THE SCIENCE BEHIND

CREATINE MONOHYDRATE

SUPPLEMENTS FOR HIGH INTENSITY EXERCISE: CREATINE

Key Points

- Creatine is an important energy source for intense bouts of exercise
- Creatine can be obtained in meats and fish but not in fruit and vegetables – so vegetarians and vegans may have lower levels of muscle creatine
- The limited stores of muscle creatine can be significantly increased by Cr supplementation
- Quick loading of muscle Cr can be undertaken by supplementation of 20g a day for 5 days whereas slower loading can be achieved by ingesting 5g a day for 10-14 days. After the loading phase, muscle concentrations can be maintained by supplementation with 2g a day
- Cr supplementation needs to be undertaken with appropriate training for maximum benefits
- Cr supplementation invariably leads to an increase in lean body mass which may present a disadvantage in weight-restricted events. This may also present a temporary problem in running based sports where an additional increase in body weight could be a problem – usually overcome when training effects are realised
- Cr supplementation is likely to significantly enhance strength and power – especially when part of an appropriate training regime
- Cr supplementation needs to be matched with training and athletes should consider cycling off Cr after 3 months or so and then recycle again
- Since Cr causes water to enter a muscle and the excess Cr is excreted by the kidneys, athletes must consume more fluids when supplementing with Cr
- If an athlete has abnormal kidney function (readily diagnosed by having a blood test via GP for kidney function) then they should avoid using Cr and indeed high protein foods too

Introduction

Creatine (Cr) is a naturally occurring substance found mainly in the skeletal muscles of vertebrates, but can also be found in smaller amounts in the liver, kidney, and brain. Creatine has been known as a constituent of food for over 150 years. However, it was not until the early 1990s that significant levels of research were undertaken examining the effects of Cr supplementation on sports performance.

Creatine can also be synthesised by the liver from three amino acids, these being arginine, glycine, and methionine (Figure 1). Once synthesised Cr is transported from the liver to muscle where it is taken up by actively. Once inside the muscle the Cr is 'trapped' by being converted to phosphocreatine (PCr), which is unable to pass through the membrane. Approximately 70% of the creatine in muscle is in the phosphorylated form (PCr), the other 30% being free Cr. It is PCr which forms an immediate source of energy during explosive bouts of exercise.

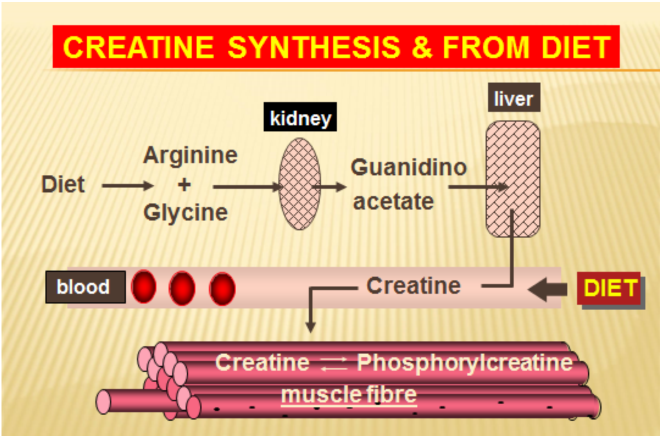

Figure 1. Creatine synthesis, intake from diet, and muscle accumulation

Creatine is constantly degraded to creatinine. The creatinine diffuses through the muscle membrane and is taken to the kidney where it is excreted in a passive process before being voided in urine. The daily urine creatinine excretion is relatively constant, although it varies between individuals due to differences in muscle mass. For a more detailed examination of creatine and creatinine metabolism, the reader should consult Wyss & Kaddurah-Daouk (2000). The daily turnover of Cr to creatinine in humans is about 2 g/day for a 70 kg person, and is replaced by endogenous synthesis and exogenous sources in the diet. Synthesis is regulated by the exogenous intake through a feedback mechanism.

Factors such as age, sex, and diet influence muscle Cr concentration. Resting PCr levels have been shown to be lower in older (60 yr) compared with younger (30 yr) subjects (Smith et al., 1998), although there is no significant difference in the total Cr concentration. In this instance it is possible that the degree of inactivity in the older subjects may have led to the attenuated PCr levels. Females have been reported to have an elevated Cr concentration compared with males (Forsberg et al., 1991). Diet can significantly influence muscle Cr concentration. However it should be noted that since the exogenous source of Cr is via consuming foods containing meat and fish, vegetarians may have lower concentrations since their only source is de novo synthesis. Studies have shown that vegetarians have marginally lower muscle Cr concentrations than those who eat meat and fish (Delanghe et al., 1989; Harris et al., 1992).

