followed by a maintenance dose of 0.07 g/kg BW. Isokinetic assessment consisted of knee extensions at a velocity of 60 degrees/second for three sets of ten repetitions with 1-minute rest between sets. A 2 × 3 repeated measures ANOVA determined a significant group by time interaction for average isokinetic knee extension and flexion power, with the Cr group demonstrating significantly greater increases. These findings are in contrast to other studies that showed no positive Cr effects on performance using isokinetic actions at higher velocities (180 degrees/second). The different findings may be explained by the greater duration of the current study[29] (36 total training sessions), which may have provided a greater time course for Cr uptake in this older population.

2.1.3 Isometric Maximal Force and Rate of Force Development

The effects of acute Cr supplementation on maximal voluntary force production (MVC), has been addressed in several articles. A MVC is typically defined as an angle-specific maximal isometric contraction. Jakobi et al.[39] recruited 12 older men (aged 65–82 years) who were randomly assigned to either a Cr group (5g Cr + 5g maltodextrin; four times daily; n = 7) or a placebo group (5g maltodextrin; four times daily; n = 5). Following 5 days of treatment, there was no significant increase in either

voluntary MVC or electrically evoked MVC between the two groups, which suggests that longer duration Cr supplementation may have been needed for the older subjects.

Kilduff et al.[38] investigated the potential ergogenic effects of acute Cr loading (20 g/day Cr + 180 g/day dextrose for 5 days) on body composition and MVC during a bench-press exercise. Thirty-two resistance-trained men were matched according to peak isometric force and then assigned in a double-blind fashion to either a Cr group or a placebo group. Following a repeated measures ANOVA, it was determined that the Cr group had no significant change in measures of peak force or total force when compared with the placebo group. However, when the Cr group was divided into responders and non-responders based on estimated intramuscular Cr storage after loading, peak isometric force and total force production was significantly higher than the placebo group. It was reported that Cr uptake was inversely proportional to training status ($r = -0.68$) suggesting that less-trained individuals uptake Cr more readily than more highly trained individuals.[38] This could be due to the near saturation of intramuscular Cr stores seen in highly trained individuals, probably through ingesting increased amounts of dietary protein in the form of red meat. Less-trained individuals may not actively seek to increase protein intake and, therefore, may have lower levels of saturation before Cr supplementation. Additionally, higher intramuscular Cr stores may also be a physiological adaptation to high-intensity resistance training. It should be noted that by partitioning the Cr group into responders and non-responders, a very different data interpretation resulted and, as such, this method may be considered biased reporting of the data and should be viewed accordingly.

2.1.4 Eccentric Induced Muscle Soreness/Damage

Eccentric action induces muscle soreness and damage at both the sarcolemmal and sarcoplasmic reticular membranes.[59,60] A change in sarcoplasmic reticulum activity can lead to an increase in proteolytic enzymes, ultimately leading to contractile protein degradation.[61] PCr has been associated with membrane stabilisation[62] leading to the notion that Cr supplementation may help lessen the degenerative effects of eccentrically induced muscle damage.

In one of the few published articles in this area, Rawson et al.[11] investigated the effects of Cr supplementation on eccentrically induced muscle damage. Twenty-three men aged between 18 and 36 years were randomly assigned to either a Cr (n = 12; 20 g/day for 5 days) or placebo group (n = 11). Fifty maximal eccentric contractions of the elbow flexors were used to induce muscle damage and elbow flexor MVC, elbow range of motion, blood creatine kinase, lactate dehydrogenase, distal arm circumference, and soreness with movement and palpation were assessed. There were no significant group or group by time interaction for any of the variables measured. These results suggest that Cr supplementation does not lessen the symptoms associated eccentric exercise[11] and the hypothesis that Cr may decrease membrane fluidity and increase membrane stability was not supported.

2.2 Power

2.2.1 Jumping and Sprinting

Cr supplementation has been reported to increase both peak and mean power output during countermovement vertical jumps (CMVJ) and static jumps (SJ).[63] Haff et al.[44] examined the effects of a 6-week resistance training programme plus Cr supplementation on dynamic rates of force development during jumping activities. Thirty-six well trained athletes (16 males and 20 females) were randomly assigned into a Cr group (n = 15; 0.3 g/kg BW for 6 weeks) or a placebo group (n = 21). Resistance training sessions were carried out three days/week utilising primarily high-power ballistic-type exercises (power cleans, power snatches) and sprint training on the other two days. Testing consisted of performing maximal CMVJ and SJ so that force-time curve characteristics such as displacement, peak force and rate of force development could be recorded. Both groups had significant improvements regarding force-time curve characteristics for the SJ following training. However, a significant group by time interaction indicated that the Cr

group had a greater rate of improvement for CMVJ height when compared with the placebo group.

Izquierdo et al.[40] investigated the potential ergogenic effects of Cr supplementation on muscle power, endurance, fatigue and sprint performance. Nineteen previously resistance-trained male handball players were randomly assigned to either a Cr (n = 9; 20 g/day for 5 days) or placebo (n = 10) group. Maximal strength was assessed using a half squat and bench press, while maximal repetitive high-power output was also determined for the half squat (70% 1RM) and bench press (60% 1RM) by performing one set of ten repetitions followed by a 2-minute rest period, then a second set until muscular failure. Lifting cadence was controlled by a metronome set at a frequency of 19Hz and measures of mean power and average velocity were recorded by a rotary encoder. A significant group by time interaction indicated a significantly greater improvement in repetitions performed to fatigue, total average power during the power endurance test, and 1RM half squat for the Cr group. Additionally, there was less of a decline in the power/velocity from CMVJ 1 to CMVJ 2 for the Cr group and a decrease in average running times over the first 5m during repetitive sprints.

