CREATINE:

A Review of the Literature on Creatine Supplementation and its Influence on Athletic Performace

ABSTRACT

The recent escalation of creatine (Cr) supplementation has inspired a variety of studies. Through the oral ingestion of creatine monohydrate the body's natural Cr and phosphocreatine (PCr) muscle stores can be augmented. Muscle uptake appears to be increased by insulin and muscle contractions. Higher concentrations of Cr in the muscle are associated with increased PCr resynthesis, decreased lactate accumulation, and reduced adenine nucleotide losses. Therefore, Cr supplementation appears to assist in the maintenance of ATP levels and combat the effects of muscle fatigue. Consequently, Cr ingestion has been implicated as an ergogen for intermittent, high-intensity, short duration exercise. Research on creatine supplementation's effect on human performance has shown increased peak power output, mean power output, speed and strength. An increase in body mass is also related to Cr ingestion. The following review seeks to establish the theoretical benefits of Cr supplementation, the current evidence on Cr supplementation and performance, practical applications for athletes and suggestions for future research.

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Introduction

Creatine has become the one of the "hottest" ergogenic aids taunted to make athletes faster, stronger, and more powerful through quicker recovery. Increased body weight and possibly muscle synthesis are other implications associated with increased ingestion of creatine (Cr). Its natural presence in the human body makes Cr an ideal ergogen because its supplementation is unlikely to be regulated for sport competition.

Numerous studies have been conducted to refute or validate the claims surrounding Cr. The following review seeks to establish the theoretical benefits of Cr supplementation, the current evidence on Cr supplementation and performance, practical applications for athletes and suggestions for future research.

Creatine Biosynthesis

Creatine is a nitrogenous compound formed from the three amino acids: glycine, arginine, and methionine. The pancreas, liver, and kidney are all sites of creatine production. It is biosynthesized through the transfer of a amidine group from arginine to glycine to form orinthine and guanidoacetate or glycocyamine in the kidney. This reversible reaction is facilitated by the enzyme transamidinase. The only identified regulator for this step appears to be dietary creatine which serves as an end product suppresser (84). The final step occurs in the liver and involves the irreversible methylation of guanioacetate by S-adenosylmethionine to create creatine (5, 9).

Approximately half of creatine stores are also replenished through exogenous sources. Creatine can be found primarily in meat and fish in values ranging from trace amounts to 10g/kg in uncooked meat[1] (4). In its supplemental form of creatine monohydrate, it is a synthetic, odorless, tasteless, white powder.

Creatine's Location and Transport in the Body

Skeletal muscle contains 95% of total creatine stores (TCr) (5). In this pool, 60% of creatine is in the phosphorylated form of phosphocreatine (PCr) and 40% exists as free creatine (82). The remaining 5% of the total creatine pool lies in the heart, brain, and testes (5). Normal levels in the muscle are 90 to 160 mmol/kg of dry muscle (dm) and average at 125 mmol/kg dm. Vegetarians usually have significantly lower levels than meat-eaters (5, 20, 82, 44).

Since creatine is not synthesized where it is stored, it must be transported. The blood stream serves this purpose and normal creatine concentrations in plasma range from 50 to 100 μmol/L (5) with a half-life of 1-1.5 hours (44). Vegetarians' levels of serum creatine tend to be significantly lower than meat-eaters. In a study by Delanghe et al. (21), the values for vegetarian males and females were 25.1 and 32.4 μmol/L respectively in contrast to 40.8 and 50.2 μmol/L for male and female meat-eaters respectively.

Two pathways which may explain the high concentration of creatine in the muscle are a specific saturable entry process or intracellular trapping in the muscle (37).

[1] ~65% of the Cr in meat is lost through cooking (80)

In the first mechanism, Cr enters the muscle cell primarily through an endergonic transport process that requires extracellular-Na^+. The structure and function of this transporter has recently been identified (83). However, it has be demonstrated *in vitro* in rat L-6 cells and in human cultures of myoblasts and myotubes that transport can be inhibited by high concentrations of intracellular creatine which activate the synthesis of proteins (57). These proteins either obstruct transport or remove the transporters from the plasma. In contrast, to the Na^+-dependent transport which is a saturable, high-capacity, high-velocity process, there is another form of creatine transport. This second transport is Na^+-independent and is a low-capacity, low velocity process and does not appear to be regulated by intracellular creatine concentrations (57). In the second mechanism of Cr uptake, 60% of the Cr that enters the muscle is phosphorylated into PCr, becoming polar and therefore unable to pass through the membrane (37). In essence, through phosphorylation Cr becomes trapped in the cell.

