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Creatine Supplementation

Summary

In the phosphorylated form, creatine serves as an energy source that contributes to the body's energy stores during maximal exercise. Depletion of phosphocreatine has been implicated as a causative factor in the development of muscular fatigue. In 1992, it was clearly shown that a regimen of creatine supplementation significantly enhances accumulation of creatine and phosphocreatine in skeletal muscle. Since that time, numerous studies have examined the acute effects on exercise performance. Generally, these studies indicate ingestion of 20-25 g creatine/day for 5-7 days decreases the normal decline in force or power production during short-duration, maximal bouts of exercise. Muscle creatine is maintained with a 3-5 g maintenance dose per day.



Creatine supplementation has not been shown to improve longer duration aerobic-type exercise. The mechanism by which elevated muscle creatine enhances exercise performance is via an increased ability to match ATP supply to ATP demand. An increase in the rate of phosphocreatine resynthesis during recovery between bouts of exercise may also contribute to the ergogenic value of creatine supplementation during intense intermittent protocols. These beneficial effects are directly related to the extent of creatine loading in muscle. An increase in body mass ranging from 1 to 3 lbs is frequently observed after one week of creatine supplementation, attributable to an increase in total body water. There is limited data describing the effects of long-term creatine supplementation.

Recent data indicate that creatine supplementation may enhance the physiological adaptations to resistance training in men and women, most likely a result of being able to train more intensely. Athletes most likely to gain from creatine supplementation are those who participate in sports or activities that are short-term, intense bouts of exercise. Nearly all the research examining creatine supplementation has been obtained in the laboratory. There are few field studies documenting beneficial effects of creatine supplementation during specific sports and competitions. Increasing use of nutritional supplements by athletes spanning several age levels and performance capabilities enforces the need to acquire answers related to the potential long-term value and risks associated with creatine supplementation.

Introduction

Creatine and phosphocreatine participate in a single reversible reaction enhanced by an enzyme that serves to replenish cytosolic ATP during periods of rapid ATP turnover. While several mechanisms probably contribute to the development of fatigue, failure to maintain a high ATP:ADP ratio is generally accepted as a feature in theories that attempt to explain reductions in force production during short-term maximal exercise. Breakdown of phosphocreatine has been directly correlated to decreases in force production in both animal and human experimental models. The potential of creatine supplementation to enhance short-term maximal exercise is based on the notion that an increase in

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the availability of free creatine and phosphocreatine can buffer the rapid accumulation of ADP resulting from ATP hydrolysis, especially in fast type II muscle fibers. Indeed, creatine supplementation has been shown to lessen the accumulation of hypoxanthine and ammonia (e.g., markers of adenine nucleotide degradation) following brief maximal exercise, indicating an enhanced ability to match ATP supply with ATP demand.

Creatine Metabolism

Nearly all of the total creatine in the body is contained within skeletal muscle. About two thirds of the total creatine in muscle exists in the phosphorylated form, phosphocreatine. Degradation of creatine into creatinine occurs at a constant rate of 1.6% per day (about 2 g/day) and is excreted in the urine. Creatine balance is maintained by endogenous synthesis (1 g/day) in the liver from precursor amino acids and dietary intake (1 g/day) predominantly from animal products. Uptake of creatine from the circulation occurs via a specific creatine receptor located on the sarcolemma that is unregulated in the presence of insulin.

Creatine Concentration in Skeletal Muscle

Normal concentrations of total creatine in skeletal muscle are 120 mmol/kg but may range from 100 to 150 mmol/kg. Ingestion of a 5-g dose of creatine monohydrate increases blood creatine concentrations nearly 10-fold over several hours. A single 5-g dose of creatine consumed 4-5x/day (20-25g creatine/ day) for 5-7 consecutive days enhances uptake of creatine into muscle by as much as 30%. Lower dose supplementation with 3 g/day will also significantly elevate muscle creatine; however, the increase occurs gradually over several weeks rather than days. The variability in creatine accumulation between individuals is quite large, which explains why some athletes may not experience an ergogenic effect. Individuals with lower total creatine values exhibit the greatest increases in creatine accumulation. The extent to which muscle creatine increases is directly related to measures of performance and the rate of phosphocreatine resynthesis during recovery, emphasizing the importance of maximizing creatine uptake. Ingestion of a carbohydrate solution with creatine has been shown to reduce the variability in uptake between individuals and to enhance creatine accumulation further. The upper limit of creatine accumulation in muscle is near 155-160 mmol/kg and reachable for many individuals when consumed with carbohydrate.

While the effectiveness of acute creatine loading protocols to increase muscle creatine levels has been well documented, there is an uncertainty regarding the optimal dosage of creatine to maintain elevated creatine stores. Once creatine is increased in muscle, the breakdown occurs relatively slowly over about one month. In sedentary individuals, 2 g/day of creatine was an adequate dose to prevent muscle creatine concentrations from declining toward pre-supplementation values. Limited data suggests that a 5 g maintenance dose is effective in maintaining elevated creatine stores and enhancing physiological adaptations to resistance training. Since the daily turnover of creatine is about 2 g, there is no reason to believe that large doses would be necessary or beneficial to maintain elevated muscle creatine stores. Large doses of creatine consumed regularly may increase the incidence of potentially unknown detrimental side effects.