Similar improvements in sprint performance were reported by Skare et al.[42] Eighteen male track sprinters, with at least 3 years of experience in regional competition were randomly assigned to either a Cr group (n = 9; 20g Cr + 20g glucose/day) or a placebo group (n = 9; 40g glucose/day). There were significant increases in 100m sprint performance and repeated sprint performance for the Cr group, while the placebo group had no improvement from pre- to post-conditions. One problem with the data analyses is that it was unclear if a group by time interaction was evaluated or if only paired t-tests were used to evaluate the data.

Improved sprint performance was also demonstrated by Cox et al.[41] using elite soccer players. Twelve subjects with a mean age of 22.1 years were given a standard diet that provided 7g carbohydrate/kg BW for a 24-hour period before each test session. Each of the two test sessions were separated by 7 days and included 11 all-out 20m sprints, two agility runs and one ball-kicking drill, each separated by 20m walks, jogs or runs during a 1-hour time period. After the first test session, the subjects were randomised into a treatment (5g Cr four times daily for 6 days) or a placebo group in a double-blind fashion and were then re-tested on the original test items. Body mass was increased significantly more for the Cr group yet they had better repeated sprint times and better agility runs with lower heart rates and lower lactate levels than the placebo group.[41]

Sprint performance was also significantly improved when a sample of squash players were supplemented with Cr (0.075 g/kg BW, four times daily for 5 days) in a double-blind, placebo-controlled, crossover study.[43] Sprint times that were assessed in a simulated squash protocol improved for both groups, but improved to a greater extent following Cr supplementation; however, unlike the Cox et al. results,[41] heart rates and lactate levels were unaffected by Cr. In general, the literature seems to support the use of Cr supplementation for short-term, intense activities such as jumping and sprinting

2.2.2 Cycling

The use of cycle ergometry to assess indices of anaerobic power has commonly been used in previous Cr research. Measures of peak and mean power (W), time to peak power (seconds), total work (J) and fatigue index (%) have been shown to be positively affected by Cr supplementation.[64] Additionally, a number of studies have addressed the effects of Cr ingestion upon indices of Wingate performance since the year 2000.

Green et al.[46] randomly assigned 19 physically active men to either a Cr group (n = 9; 20 g/day for 6 days) or a placebo group (n = 10; 20g sucrose + maltodextrin/day). Before and after supplementation, subjects performed three arm Wingate tests (AW1, AW2, AW3), then three leg Wingate tests (LW1, LW2, LW3) on consecutive days. Each Wingate trial was separated by 2 minutes of recovery. Test variables compared between groups included peak power (W), mean power (W), and percentage power decline (%). There was no significant differ-

ence from pre- to post-test for mean power output for both the arm and leg trials. There was no change in peak power for either groups Wingate tests; however, peak power increased significantly for the Cr group during AW1, and for the placebo group during AW1 and AW3. Percentage decline for the Cr group was significantly decreased (pre- to post-test) and was significantly less than the placebo group after LW2.[46] Unfortunately, no interaction term could be assessed since the authors only used t-tests to statistically analyse the data.

Ziegenfuss et al.[45] studied highly anaerobically trained collegiate athletes to assess the effects of 3 days of Cr ingestion on cycle ergometer power output. Twenty division I athletes (ten males and ten females) were selected and randomly assigned to a Cr group (n = 10; 0.35g Cr/kg fat-free mass) or placebo group (n = 10; 0.35g maltodextrin/kg fat-free mass). Subjects completed six maximal 10-second cycle sprints with 60 seconds recovery between sprints prior to treatment and after 3 days of the treatment. MRI techniques were used to obtain ten transaxial images of both thighs pre- and post-treatment. Repeated measures analysis revealed that Cr supplementation resulted in significant increases in total body mass (0.9 ± 0.1kg) compared with the placebo group. There was also a significant 6.6% increase in thigh volume for the Cr group that was attributed to an increase in intracellular water with no change for the placebo group. A significant increase was also seen in total work performed during the first sprint as well as peak power output during sprints two through six, the total amount of work performed, and the peak power produced during the repeated cycle sprint protocol. When male and female subgroups (within the Cr group) were examined, the males exhibited the highest initial peak power relative to lean body mass; however, after three of the sprints had been completed, the reverse trend was seen, that is, females exhibited the greater relative peak power output.[45] The drop in power output relative to body mass is similar to the findings presented by Linnamo et al.[65] who used explosive repetitive weight-lifting tasks. Although males exhibit both higher absolute and relative power outputs, they also experience a greater amount of central fatigue than females. Additionally, the greater initial power output seen with males has previously been shown to be related to greater systemic testosterone levels and greater amounts of fat-free mass.[63]

Deutekom et al.[50] assessed the effects of Cr supplementation on muscle properties and sprint performance. Twenty-three well trained rowers were randomly assigned to either a Cr group (n = 11; 20 g/day for 6 days) or a placebo group (n = 12). Testing consisted of 40 consecutive electrical stimulations of the quadriceps at an activation frequency of 150Hz, which was equal to 30% of maximal voluntary isometric peak torque. Repeated measures ANOVA indicated that there was a significant increase in body mass for the Cr group compared with the placebo group. However, there was no group difference for maximal voluntary torque generation, muscle activation as elicited by electrical stimulation, and recovery from the electrically stimulated exercise. Additionally, there were no differences between groups peak power, time to peak power, or work to peak power[50] during the sprint tests.