Creatine Turnover Rate

The rate of creatine turnover appears to be 1.5-2.0% of total creatine pool per day which amounts to approximately 2g (18, 19). This creatine is excreted as creatinine from the kidneys and is replaced by previously described endogenous biosynthesis and exogenous sources.

Creatine's Role in the Body

PCr has several roles in skeletal muscle. It serves as a high-energy reserve by buffering the ATP/ADP ratio. It accomplishes this through the popularly known creatine kinase (CK) facilitated reaction:

$$PCr + ADP \overset{CK}{\leftrightarrow} Cr + ATP \qquad (84)$$

Cr often serves as a pH buffer often to offset the effects of lactic acid in the muscle. This occurs through the following reaction:

$$P^{2-}Cr + H_2O \rightarrow Cr + P_i^{2-} \leftrightarrow P_i^{-}$$
$$\downarrow$$
$$H^+ \qquad (84)$$

Greenhaff et al., Volek et al. and Balsom et al. (5, 37, 82) describe the two former processes through the following equation:

$$PCr + ADP + H^+ \leftarrow (CK) \rightarrow Cr + ATP$$

The previous reaction also serves to regulate glycolysis and oxidative phosphorylation by stimulating these processes with increasing P_i concentrations or decreasing PCr concentrations. There is *in vitro* evidence that supports the partial inhibition of the glycolytic enzyme phosphofructokinase (PFK) with increasing levels of PCr. When PCr concentration decreases and P_i concentrations increase, this inhibition of PFK is removed (82, 84).

Finally, Cr is proposed to be a spatial energy buffer in skeletal muscle (82). Theoretically, this is accomplished through the PCr energy shuttle which was first proposed by Bessman in 1954 (10, 61). Basically, the PCr shuttle serves to connect areas of energy production with areas of energy utilization by means of PCr (10, 82). There are three primary locations in the PCr shuttle - the peripheral terminus or site of energy utilization (i.e. the myosin head in muscle contraction), the energy-generating terminus or mitochondria, and the space between these two sites. At the peripheral terminus PCr reacts with ADP to form ATP and free Cr. The free Cr then diffuses to the energy-generating terminus. At this site Cr is rephosphorylated to PCr which diffuses towards the peripheral terminus and the shuttle repeats (10).

Therefore, Cr/PCr serves four primary roles. It can function as a high-energy reserve, a pH buffer, a regulator of glycolysis, and a spatial energy buffer.

Creatine's Role in Muscle Metabolism and Fatigue

The accessibility of PCr has been proposed as a major limitation to performance during high intensity, short duration, fatiguing physical activities (37, 58, 62, 76). Free creatine availability is vital to the resynthesis of PCr, and both interact to maintain levels of ATP (37). Studies in which rats have been depleted of their Cr stores through ingestion of the Cr-analogue β-guanidonopropionate (β-GPA) and undergone maximal electrical stimulation of the muscles support this concept (25, 60). However, Cr-depletion studies showed no substantial affect on submaximal contractions, oxygen

consumption and energy metabolism (37). These findings further suggest that Cr-PCr has little effect on submaximal longer duration exercise (4).

Hultman et al. (47) reports that in exercise of 0 - 30, 60 - 90, and 120 - 192 s the contribution of energy from the anaerobic sources of glycolysis and the PCr energy system is 80, 45, and 30% respectively. The remainder of the energy is produced from aerobic sources. During high intensity exercise, there is an increased degradation of ATP. The majority (80 - 90%) of this ATP resynthesis must come from these anaerobic sources which share the responsibility equally (71, 47). However, during intense exercise the level of glycogen in the muscle remains at adequate levels, yet PCr becomes depleted. This suggests that PCr may be limiting. Further support for this assumption is Hultman et al.'s (47) statement that PCr limits ATP availability after 10 s of electrical stimulation. Glycolysis is unable to compensate for this reduction because it is already working at maximal capacity after 1 s of stimulation (47).

Studies suggests that the rapid fatigue properties of Type II fibers may be the culprit in short duration high intensity activities and PCr is crucial in the continuance of Type II fiber activity (37, 76). When Greenhaff et al. (37) electrically stimulated both Type I and II fibers for 32 s to perform a maximal isometric contraction, the Type II fibers showed a significantly greater PCr degradation and lower ATP levels than Type I. This finding was further verified by Tesch et al. (76) in a study where subjects voluntarily performed 30 maximal isokinetic knee extensions.