Muscle creatine loading

Muscle Cr is restored at a rate of approximately 2 g/day by a combination of dietary Cr ingestion from sources such as meat and fish, and from endogenous synthesis. Muscle Cr content has been found to increase significantly following Cr ingestion (Harris et al., 1992). In this study, ingestion of 5 g of Cr 4 to 6 times a day for two days resulted in an increase in total Cr from 127 to 149 mmol/kg. These increases were individual responses, in which some subjects increased significantly and others less so (Figure 2). The term 'responders' and 'non-responders' applies in this instance, and a relationship between the initial resting level and the level of increase was established. Two vegetarians in the study possessed the lowest initial resting levels and responded with significant increases.

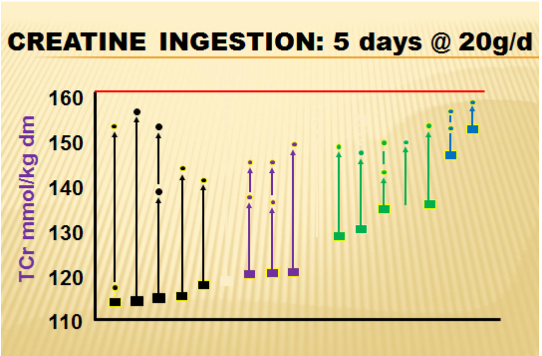

Figure 2. Effect of 5 days of creatine ingestion on total muscle creatine.

Furthermore, Harris et al (1992) were also able to demonstrate that whereas on the first 2 days the Cr storage was approximately 30% of that ingested, the amount stored in the following 2 days diminished to around 15% of the Cr ingested (figure 3).

Studies have shown that muscle Cr concentrations can be significantly enhanced using lower daily doses for a prolonged time period. Hultman et al. (1996) reported that Cr ingestion of 3 g/day over a 4 week period produced muscle Cr concentrations similar to those found when 20 g/day were ingested over a 5 day period. Most recent studies have employed a regimen in which 5 g of Cr are administered in a warm solution during 4 equally spaced time intervals through a day. See Figure 3.

There is considerable variation between subjects to the extent muscle Cr concentrations are elevated following supplementation, although it appears that there is an upper limit of 160 mmol/kg dry muscle. In order to achieve this level, creatine should be ingested in combination with at least 370 g of simple carbohydrates in a day (Green et al., 1996). It seems likely that the increase in muscle Cr stores when taken with carbohydrates is as a result of insulin action. Hyperinsulinaemia results in enhanced muscle Cr storage.

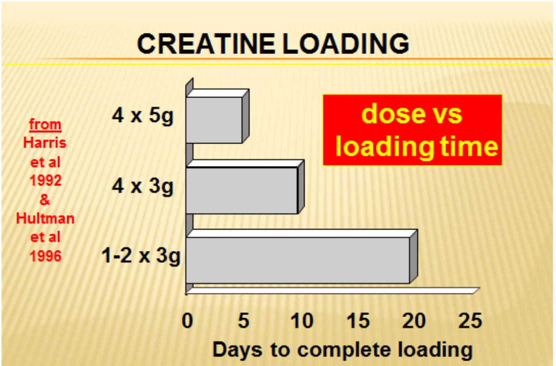

Figure 3. Muscle creatine loading using different doses.

Following the Cr loading phase of 20 g/day for 5 days, recommended maintenance doses are considerably lower. Most studies have used doses ranging from 2 to 5 g/day during the maintenance phase. Hultman et al. (1996) recommend a maintenance dose of 0.03 g/kg body mass per day, which for a 70 kg person amounts to approximately 2 g/day. When an athlete stops ingesting creatine, the muscle Cr levels diminish to normal levels after 4 weeks (Greenhaff, 1997).