Wiroth et al.[47] examined the potential ergogenic effects of Cr supplementation on maximal pedalling performance by recruiting three groups of subjects (G1 = sedentary, n = 14, mean age 70.1 years; G2 = trained cyclists, n = 14, mean age 66.4 years; and G3 = young sedentary, n = 14, mean age 26.0 years). Within each group, Cr was administered (5g three times daily for 5 days) using a double-blinded, randomised design. Subjects performed five maximal 10-second sprints with 60 seconds of passive recovery between each sprint, with power output, work done and heart rate being recorded during each sprint. Maximal power was significantly increased only for G1 and G3, suggesting that Cr was beneficial in previously untrained older and younger populations but not in previously trained individuals.[47] This is in contrast to the findings of Rawson et al.[11] who reported no significant increases in force or power output in older subjects during an isokinetic test following 5 days of Cr loading. It is possible that the increased training status of the trained cyclist

group may have reduced the responsiveness to Cr loading. Assessment of intramuscular Cr stores during future studies of this type may help explain some of the discrepancies.

Within the cycling literature, authors have also attempted to delineate the effects of Cr under conditions that might be exhibited during performance, such as dehydration and energy restriction. In one such paper, Vogel et al.[51] examined the effects of cycle performance at two levels of acute hydration. Sixteen men were randomly assigned to either a Cr group (n = 7, 20 g/day for 5 days) or a placebo group (n = 9). Subjects were required to perform five, 5-second maximal sprints on a cycle ergometer in an environmental chamber with the temperature at 32°C and 50% humidity. To induce a state of hypohydration, subjects then performed a 75-minute exercise session followed by the same sprint protocol, then an additional 75 minutes of exercise. It was determined that the two 75-minute exercise sessions elicited similar significant losses in body mass (−2.5% for the Cr group and −4% for the placebo group) as well as plasma volume (−7% for the Cr group and −9% for the placebo group) for the Cr and placebo groups. Additionally, there were no significant differences for either group for any of power measures. Reports of muscle cramping and tightness were not different between the groups and it was concluded that Cr supplementation did not appear to negatively affect hydration status during extended cycling exercise.[51]

To examine the issue of Cr usage during a period of energy restriction, Rockwell et al.[48] randomly assigned 16 men to either Cr group or a placebo group. Cr was administered at 20 g/day and both the Cr and placebo group consumed a formula diet of 75.3kJ (18 kcal/kg/day; 57% carbohydrate, 21% protein and 24% fat). Subjects were then required to perform ten, 6-second maximal sprints with 30 seconds of recovery between sets. Both the Cr and placebo groups lost similar amounts of body mass and percentage body fat, but the placebo group had a significant decrease in percentage change of fat-free mass when compared with the Cr group. Nitrogen loss (total urinary nitrogen and estimated faecal loss relative to nitrogen content of the diet) was found to be similar in both groups. Cr and PCr concentrations were determined by muscle biopsy from the vastus lateralis and all samples were adjusted for the highest ATP concentrations at pre- and post-treatment. The Cr group had significantly greater total Cr content when compared with pre-treatment measures (15–16%), while there was no change for the placebo group. It is interesting to note that there were no significant differences or interactions between the groups, either before or after energy restriction and supplementation, for any of the cycle performance measures. The authors suggest that the brief 6-second sprints that are dependent on the phosphagen system are less affected than longer sprint periods that might rely on anaerobic glycolysis.

Dealing with the issue of Cr supplementation and exercise in a hot environment, Volek et al.[49] examined the physiological responses to short-term exercise at 37°C (80% humidity) after 7 days of Cr loading. Twenty-two males were randomly assigned to either a Cr group (n = 10; 0.3 g/kg BW) or a placebo group (n = 10) in a double-blind fashion. The exercise session consisted of cycling for 30 minutes at 60–70% of peak oxygen consumption and then, immediately perform three, 10-second maximal sprints. Repeated measures ANOVA revealed no significant differences between groups for heart rate, blood pressure and sweat rate responses to exercise. Urine excretion rates for Cr, sodium and potassium obtained over 24 hours were also not different between the two groups. The exercise bouts significantly increased levels of cortisol, aldosterone, renin, angiotensin I and II, atrial peptide and arginine vasopressin for both groups but there was a significant interaction term indicating that peak power during cycling was significantly greater during all three sprints for the Cr group but unchanged for the placebo group.

2.3 Continuous Endurance

Much of the previous Cr literature has focused on improvements in anaerobic and intermittent physical activity. In terms of sport performance, there is less evidence to support the use of Cr with activities

that are longer in duration than 3 minutes. The potential positive ergogenic effects that Cr might have on submaximal endurance performance have been addressed in only a few papers since the year 2000. Jones et al.[52] investigated the effects of Cr loading on oxygen uptake ($\dot{V}O_2$) kinetics during submaximal cycle exercise. Five subjects received Cr (20 g/day for 5 days followed by 5 g/day maintenance dose) while four subjects served as controls. Following all testing conditions, 35–50 days later, the five subjects initially supplemented with Cr now served as controls and the initial four control subjects were now supplemented with Cr. Paired t-tests revealed that there were no significant differences between groups for the $\dot{V}O_2$ kinetic response during the moderate exercise protocol and that Cr had no ergogenic effect. The limitations of this study involve the statistical analyses and the small sample size.