Other changes in muscle during high intensity fatiguing activity include increases in lactate accumulation and decreases in pH. These factors are also accused of

contributing to the decrease of power output through the interference with the contractile apparatus either through Ca^{2+} or myosin ATPase (21). In addition, these conditions may affect equilibrium reactions such as the creatine kinase reaction and inhibit the glycolytic enzymes PFK and phosphorylase. However, Gollnick et al. (29) argues that humans appear to have a capacity to maintain glycolysis until a low muscle pH is reached. As a pH buffer PCr may serve to offset some of these detrimental effects to exercise performance.

Adenine nucleotide loss is another consequence of high intensity exercise. In a study by Balsom et al. (4), levels of plasma hypoxanthine and uric acid, substances which are indicative of adenine nucleotide loss, were measured. Both substances increased following repeated 30m and 40m sprints with 30 s of rest. Normally, PCr minimizes these losses through buffering the concentration of ADP by rephosphorylation (4).

Phosphocreatine is a major regulator of muscle fatigue. The PCr rate of PCr resynthesis is responsible for maintaining the PCr concentration and hence ATP levels. It also serves to buffer against both lactic acid and adenine nucleotide losses.

Creatine Monohydrate Supplement Dosage

Because approximately half of human creatine is obtained exogenously, it has been postulated that ingestion of large amounts may increase skeletal muscle stores. Several studies support such a conclusion (18, 19, 44), but minimal dosages that will elicit maximal gains are still undetermined.

Harris et al. (44) conducted a study to ascertain what regimen of supplementation would produce the greatest increases in TCr concentration in the muscle. They determined that a 5g dose of Cr (which is the equivalent to the amount of Cr in 1 kg of uncooked meat (5)) increased plasma concentration to 795 μmol/L, whereas a 1g dose only "produced a modest rise" (44). In addition, by repeating the 5g dose every two hours the Cr plasma concentration remained above 1000 μmol/L. Harris et al. (44) felt these high concentrations of 10 - 20 time normal levels in the blood were necessary to maximize stores.

In the study, dosage protocol ranged from 5g of Cr 4-6 times a day for 3 to 20 days (44). Mean results indicated a 26% in TCr of which at least 20% was PCr, but there was considerable variation among individual subjects. Also, from the analyzed urine of three subjects, it was determined that 40, 61, and 68% of Cr supplementation was excreted on day 1, 2, and 3 respectively (44).

Because Cr stores appear to maximized within 5 to 6 days of supplementation of 20g/day (44), subjects can ingest a much smaller quantity after the loading phase to maintain these levels. Hultman et al.(48) studied Cr dosages to determine this amount. They concluded that a dosage of 2g a day for 28 days would sustain the elevated Cr stores after 6 days of supplementation with 20g/day. To account for individual differences in body weight the authors recommended a loading dose of .3/kg of body weight (bwt) and a maintenance does of .03g/kg of bwt (48). In addition, the study determined that if taken for 28 days, ingestion of 3g of Cr a day would cause the same rise in tissue Cr levels as the former dosage. Finally, this study discovered that the skeletal muscle does

not return to pre-supplementation levels until 30 days after the cessation of Cr supplementation.

Augmentors and Reducers of Creatine Uptake

Both insulin and muscle contraction have been shown to increase creatine uptake into the muscle (31, 32, 44, 46, 53). The mechanisms remain unknown, but they may be related to the Cr membrane transporter which has recently been identified in animal studies (37, 67, 46, 53). Green et al. (31) significantly raised plasma insulin levels when 93g of carbohydrate was ingested 30 minutes after a 5g dose of creatine 4 times daily for 5 days. They found Cr with carbohydrate presented a 60% increase in TCr and decreased creatinine excretion above creatine supplementation alone. A second study by Green et al. (32) that measured serum Cr levels supported this finding (32).

In the previously mentioned study by Harris et al. (44), researchers also measured the effect of muscle contraction on Cr uptake through biopsy samples of the leg. One leg exercised on a cycle ergometer for 1 hour while the other rested. Levels of TCr increased an extra 9.2% in the exercised leg, while the control leg remained the same. However, biopsies were only taken in one leg before exercise which has a coefficient of variance of 5% on collateral legs. Consequently, increases in uptake may not be as large as reported. In addition, there was no additive effect of carbohydrate and exercise in the before mentioned study by Green et al. (32).