Creatine and performance

The theoretical benefits of creatine supplementation are related to the role of Cr and PCr in the energetics of muscle contraction, and also to the potential for buffering increases in [H^+] as a consequence of raised intramuscular lactic acid concentrations. Specifically, mechanisms purported to provide an ergogenic effect of creatine include the fact that supplementation results in elevated PCr levels in muscle and hence a greater immediate source of generation of ATP, that increased levels of Cr would facilitate an enhanced rate of PCr resynthesis in recovery bouts, and that there is enhanced buffering of H^+.

Intramuscular stores of ATP and PCr are limited, and it has been estimated that these phosphagen stores could supply sufficient energy for high-intensity exercise for not more than 10 seconds (Balsom et al., 1994). Furthermore, Sahlin (1998) has suggested that the maximum rate of PCr hydrolysis decreases as PCr content of muscle decreases, and that complete depletion is not necessary to cause a reduction in power production. In fact, a number of researchers have concluded that PCr availability is a limiting factor during high-intensity exercise (Greenhaff, 1997; Balsom et al., 1995).

Creatine supplementation, by increasing both Cr and PCr, particularly in the FG fibres, should prolong either single bouts of high-intensity exercise and in particular repeated bouts of high-intensity exercise. Probably the first two studies which reported on Cr supplementation and intense exercise were those of Greenhaff et al. (1993) and Earnest et al. (1995). Greenhaff and colleagues (1993) employed 5 bouts of 30 maximal isokinetic knee extensions with 1 minute recovery between the bouts (Figure 4). When subjects were loaded with 20 g/day of Cr for 5 days, peak muscle torque was significantly enhanced in the final 10 contractions during the first bout, and during the whole of the next 4 bouts. The authors concluded that Cr supplementation accelerated PCr resynthesis and that the increased availability of PCr was responsible for the higher peak torque production.

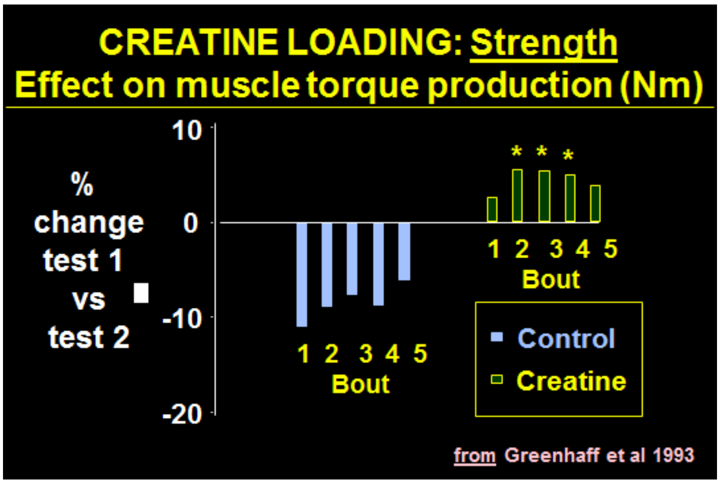

Figure 4. Effect of 5 days of creatine or placebo on repeated bouts of knee extension exercise.

Earnest et al. (1995) used three 30 second bouts of all-out cycling with 5 minutes recovery between the tests. The test was undertaken by a placebo group and a creatine group in a random, double-blind design. Creatine loading entailed 5 days of 20 g/day of Cr. The creatine-loaded group increased the work done during the three bouts compared with their non-loaded values, whereas those on placebo failed to do so (Figure 5).

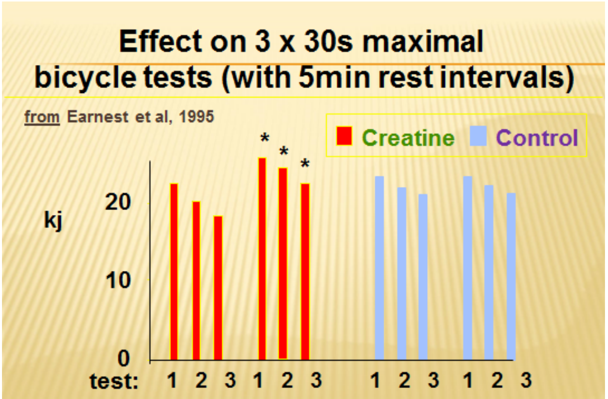

Figure 5. Effect of creatine or placebo on repeated sprint cycling.

In the same study, Earnest et al. (1995) had the participants undertake a maximal bench press and also determined the number of repetitions of bench press at 70% of the maximum i.e. 70%-RM. Figure 6 highlights the significant findings following creatine but not placebo.