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Effects on Exercise Performance and Body Composition

Acute Effects. The effects of creatine on performance have been limited to the investigation of several exercise protocols after short-term (<1 week) supplementation. The majority of research indicates that creatine significantly enhances the ability to maintain power output during short-term maximal bouts of exercise, including cycling, sprinting, jumping, and weightlifting protocols. These findings are consistent with the function of creatine as a buffer to replenish ATP during conditions of rapid energy turnover. Other studies have failed to detect a positive effect of creatine supplementation using various swimming, cycling, and longer duration running protocols. Such data support the notion that only certain exercise modes and configurations are influenced by creatine supplementation and/or that supplementation does not enhance creatine accumulation in all individuals. Evidence exists supporting both explanations. Another finding often reported in short-term creatine studies is an increase in body mass. An increase in body mass of 1 to 2 lbs. after ingestion of 20-25 g creatine per day for 5-7 days is often observed. This is most likely a reflection of increased retention of body water although direct evidence for this contention is lacking.

Chronic Effects. There is limited data on the long-term benefits and risks of creatine supplementation. Consumption of creatine in conjunction with resistance exercise enhances the physiological adaptations to weight training. Creatine supplementation (5 g/day) during 10 to 12 weeks of resistance training enhances maximal strength, body mass, and fat-free mass, while percent body fat and fat mass remain relatively constant in both men and women. The increase in strength and fat-free mass is associated with greater increases in individual, cross-sectional areas of muscle fiber in men.

Mechanisms

The primary mechanism explaining the acute ergogenic value of creatine supplementation is an enlargement of the phosphagen pool available for rapid resynthesis of ATP during periods of extremely high ATP turnover. Depletion of phosphocreatine, especially in fast type II fibers, and subsequent declines in force production, are thus delayed. During maximal intermittent exercise, the enhanced rate of phosphocreatine resynthesis during recovery allows for higher levels of phosphocreatine at the beginning of each subsequent bout. The beneficial effects of creatine on muscular strength and body composition responses to resistance training are probably mediated by the following sequence of events: increased muscle creatine, increased training intensity, greater training stimulus, and enhanced physiological adaptations to training.

Side Effects

While no direct cause-and-effect relationships between creatine ingestion and any negative side effects have been documented in the scientific literature, adverse reactions including minor gastrointestinal distress, nausea, and muscle cramping have been anecdotally attributed to creatine supplementation. These anecdotal claims are not supported by data collected in a scientific manner and published in peer-reviewed journals. Short-term oral creatine supplementation (20 g/day for 5 days) does not adversely affect several measures of renal function in healthy men. However, circumstantial evidence linking creatine supplementation to deterioration in kidney function in a 25-year-old man with pre-existing renal problems (focal segmental glomerulosclerosis) was recently published as a research letter in *Lancet*. When large doses of creatine are consumed in the diet, endogenous synthesis is dramatically reduced probably via feedback regulation.

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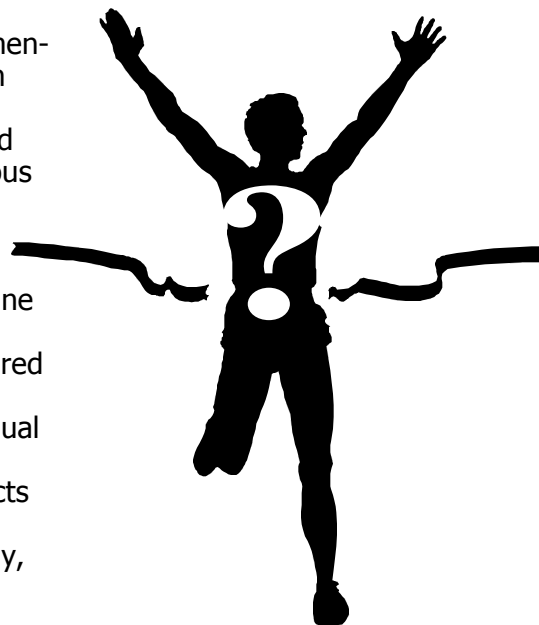
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CREATINE (cont.)

Animal and human data indicate that enzymes involved in creatine biosynthesis are re-activated when creatine supplementation is discontinued. In summary, the verdict is still out on the safety of creatine supplementation, especially over long periods of time. More research is needed in both animal and human studies to thoroughly evaluate any potential deleterious side effects.

Future Research

There are still many unanswered questions concerning creatine supplementation, including issues related to 1) strategies to maximize creatine accumulation in muscle, 2) dosages required to maintain elevated creatine stores in muscle, 3) aspects related to the matrix of delivery, timing of intake, and individual variability in creatine accumulation, 4) factors regulating the creatine receptor on muscle, 5) long-term physiological effects of creatine supplementation, including potential side effects, and 6) responses in various populations (e.g., women, elderly, catabolic patients).



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