It has been concluded that upper limits of TCr stores may be between 145 to 160 mmol/kg of dm (5, 37, 44, 82). Additionally, there is a large variation among individuals

in the amount of creatine uptake. Several studies noted the largest gains in both retention and performance in those subjects with normally low muscle Cr stores (10, 40). Such subjects are often vegetarians who do not receive as much creatine from their diet as meat eaters (20, 44). In the previously mentioned study, Harris et al. (44) noticed the greatest gains in a vegetarian whose exercised leg reached levels of 182.8 mmol/kg dm. Evidence from Green et al.'s (31) research with Cr plus carbohydrate suggests stores can surpass the previously reported limits. One subject whose stores were already at 152 mmol/kg dm before supplementation reached 195 mmol/kg dm. Furthermore, the level of creatine in the muscle before supplementation appeared to have no effect on uptake when creatine was supplemented with carbohydrate (31). The only other reported potential reducer of creatine uptake besides high muscle concentrations is vitamin E deficiency. This was demonstrated by Gerber et al. in rats (27).

Creatine Supplementation and PCr Resynthesis

PCr resynthesis is an oxygen-dependent process consisting of a fast component (~21-22 s) and a slow component (>170 s) (82). When Cr is supplemented, between 20-30% of increase of TCr is in the form of PCr (44). In addition, Cr supplementation has shown increases in work production which has been postulated to occur from increase PCr resynthesis (10, 13, 23). Therefore, Greenhaff et al. (39) studied the rate of PCr resynthesis before and after oral Cr supplementation of 20g for 5 days. Subjects were administered 50 Hz of electrical stimulation to instate isometric contractions of the vastus lateralis or tibialis anterior. Blood flow to the muscle was occluded during the

trial. Each contraction lasted 1.6 s and was proceeded by 1.6 s of rest. A needle biopsy of the vastus lateralis or a magnetic resonance spectroscopy (MRS) of the tibialus anterior was taken following electrical stimulation. Results concluded that PCr was 20% higher in muscle biopsies and 11% greater in MRS scans in the Cr supplemented group. Also, 10 out of 12 subjects had greater PCr resynthesis rates following supplementation. In a follow-up study by the same lab (38), muscle biopsy samples were taken after 0, 20, 60, and 120 s of electrically induced isometric contraction intended to deplete PCr stores. In those subjects whose TCr stores were augmented by greater than 15%, PCr resynthesis was increased. During the first 40s of recovery, rates of PCr resynthesis were similar for both pre- and post-supplementation. However, the results soon separated yielding a 42% increase in the rate resynthesis after Cr ingestion. At the end of 2 minutes, there was a 30% increase in PCr stores above the placebo group. The authors postulated that the heightened free Cr concentration was the mechanism for this occurrence. During the second half of recovery the muscle was more likely to keep the level of free Cr above the K_m for (CK). Therefore, the rate of the reaction was maintained and more PCr was resynthesized and ADP formed (38).

Creatine Supplementation's Effect on Performance

Creatine supplementation[2] has been shown to improve performance especially in high intensity, intermittent, short duration exercise (6, 10, 13,17, 23, 24, 45, 52). Research on exercise of longer duration yields mixed results (2, 25, 22, 45, 75).

[2] Cr Supplementation Dosage = 5g x4-6 times daily for 5-7 days unless otherwise noted. 1-20g of carbohydrate may also be administered with each dose.

The Wingate test[3] was used repeatedly to assess creatine supplementation's effect on performance. This test assesses peak power output, mean power output and fatigue which are parameters that creatine supplementation is postulated to affect. Earnest et al. (23) used the Wingate test and determined that the 14-day creatine supplemented group yielded consistently greater anaerobic work outputs of 13, 18, and 18% on bouts 1, 2, and 3 respectively from pre- to post-supplementation. However, the placebo group showed no change. In a second study by the same research group (24), increases of 15, 20, and 23% in anaerobic capacity after creatine supplementation were noted. Male and female intercollegiate track and field athletes were subjects in a third study applying the Wingate test. They produced greater average peak power increases with Cr ingestion (13%) than with the placebo (5%) (52). Finally, Odland et al. (63) used the Wingate test and found no change in performance across creatine, placebo and control groups. However, these subjects were only supplemented for 3 days whereas the other studies supplemented for at least twice that time. A more salient confounding variable is that all subjects cycled through each group with only 14 days between either creatine, placebo or control conditions. It has been demonstrated that it takes 30 days after supplementation for skeletal muscle Cr levels to return to pre-supplementation levels (48).