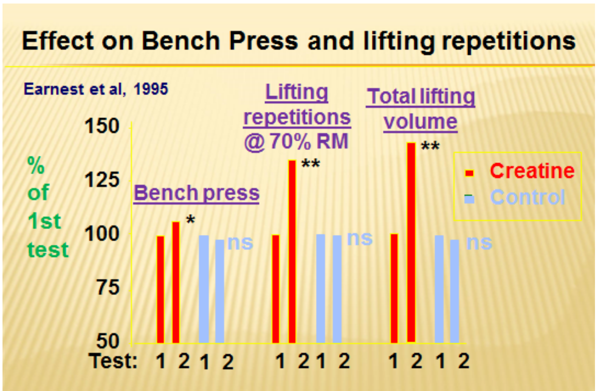

Figure 6. Effect of creatine or placebo on bench press and lifting repetitions.

Since these early reports, in excess of 400 studies have been published in peer reviewed articles. The majority of these studies highlight the effectiveness of Cr supplementation for enhancing sports performance (Bemben & Lamont, 2005) and being of potential use for ageing athletes too (Tarnopolsky, 2008). These studies have examined the effects on high-intensity exercise (both single bouts and repeated bouts), strength and power, field based activities, and endurance (Deldicque & Francaux, 2008). Other studies have purely examined the effects of supplementation on lean body mass and body composition, although many of the other studies have also reported data on body mass changes. The reader may wish to explore reviews on creatine and performance (Bemben & Lamont, 2005; Hespel & Derave, 2007; Deldicque & Francaux, 2008) for a broader exploration of studies.

Creatine and single bouts of high intensity exercise

In spite of the fact that Cr supplementation leads to increases in muscle Cr and PCr, it would be expected that single bouts of high intensity exercise produce enhanced performance. In general, this is not the case. Some studies have shown significant improvements in sprint running (Goldberg & Bechtel, 1997; Kendall et al., 2009; Law et al., 2009; Noonan et al., 1998), or vertical jump performance (Stout et al., 1999), whereas the majority of studies using single bouts of running, cycling, swimming, and jumping have failed to show significant improvements. It appears that the possibility of elevated Cr stores in muscle being available to maintain a short, sharp burst of activity when not fatigued does not happen. Interestingly a study in which a single bout of 10 seconds of sprint cycling was assessed following 5 bouts of 6 s sprinting with a 30 s recovery between bouts showed an increase in power (Balsom et al., 1995). So when there is an element of fatigue due to previous activity, creatine may help to improve single bouts of intense exercise.

Creatine and repeated bouts of high intensity exercise

Since enhanced stores of Cr and PCr result from creatine loading, there is the possibility that during recovery phases of repeated bouts of exercise, the elevated Cr will be more rapidly phosphorylated. Enhanced performance may then result in subsequent bouts of exercise. Positive ergogenic effects of Cr loading have been exhibited for repeated bouts of high intensity cycling (Earnest et al., 1995), running (Aaserud et al., 1998), swimming (Peyrebrune et al., 1998), and vertical jumping (Bosco et al., 1997). In most cases, the significant effects are noted in the later bouts of exercise and not usually in the first bout. Furthermore, the effects are normally associated with mean power or total work done rather than peak power values. All in all, these findings do support the notion of greater re-phosphorylation in the recovery period when Cr stores have been enhanced.

It should be noted however, that not all studies have reported significant effects. Some studies on repeated sprint cycling have shown no significant effect of Cr ingestion (Barnett et al., 1996; Cooke et al., 1995). Similar non-responses were obtained for investigations using repeated running (Smart et al., 1998), and swimming (Leenders et al., 1999).

It is difficult to fathom out the reasons why the majority of studies highlight positive ergogenic effects whereas a significant, though smaller, number find no such differences. Examination of the dose of Cr ingested and whether carbohydrates were ingested in addition, together with the types of subjects used (i.e level of training), the sex of the subjects, the dietary habits of the subjects, the number of subjects employed, and variations in the mode of testing are all possible confounding variables. On balance, Cr supplementation results in an approximate 4-10% improvement in repeated high intensity activities. Even some of the studies which reported no significant findings, reported 2-4% improvements in performance, but due to the low power of the experimental design produced non-significant results.