However, similar results were obtained by Syrotuik et al.[53] when they examined the effect of Cr supplementation (0.3 g/kg BW/day, ingested in four equal portions throughout the day, for 5 days, then a maintenance phase of 0.03 g/kg BW/day for 5 weeks) on training volume for male rowers. The initial 5-day loading period of Cr did not improve repeated interval rowing performance, 2000m rowing times or any strength measures. Following an additional 5 weeks of Cr supplementation, still no differences were noted between the two groups relative to any of the performance parameters.

In contrast to these two previous studies, Rico-Sanz and Marco[54] investigated the effects of Cr supplementation on $\dot{V}O_2$ and performance during alternating bouts of exercise at different intensities. Fourteen male subjects were randomly assigned to either a Cr group (n = 7; 20 g/day for 5 days) or a placebo group (n = 7). Cycling tests were carried out at intensities equal to 30% and 90% of peak power until exhaustion. After a standardised warm up, subjects cycled for a total of five, 3-minute stages (alternating 30% and 90% of maximal power output). Blood samples were taken at four separate timepoints (rest, just before the end of each cycling load, at exhaustion, and at 5 minutes post-exercise). There was a greater $\dot{V}O_2$ for the Cr group and lower blood ammonia concentrations. Plasma uric acid was also found to be lower for the Cr group at the cessation of exercise and 5 minutes post-exercise. From a performance standpoint, the Cr group increased their time to exhaustion from 29.9 ± 3.8 minutes to 36.5 ± 5.7 minutes, while there were no changes seen with the placebo group. It appeared that Cr supplementation during the current study was able to increase the total amount of work that could be performed during alternating bouts of different intensity exercise by effecting oxygen utilisation and enhancing oxidative phosphorylation at these varying intensities.[54]

2.4 Intermittent Endurance

The role Cr might have in improving bouts of intermittent anaerobic exercise has been addressed in a number of studies since 2000, with conflicting results. Yquel et al.[15] described the effects of Cr supplementation on PCr resynthesis and inorganic phosphate accumulation during intermittent exercise. Nine male subjects consumed 20 g/day Cr for 6 days in a non-blinded fashion. Using an isokinetic dynamometer, subjects performed five, 8-second bouts of dynamic plantar flexion exercise with 30 seconds of recovery between bouts. An additional two bouts (bouts six and seven) were then carried out for a total of 8 and 16 seconds, respectively. The rest interval between the end of bout five and the start of bout six was 1 minute with 2 minutes allowed between bouts six and seven. Muscle PCr and inorganic phosphate were estimated every 16 seconds using ^{31}P magnetic resonance spectroscopy. Results indicated that after Cr ingestion, power output significantly increased by 5% from exercise bouts three to seven and total PCr resynthesis was also significantly increased following 10 minutes of recovery. There was also a strong positive relationship between inorganic phosphate concentration and muscle pH after Cr ingestion. It appeared that Cr ingestion helped maintain power output over repeated bouts of intermittent anaerobic activity by reducing acidic conditions.

In a similar protocol, Cottrell et al.[55] studied the effect of Cr ingestion and recovery interval on multiple bouts of sprint cycling performance in adult males. Well trained cyclists were randomised to either a Cr group (0.3 g/kg BW/day for 6 days) or a placebo group. Three separate trials of maximal cycling sprints were used. Cycling bouts consisted of eight, 15-second, maximal efforts. Subjects were randomly assigned to recovery interval groups of 1, 3 or 6 minutes, and the same protocol was carried out again, 7 days later. The use of paired t-tests indicated that between-trial mean power significantly increased for the Cr groups with 1 and 3 minutes of recovery, and for the placebo group with 6 minutes of recovery. It appeared that during this study, Cr supplementation had a positive effect on mean power maintenance as long as the rest interval was no longer than 6 minutes, but the lack of assessing an interaction term following supplementation, should lead one to closely scrutinise the interpretation of these results.

Contrary to the previous studies, Edwards et al.[58] examined the effects of Cr supplementation on anaerobic performance in moderately active men. Twenty-one subjects were randomly assigned to either a Cr group (n = 11; 20 g/day for 6 days) or a placebo group (n = 10). Subjects were tested using an anaerobic speed test (AST), which required them to run to fatigue on a treadmill at a constant speed of 13 km/h and 20% gradient. Prior to performance of the AST, four 15-second bursts of high-intensity running, each separated by 30 seconds of passive recovery, were performed to ensure depletion of PCr stores. Statistical analysis revealed that there were no significant group or interaction effects for performance times on the treadmill or blood lactate concentrations. There was a significant interaction for plasma ammonia concentrations indicating a trend for plasma ammonia to decrease for the Cr group. These data suggest that, during the present study, Cr supplementation offered no ergogenic advantage over the placebo condition with regard to exercise performance.