[3] In the Wingate test subjects pedal on a cycle ergometer for 30s bouts of supermaximal exercise with a 5 minute rest between bouts. The resistance is determined by body weight (.075 kg/kg of bwt) and is not applied until inertia and the unloaded bike resistance is overcome (59). Peak power output is assessed as the highest mechanical power achieved for any 3-5s period during the test and is assumed to measure the high energy phosphate's capacity to produce energy. Average power equals the mean of the total power produced during the trial and is thought to represent glycolytic capacity. Fatigue is computed as the rate of decline from peak power output.

Other cycling protocols have been used to demonstrate creatine's influence on performance. In a study by Casey et al. (13), maximal isokinetic cycling was used . After assessing that TCr concentrations were increased by an average of 23.1±4.7 mmol/kg dm (1/3 in the form of PCr) through muscle biopsies, subjects performed two 30 s bouts of cycling at 80 rpm with 4 minutes of rest between bouts. After creatine ingestion the subjects produced approximately 4% more work which was correlated to the increased TCr concentration. Despite performing more work, the ATP loss was 30.7 % less in the Cr group. The authors attributed their findings to increased ATP resynthesis and a heightened availability of PCr in Type II muscle fibers (13). Birch et al. (10) used the same exercise protocol but added one more 30 s bout. Their results showed a significant increase in peak power output of 8% in bout 1 and a significant increase in mean power output of 6 % in bouts 1 (251.9±10.5 to 267.0±10.3 J/kg) and 2 (227.0±11.1 to 239.6±11.9 J/kg) but no changes in bout 3 with Cr ingestion. Also, there were no changes in lactate, but peak plasma ammonia was significantly reduced in the Cr supplemented group suggesting a lowered adenine nucleotide loss. Again, the authors ascribe their results to increased ATP production from greater PCr accessibility and resynthesis (10).

Balsom et al. (6) looked at sprint cycling over 2 trials of 6s at 140 rpm with a 30 s rest in between, followed 40 s later by a 10 s trial. Muscle biopsies determined that TCr stores were raised from 128.7±4.3 to 151.5±5.5 mmol/kg dm and PCr from 45.6±7.5 to 69.7±2.7 mmol/kg dm by Cr ingestion. The authors assessed that supplementation allowed subjects to maintain greater power during the 10 s trial (132.3 vs. 125.9 rpm).

Also, lactate concentration after the two 6s trials was significantly less after supplementation (25.2 vs. 44.3 mmol/kg dm). Balsom et al. suggested the enhanced performance was due to increased PCr availability and decreased lactate accumulation (6). In contrast, Cooke et al. (17) found no changes in performance on 2 sets of 15 s sprints separated by 20 minutes of recovery on a cycle ergometer. However, the short duration of the exercise coupled with the long recovery may have prevented PCr resynthesis rate from becoming a limiting factor in the placebo group.

Studies evaluating Cr supplementation on resistance exercise have found positive effects on performance. Volek et al. (83) demonstrated an increase in total number of repetitions in 5 sets of bench press to failure with Cr supplementation. In another study using the bench press, subjects performed 26% more repetitions of their 70% 1RM after Cr ingestion (23). The subject's bench press 1RM also increased 6%, but this yielded no change when corrected for weight gain. Goldberg et al. (29) used a reduced dose of Cr (3g/day) to supplement and still found a 2.95% increase in 1RM bench press, however, no significant differences were found in the single leg extension or leg sled. An abstract by Becque et al. (8) reports that after subjects trained on a periodized resistance program for biceps curls, those who ingested Cr significantly improved over the placebo group. Finally, Greenhaff et al. (40) assessed Cr supplementation on 5 sets of 30 isokinetic knee extensions. They discovered increases over the placebo in torque during the last 10 extensions of bout 1, throughout bouts 2, 3, and 4 and during repetitions 11-20 of bout 5. Creatine supplementation also produced lower plasma ammonia concentrations in the 4th and 5th bouts. However, no differences in lactate were observed.