Creatine and strength

Phosphocreatine and ATP are likely to be the major energy sources during strength-based activities which are isometric, isotonic, or isokinetic. In the cases of isotonic or isokinetic exercise, the activity is repeated in either fast or slow modes, whereas isometric activity involves either an all-out fast action or a hold of the tension for a period of time. The majority of studies in which some form of strength has been assessed, have shown positive ergogenic effects. Such studies include the use of isometric (Maganaris & Maughan, 1998), isotonic (Noonan et al., 1998), or isokinetic (Vandenberghe et al., 1997) modes of testing. Improvements of between 6 and 28% in strength were reported in the above studies. Studies in the elderly have shown the potential for significant improvements in strength and lean body mass with creatine ingestion (Tarnopolsky, 2008).

The study by Vandenberghe et al. (1997) is of particular interest in so far as it illustrates a number of key features regarding Cr supplementation, muscle Cr content, body mass, strength, and washout period (Figure 7a, b, c). Participants engaged in a study lasting 24 weeks in which they first 'loaded' with Cr for 5 days before undertaking a 10 week resistance training period with a 2g maintenance dose of Cr followed by continued training of 10 weeks without Cr, and finally 4 weeks of no training (and no Cr). An matched group carried out the programme but on placebo. From Figure 7a it is seen that muscle PCr levels increased in concordance with taking Cr, whilst Figure 7b highlighted the impact of Cr and training on increases in lean/muscle tissue – which remained elevated even after Cr supplementation had ceased. The effect of Cr and training on muscle power can be seen in Figure 7c, although strength decreased somewhat once Cr was removed. Finally (in Figure 7a) it is worth pointing out that 4 weeks of no Cr resulted in muscle PCr returning to pre-administration levels i.e. wash-out.

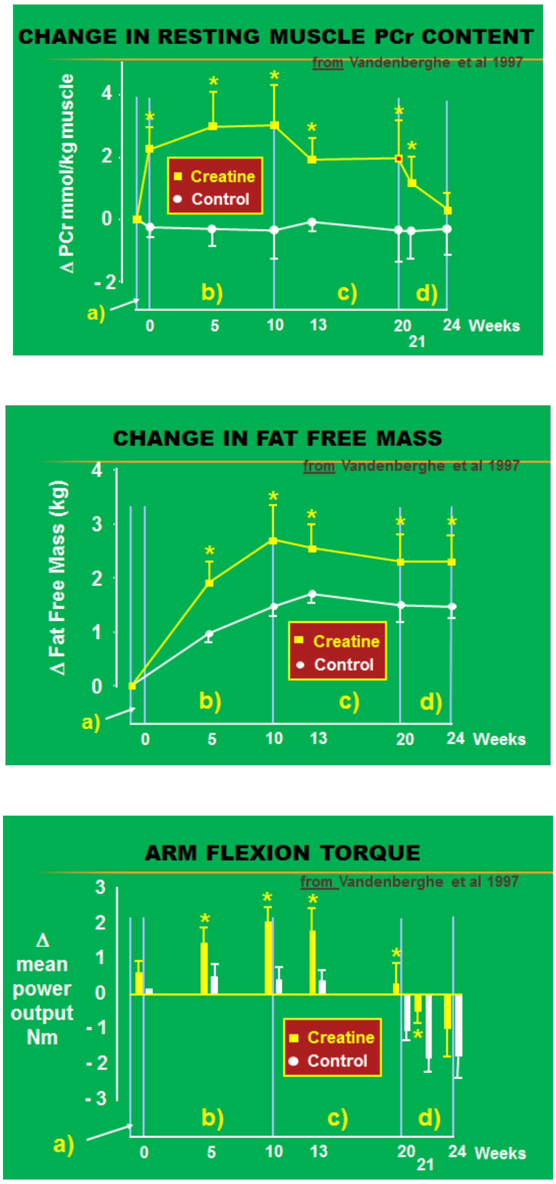

Figure 7. Changes in resting muscle PCr content (7a); changes in fat free or lean mass (7b); changes in arm muscle isometric strength (7c).

However as with the studies on repeated bouts of high intensity exercise, there are a number of studies which reported no significant benefits of Cr on isometric strength (Rawson et al., 1998), isotonic strength (Stout et al., 1999), or isokinetic strength (Kreider et al., 1996).

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