No improvements in performance were also demonstrated by Preen et al.,[56] who studied the effect of pre-exercise Cr supplementation on intermittent sprint performance. Eight active, but not well trained men either received Cr (15g + water) or a placebo treatment during their first day of testing. Fourteen days later, in a randomised, double-blind, crossover design, subjects were then re-tested before ingesting the other treatment that was not received on the first test. Cr or placebo treatments were ingested 60 and 120 minutes prior to the start of an 80-minute sprint cycle task. The protocol consisted of ten sets of multiple 6-second sprints, with recovery periods varying from 24 to 84 seconds. Subjects carried out the same protocol 14 days later and received the alternative treatment to what was received previously. Variables recorded and analysed included work done and peak power. Muscle biopsies were also taken from the vastus lateralis prior to exercise and at 1 and 3 minutes post-exercise. Data analyses revealed that there were no significant changes in cycling performance after ingestion of Cr and that muscle ATP concentrations and total Cr levels were not different between the two groups.

Finn et al.[57] also reported no difference in intermittent cycle performance following Cr ingestion. Sixteen currently active triathletes performed four 20-second all-out sprints on an air-braked cycle ergometer with each trial separated by 20-second recovery periods. Muscle biopsies were obtained so that subjects could be matched for intramuscular Cr content before they were randomly assigned to receive either a Cr (n = 8; 20 g/day for 20 days) or a placebo group (n = 8). Results indicated that free Cr was significantly higher in the Cr group compared with no change in the placebo group; however, there were no significant differences between groups regarding test performance parameters.

3. Potential Adverse Effects

It appears as though the consensus, regarding issues of possible adverse effects from Cr supplementation, is that there is no strong scientific evidence to support any reported adverse effects. Most of the reports have been rather minor in nature and purely anecdotal; however, it is critical to note that well controlled, long-term studies in humans are

lacking, therefore, caution should still be used if Cr is to be used on a long-term basis.

3.1 Gastrointestinal (Stomach Cramping, Nausea, Diarrhoea, Vomiting)

Perhaps the most often reported adverse effect of Cr supplementation is gastrointestinal (GI) distress. It appears that, if the Cr is insufficiently dissolved[9,18] or if it is ingested during or immediately after exercise,[66] there seems to be more reports of stomach upset. However, when a placebo group has been included and the study has been double blinded, there appears to no detrimental effect on the GI system.[43]

In a recent double-blind study completed by our laboratory that examined the effects of Cr supplementation, protein supplementation, a combination of both Cr and protein supplements, or a placebo supplementation in 40- to 60-year-old men, we had essentially no reports of any GI upset (nausea, vomiting or diarrhoea) when the drinks were consumed immediately following a resistance training programme designed to facilitate muscle hypertrophy (three sets, ten exercises, 80% 1RM). Subjects lifted three times/week and consumed drinks that contained either 5g of Cr in 250mL of Gatorade™[1] following a 5-day loading period of 7g Cr/day, 35g of protein in 250mL Gatorade™, or a combination of 5g Cr and 35g protein in 250mL Gatorade™, or 250mL Gatorade™.

3.2 Renal and Liver Function

It has been established that studies that have investigated renal function following Cr supplementation by assessing urinary creatinine clearance have found no indication of impaired function;[18,67-72] however, it has been suggested that care should be taken if an individual has a pre-existing compromised renal function.[14]

There is no scientific evidence that liver function is impaired by either short-term, high-dosage Cr ingestion or longer term, low-dosage programmes.[8,73-76]

3.3 Muscle Cramping

Most reports of muscle cramping following Cr supplementation have been anecdotal in nature and unsubstantiated, especially when research designs have included control groups and blinding. There is no direct evidence that Cr supplementation can induce muscle cramping and that if cramps are experienced that it is most likely due to either the high intensity of the workout[8,9,18] or to a disruption in electrolyte balance. Most authors agree that adequate hydration during exercise is likely to significantly reduce the chance of getting muscle cramps.

3.4 Body Mass/Water Retention

The early changes observed in BW following Cr ingestion is probably explained by increases in body water, especially in the intracellular compartments (within the muscle cell). Authors have speculated that the reason for the increase in intracellular water is the increased osmotic load associated with the increased Cr concentrations within the cell.[9,26,77,78] This does have implications for body composition measurements taken in conjunction with resistance training studies. Increases in muscle cross-sectional area may be attributed to increased muscle hypertrophy whereas the increase in size may be primarily due to intracellular water retention. These same authors have suggested that the initial intracellular swelling may be a preparatory phase of compensatory hypertrophy in response to resistance training. Also, the increased water retention within the intracellular compartments may contribute to increased force production by increasing interstitial leverage advantage.

In summary, it appears that most reports of adverse effects regarding Cr supplementation have been anecdotal. When studies employ research designs that include control groups and blinding, there appears to be no consistent finding of any detrimental effects of Cr supplementation in normal, healthy individuals.

1 The use of trade names is for product identification purposes only and does not imply endorsement.

4. Conclusion

In general, recent studies are similar to the older literature discussing Cr supplementation; however, better statistical analyses utilising repeated measures designs and the examination of interaction terms are much more common in the newer literature. Other improvements in methodologies include double blinding, greater varieties of subjects (e.g. female, older) and better attempts at understanding the mechanisms responsible for improved performances.