The evidence concerning Cr supplementation and jumping has been inconclusive (6, 29, 83). Volek et al. (83) reported an increase in peak power output in 5 sets of jump squats. However, Balsom et al. (6) found no changes in counter movement jumps or jump squats and Goldberg et al. (29) reported no change in vertical jump.

Creatine supplementation studies on anaerobic running have been limited. In a field study, Harris et al. (45) measured the effect of creatine ingestion on interval training. Subjects performed 4x 300m and 4x1000m runs with 4 and 3 min. rests between runs respectively. It was found that Cr supplementation improved final 300m and 1000m times and total 4x1000m time. Also the Cr group decreased their best 300m time by .3 s and their 1000m time by 2.1 s. There were no significant changes in the placebo group. Earnest et al. (22) had subjects perform two runs to exhaustion separated by 48 hours. When data for the two runs were combined subjects who supplemented with creatine increased their time by 5.7s (176.5 ± 11.4 s to 182.2 ± 14.6 s), whereas the placebo group actually decreased in performance (166.0 ± 11.6 s to 163.8 ±11.4 s). However, no significant differences were found when each run was analyzed alone. In a similar experiment, Balsom et al. (2) found no significant changes in a run to exhaustion times at 120% VO_2max with creatine supplementation. The influence of Cr supplementation on performance in either the Earnest or Cooke studies is questionable since anaerobic sources only provide 30% of the energy in exercise of this duration (47). Also, measures of blood lactic acid in both studies does not indicate that increase Cr facilitated exercise in any pH buffering capacity (6, 17).

Creatine supplementation's supposed benefits would not suggest an advantage to supplementation with endurance exercise, however the research has been equivocal (2, 15, 45). Balsom et al. (2) found a significant decrease in performance on a 6 km run with creatine supplementation. Also, no changes were found in blood lactate between pre- and post-creatine ingestion trials. In contrast, Coleman et al. (15) saw an increase in performance with 16 km cycling. The Cr supplemented group gained a significant 5 W increase in mean power output where as the placebo group improved an insignificant 2 W. Although the Cr group produced more work, no differences in blood lactate concentrations were observed. Stroud et al. (75) also observed no changes in blood lactate concentration or gas exchange when subjects ran 10 k m at various intensities (50-90% VO_2max).

Side Effects of Creatine Supplementation

No long terms studies with the high doses of Cr reported in this paper have been conducted. Therefore, side effects associated with these practices may emerge later. The only long term studies with creatine supplementation have been in diseased patients who could not adequately biosynthesize Cr. In a study on gyrate atrophy patients who supplemented 1.5g/day for 5 years, no detrimental effects were noted (70, 79). In a second study, no ill effects were discovered from supplementing a guanidineoacetate methyltransferase deficient 23 month old child (74). The supplementation regimen consisted of 4g/day for 13 months and 8g/day for 12 months.

The only reported side effect of Cr supplementation appears to be weight gain (2, 6, 8, 23, 29, 64, 66, 83). Average reported weight increases ranged from .6 kg to 1.7 kg (23, 66). Earnest et al. reported no increase in weight among its subjects after Cr ingestion, however, there were no measures to prove the supplemented Cr was actually taken into the muscle (22).

To further prove that this weight gain is related to Cr supplementation, Pearson et al. (64) noted that 6 days after the cessation of Cr loading the subject's weight returned to prior levels. In contrast, Greenhaff et al. (38) found an increase in body weight in 7 of 8 subjects, yet only 5 subjects increased their stores above 15% of [TCr]. This may suggest that even a small amount (5-7%) of uptake into the muscle will still elicit an increase in weight.

Most researchers attribute this weight gain to an increase in fat free mass and more specifically water weight gain (8, 23, 66, 83). These assumptions are based on skinfold measurements and hydrostatic weighing (8, 23, 66, 83). Several theories exist to explain the greater fat free mass as either an increased protein synthesis or increased hydration of the muscle cells (82). Volek and Kraemer (82) report on Balsom's theory that some of the weight gain could be attributed to the enlargement of Type II muscle fibers. Balsom supports his theory with evidence of decreased Type II muscle fibers in studies where rats were Cr-depleted (68) and the rise in Type II fibers in gyrate atrophy patients who were supplemented with 1.5g of Cr a day for a year (70). Finally, Balsom suggests that the increased diameter of Type II fibers may be due to Cr regulation of contractile protein synthesis. Research by Ingwall et al. (49) supports this idea. These

researchers have studied Cr effect on mononucleated muscle cells from the breast tissue of chick embryos suspended in a cultural medium. From their studies they have determined that Cr increases the rate of synthesis of contractile proteins, but not the degradation of these proteins.