Basically, Cr seems to provide the most beneficial effects for sport performance when the activity involves repeated, short bouts of high-intensity exercise. It appears that athletes who perform in sports that are most similar to this type of activity have the greatest benefit from Cr supplementation. Sports like football, soccer, squash and lacrosse are the types of sport most often involving Cr usage.

Part of the documented findings associated with Cr supplementation seem to be related to the outcome measures that are selected for any particular study. If dynamic or isotonic peak force is assessed, it generally appears that Cr supplementation can provide a benefit. However, if isokinetic parameters are measured, there is more discrepancy in the findings, and if isometric parameters are assessed it seems that there is little benefit from Cr supplementation.

It also appears that both men and women can benefit from Cr, as well as both young and old participants, although some conflicting evidence with regard to age exists in the published literature. Training status may impact Cr uptake during a loading phase, in that highly trained individuals may not require a loading period since intramuscular levels may already be elevated. Finally, it should be remembered that there are both responders and non-responders in all groups and that this can impact the potential ergogenic effects of Cr.

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References

1. Grindstaff PD, Kreider R, Bishop R, et al. Effects of oral creatine supplementation on repetitive spring performance and body composition in competitive swimmers. Int J Sport Nutr 1997; 7: 330-46
2. Berman S, Venembre P, Sachet C, et al. Effects of creatine monohydrate ingestion in sedentary and weight-trained older adults. Acta Physiol Scand 1998; 164: 147-55
3. Rawson ES, Clarkson PM. Acute creatine supplementation in older men. Int J Sports Med 1999; 21: 71-5
4. Rawson ES, Wehnert ML, Clarkson PM. Effects of 30 days of creatine ingestion in older men. Eur J Appl Physiol 1999; 80: 139-44
5. Smith SA, Montain SJ, Matott RP, et al. Creatine supplementation and age influence on muscle metabolism during exercise. J Appl Physiol 1998; 85: 1349-56
6. Unnithan BV, Veehof SHE, Vella CA, et al. Is there a physiologic basis for creatine use in children and adolescents? J Strength Cond Res 2002; 15 (4): 524-8
7. Demant TW, Rhodes FC. Effects of creatine supplementation on exercise performance. Sports Med 1999; 28 (1): 46-60
8. Terjung RL, Clarkson P, Eichner ER, et al. The physiological and health effect of oral creatine supplementation. Med Sci Sport Exerc 2000; 32 (3): 706-16
9. Mesa JLM, Ruiz JR, Gonzalez-Gross MM, et al. Oral creatine supplementation and skeletal muscle metabolism in physical exercise. Sports Med 2002; 32 (14): 903-44
10. Pastoris O, Roschi F, Verri M, et al. The effects of aging on enzyme activities and metabolite concentrations in skeletal muscle from sedentary male and female subjects. Exp Gerontol 2000; 35: 95-104
11. Rawson ES, Gunn B, Clarkson PM. The effects of creatine supplementation on exercise-induced muscle damage. J Strength Cond Res 2001; 15 (2): 178-84
12. Silber ML. Scientific facts behind creatine monohydrate as a sport nutrition supplement. J Sports Med Phys Fitness 1999; 39: 179-88
13. Andres LP, Andy J, Sachek AJ, et al. A review of creatine supplementation: side effects and improvements in athletic performance. Nutr Clin Care 1999; 2 (2): 78-81
14. Hespel P, Eijnde BO, Derave W, et al. Creatine supplementation: exploring the role of the creatine kinase/phosphocreatine system in human muscle. Can J Appl Physiol 2001; 26 Suppl.: S79-S102
15. Yquel RJ, Arsac LM, Thiaudiere E, et al. Effect of creatine supplementation on phosphocreatine resynthesis, inorganic phosphate accumulation and pH during intermittent maximal exercise. J Sports Sci 2002; 20: 427-37
16. Wyss M, Kaddurah-Daouk R. Creatine and creatinine metabolism. Physiol Rev 2000; 80: 1107-213
17. Haussinger D, Roth E, Lang F, et al. Cellular hydration state: an important determination of protein catabolism in health and disease. Lancet 1993; 341: 1330-2
18. Poortmans JR, Francaux M. Adverse effects of creatine supplementation: fact or fiction. Sports Med 2000; 30 (3): 155-70
19. van Leemputte M, Vandenberghe K, Hespel P. Shortening of muscle relaxation time after creatine loading. J Appl Physiol 1999; 86: 840-4
20. Hespel P, Eijnde B, van Leemputte M. Opposite actions of caffeine and creatine on muscle relaxation time in humans. J Appl Physiol 2002; 92: 513-8

21. Greenhaff PL, Bodin K, Soderlund K, et al. Effect of oral creatine supplementation on skeletal muscle PCr resynthesis. Am J Physiol 1994; 266: E725-30
22. Gordon A, Hultman E, Kaijser L, et al. Creatine supplementation in chronic heart failure increases skeletal muscle creatine phosphate and muscle performance. Cardiovasc Res 1995; 30: 413-8
23. Andrews R, Greenhaff PL, Curtis S, et al. The effects of dietary creatine supplementation on skeletal muscle metabolism in congestive heart failure. Eur Heart J 1998; 19: 617-22
24. Matthews RT, Yang L, Jenkins BG, et al. Neuroprotective effects of creatine and cytocreatine in animal models of Huntington's disease. J Neurosci 1998; 18: 156-63
25. Tarnopolsky MA, Roy BD, MacDonald JR. A randomized, controlled trial of creatine monohydrate in patients with mitochondrial cytopathies. Muscle Nerve 1997; 20: 1502-9
26. Wilder N, Deiuert RG, Hagerman F, et al. The effects of low-dose creatine supplementation versus creatine loading in collegiate football players. J Athl Train 2001; 36 (2): 124-9
27. Wilder N, Gilders R, Haterman F, et al. The effects of a 10-week, periodized, off-season resistance-training program and creatine supplementation among college football players. J Health Res 2002; 16 (3): 343-52
28. Bemben MG, Bemben DA, Loftiss DD, et al. Creatine supplementation during resistance training in college football athletes. Med Sci Sports Exerc 2001; 33 (10): 1667-73
29. Chrusch MJ, Chilibeck PD, Chad KE, et al. Creatine supplementation combined with resistance training in older men. Med Sci Sports Exerc 2001; 33: 2111-7
30. Tarnopolsky MA, Parise G, Yardley NJ, et al. Creatine-dextrose and protein-dextrose induce similar strength gains during training. Med Sci Sports Exerc 2001; 33: 2044-52
31. Becque MD, Lochmann JD, Melrose DR. Effects of oral creatine supplementation on muscular strength and body composition. Med Sci Sports Exerc 2000; 32: 654-8
32. Brenner M, Rankin JW, Sebolt D. The effect of creatine supplementation during resistance training in women. J Strength Cond Res 2000; 14 (2): 207-13
33. Larson-Meyer DE, Hunter GR, Trowbridge CA, et al. The effect of creatine supplementation on muscle strength and body composition during off-season training in female soccer players. J Strength Cond Res 2000; 14 (4): 434-42
34. Rossouw F, Krüger PE, Rossouw J, et al. The effect of creatine monohydrate loading on maximal intermittent exercise and sport-specific strength in well trained power-lifters. Nutr Res 2000; 20 (4): 505-14
35. Syrotuik DG, Bell GJ, Burnham R, et al. Absolute and relative strength performance following creatine monohydrate supplementation combined with periodized resistance training. J Strength Cond Res 2000; 14 (2): 182-90
36. Stevenson SW, Dudley GA. Dietary creatine supplementation and muscular adaptation to resistive overload. Med Sci Sports Exerc 2001; 33: 1304-10
37. Gilliam JD, Hohzorn C, Martn D, et al. Effect of oral creatine supplementation on isokinetic torque production. Med Sci Sports Exerc 2000; 32: 993-6
38. Kilduff LP, Vidakovic P, Cooner G, et al. Effects of creatine on isometric bench-press performance in resistance-trained humans. Med Sci Sports Exerc 2002; 34: 1176-83
39. Jakobi JM, Rice CL, Curtin SV, et al. Neuromuscular properties and fatigue in older men following acute creatine supplementation. Eur J Appl Physiol 2001; 84: 321-8
40. Izquierdo M, Ibanez J, Gonzáles-Badillo JJ, et al. Effects of creatine supplementation on muscle power, endurance, and spring performance. Med Sci Sports Exerc 2002; 34: 332-43
41. Cox G, Mujika I, Tumilty D, et al. Acute creatine supplementation and performance during a fixed test simulation match play in elite female soccer players. Int J Sport Nutr Exer Metab 2002; 12: 33-46
42. Skare OC, Skadberg O, Wisnes AR. Creatine supplementation improves sprint performance in male sprinters. Scand J Med Sci Sports 2001; 11: 96-102
43. Romer LM, Barrington JP, Jenkendrup AE. Effects of oral creatine supplementation on high intensity intermittent exercise performance in competitive squash players. Int J Sports Med 2001; 22: 546-52
44. Haff GG, Kirksey KB, Stone MH, et al. The effect of 6 weeks of creatine monohydrate supplementation on dynamic rate of force development. J Strength Cond Res 2000; 14 (4): 426-33
45. Ziegenfuss TN, Rogers M, Lowery L, et al. Effect of creatine loading on anaerobic performance and skeletal muscle volume in NCAA division I Athletes. Appl Nutr Invest 2002; 18: 397-402
46. Green JM, McLester Jr JR, Smith JE, et al. The effects of creatine supplementation on repeated upper- and lower-body wingate performance. J Strength Cond Res 2001; 15 (1): 36-41
47. Wiroth JB, Bermon S, Andreï S, et al. Effects of oral creatine supplementation on maximal pedaling performance in older adults. Eur J Appl Physiol 2001; 84: 533-9
48. Rockwell JA, Rankin JW, Toderico B. Creatine supplementation affects muscle creatine during energy restriction. Med Sci Sports Exerc 2001; 33: 61-8
49. Volek JS, Mazzetti SA, Farquhar WB, et al. Physiological responses to short-term exercise in the heat after creatine loading. Med Sci Sports Exerc 2001; 33: 1101-8
50. Deutekom M, Beltman JGM, de Ruiter CJ, et al. No acute effects of short-term creatine supplementation on muscle properties and sprint performance. Eur J Appl Physiol 2000; 82: 223-9
51. Vogel RA, Webster MJ, Erdmann LD, et al. Creatine supplementation: effect on supramaximal exercise performance at two levels of acute hypohydration. J Strength Cond Res 2000; 14 (2): 214-9
52. Jones AM, Carter H, Pringle JSM, et al. Effect of creatine supplementation on oxygen uptake kinetics during submaximal cycle exercise. J Appl Physiol 2002; 92: 2571-7
53. Syrotuik DG, Game AB, Gillies EM, et al. Effects of creatine monohydrate supplementation during combined strength and high intensity rowing training on performance. Can J Appl Physiol 2001; 26 (6): 527-42
54. Rico-Sanz J, Marco MTM. Creatine enhances oxygen uptake and performance during alternating intensity exercise. Med Sci Sports Exerc 2000; 32: 379-85
55. Cottrell GT, Coast JR, Herb RA. Effect of recovery interval on multiple-bout sprint cycling performance after acute creatine supplementation. J Strength Cond Res 2002; 16 (1): 109-16
56. Preen D, Dawson B, Goodman C, et al. Pre-exercise oral creatine ingestion does not improve prolonged intermittent sprint exercise in humans. J Sports Med Phys Fitness 2002; 42: 320-9
57. Finn JP, Ebert TR, Withers RT, et al. Effect of creatine supplementation on metabolism and performance in humans during intermittent sprint cycling. Eur J Appl Physiol 2001; 84: 238-43