Bessman and Savabi's (10) theory of Cr interaction of protein synthesis stems from their PCr energy shuttle. They postulate that exercise stimulates protein synthesis through the increase in contractile activity and subsequent increase in PCr transport. Because free creatine produced from muscular contraction travels to the mitochondria where it is rephosphorylated into PCr, supplementation could escalate the rate of this shuttle and make more PCr accessible for protein synthesis (82).

Another theory to explain the weight gain is an increased hydration state of the cell. Water retention could account for the decrease in urinary volume seen after creatine loading in a study by Hultman et al. (48). Because Cr is an osmotically active substance this is a plausible explanation (82). In addition, muscle edema has been linked to increased rates of protein synthesis (82, 50) .

Practical Applications for Creatine Supplementation

In the previously reported studies, Cr supplementation showed increases in peak power output and mean power output on a cycle ergometer (6, 10, 13, 23, 24, 52), faster interval run times in the field (26), and greater work production and strength in resistance training (2, 29, 40, 83). Creatine ingestion's benefit in these intermittent, short duration, high intensity activities may be from increasing the rate of PCr resynthesis and

therefore ATP production, buffering pH and reducing the loss of adenine nucleotides. Hence, Cr supplementation may enhance performance by speeding recovery and reducing fatigue. Such effects suggest that Cr ingestion may be beneficial is such pursuits as body building, power lifting, weight lifting, sprinting, rowing, swimming, long jumping, high jumping, football, wrestling, basketball, hockey, volleyball, and soccer (82). Athletes whose performance is not limited by fatigue may find supplementation beneficial in reducing exhaustion during practice and therefore, augmenting the training response.

The increase in body mass associated with Cr supplementation could be a advantage or a disadvantage depending on the activity. Individual athletes must weigh the increases in performance against the possibility of moving up in weight class. This possible increase in body mass is another reason Cr supplementation is not encouraged for endurance sports.

From the limited studies on supplemental dosages, it appears that athletes should consume 20 - 25 g/day in 5g dosages with carbohydrate for 4 to 6 days (44). After this loading phase, 2 g/day will maintain the augmented TCr levels (48). Upon cessation of supplementation muscle stores do not return to normal levels for 30 days (48). Athletes must keep in mind that individuals vary widely in their capacity to uptake creatine, and hence, no benefit may be derived from supplementation. Finally, athletes should be warned that no long term research with such large dosages has been done to determine the health implications.

Future Research

The number of questions left unanswered concerning creatine supplementation is enormous. Research needs to address the areas of optimal dosages for muscle uptake, health implications of long term supplementation of high dosages, and the mechanism causing weight gain and performance enhancement.

Information on the necessary serum levels and optimal insulin response for Cr uptake is still unknown. The greatest insulin response is produced by a blend of carbohydrate and protein (87), it should be determined if this combination enhances Cr uptake above ingestion with just carbohydrate. In addition, the affect of timing of ingestion and uptake in accordance with meals, sleep and exercise should be established. Finally, it should be ascertained if muscle Cr stores can be maintained through natural dietary sources (4, 80).

It is vital that the long term health implications of high dosages of Cr supplementation be assessed. Since approximately 30% of individuals who supplement Cr do not increase their stores (38), an easy method of determining whether Cr uptake is occurring needs to be developed. Measuring creatinine in the urine or possibly weight gain may prove effective.

More research needs to address the mechanism of body composition changes. Does this weight gain nullify some improvements in performance? Increases in power were noted using the non-weight bearing activity of cycling (6, 10, 13, 23, 24, 52), yet improvements in jumping power (6, 29, 83) were unclear. In addition, is the weight gain

related to hydration or protein synthesis? If protein synthesis does occur, is it a function of PCr availability or the enhanced ability to exercise the muscle?

Research designs need to attempt to isolate which function of Cr has the highest correlation with enhanced performance when Cr stores are elevated. Also, more field tests need to assess what sports find the greatest gains with Cr supplementation. Finally, researchers should measure the long term effects of Cr ingestion on performance, and if performance gains are maintained or return to former levels upon cessation of supplementation.

The current body of literature sheds a sliver of light on the topic of creatine supplementation. However, the available evidence is vastly inadequate considering the prevalence of this ergogen's utilization.

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