58. Edwards MR, Rhodes ED, McKenzie DC, et al. The effect of creatine supplementation on anaerobic performance in moderately active men. J Strength Cond Res 2000; 14 (1): 75-9

59. Lieber RL, Thornell L, Friden J. Muscle cytoskeleton disruption occurs within the first 15 minutes of cyclic eccentric contractions. J Appl Physiol 1996; 80: 278-84

60. Yasuda T, Sakamoto K, Nosaka K, et al. Loss of sarcoplasmic reticulum membrane integrity after eccentric exercise. Acta Physiol Scan 1997; 161: 581-2

61. Ingalls CP, Warren GL, Armstrong RB. Dissociation of force production from MHC and actin contacts in muscle injury by eccentric contraction. J Muscle Res Cell Motil 1998; 19: 215-24

62. Clark JF. Uses of creatine phosphate and creatine supplementation for the athlete. In: Conway MA, Clark JF, editors. Creatine and creatine phosphate: scientific and clinical perspectives. San Diego (CA): Academic Press, 1999: 217-26

63. Bosco C, Tihanyi J, Puespk J, et al. Effect of oral creatine supplementation on injury and running performance. Int J Sports Med 1997; 18: 369-72

64. Earnest CP, Snell PG, Rodriquez R, et al. The effect of creatine monohydrate ingestion on anaerobic power indicies, muscular strength, and body composition. Acta Physiol Scand 1995; 153: 207-5

65. Linnamo V, Hakkinen K, Komi PV. Neuromuscular fatigue and recovery in maximal compared to explosive strength loading. Eur J Appl Physiol Occup Physiol 1998; 77: 176-81

66. Vanderberie F, Vandeneynde BM, Vandonberghe K, et al. Effect of creatine on endurance capacity and sprint power in cyclists. Int J Sport Med 1998; 8: 2055-63

67. Papadopoulos C, Imamura R, Brandon LJ. The effect of creatine supplementation on repeated bouts of high-intensity exercise in the heat [abstract]. Med Sci Sports Exerc 2001; 33: s203

68. Poortmans JR, Auguer H, Renaut V, et al. Effect of short-term creatine supplementation on renal responses in men. Eur J Appl Physiol 1997; 76: 586-67

69. Poortmans JR, Francaux M. Long-term oral creatine supplementation does not impair renal function in health athletes. Med Sci Sport Exerc 1999; 31: 1108-10

70. Rasmussen C, Kreider R, Melton C, et al. Long-term creatine supplementation during football training does not affect markers of renal stress [abstract]. J Strength Cond Res 1999; 13: 431

71. Almada AL, Kreider M, Melton C, et al. Long-term creatine supplementation does not affect markers of renal stress in athletes [abstract]. J Strength Cond Res 2000; 14: 359

72. Kreider R, Melton C, Rasmussen C, et al. Effects of long-term creatine supplementation in renal function and muscle and liver enzyme efflux [abstract]. Med Sci Sport Exerc 2001; 33: s207

73. Robinson TM, Sewell DA, Casey A, et al. Dietary creatine supplementation does not affect some hematological indices, or indices of muscle damage and hepatic and renal function. Br J Sports Med 2000; 34: 284-8

74. Ransom J, Kreider R, Hunt J, et al. Effect of creatine supplementation during training on markers of catabolism and muscle and liver enzymes [abstract]. Med Sci Sport Exerc 1999; 31: s265

75. Ransom J, Kreider R, Rasmussen C, et al. Effects of long-term creatine supplementation during training on markers of catabolism and enzyme flux [abstract]. J Strength Cond Res 1999; 13: 431

76. Schilling BK, Stone MH, Utter A, et al. Creatine supplementation and health variables: a retrospective study. Med Sci Sport Exerc 2001; 33: 183-8

77. Mihic S, Macdonald JR, McKenzie S, et al. Acute creatine loading increases fat-free mass, but does not affect blood pressure, plasma creatinine or CK activity in men and women. Med Sci Sport Exerc 2000; 32: 291-6

78. Kern M, Podewils LJ, Vukovich M, et al. Physiological response to exercise in the heart following creatine supplementation. J Exerc Physiol 2001; 4: 18-27

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