INVITED REVIEW

BENEFITS OF CREATINE SUPPLEMENTATION FOR OLDER ADULTS

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ABSTRACT

STEC, M. J.; RAWSON, E. S. Benefits of creatine supplementation for older adults. Brazilian Journal of Biomotricity, v. 4, n. 4, p. 215-226, 2010. Decreases in muscle mass (i.e. sarcopenia), strength, and power due to the aging process can result in an impaired ability to perform daily tasks and ultimately lead to functional disability in older adults. While age-related declines in muscle mass and function can be attenuated by progressive resistance training, only one nutritional intervention has been identified as an effective strategy to combat sarcopenia. Creatine supplementation increases strength and power, enhances fatigue resistance, and increases fat free mass in young adults. The purpose of this review is to examine the effects of creatine supplementation on muscle function, body composition, and activities of daily living in older individuals (>60 yr). Collectively, the studies reviewed in this article indicate that creatine supplementation increases muscle creatine, enhances fatigue resistance, increases strength/power, increases fat free mass, and enhances functional performance in older adults. In addition to the beneficial effects of creatine supplementation on skeletal muscle in older adults, new data indicate a role of creatine in improving bone health and cognitive processing. Creatine supplementation, with or without concurrent resistance exercise, should be considered a safe and effective nutritional therapy to combat age-related changes in muscle.

Key Words: Aging; Elderly; Muscle; Sarcopenia; Fatigue resistance; Phosphocreatine.

INTRODUCTION

Enhanced fatigue resistance, increased fat free mass (FFM), and increased strength in young adults ingesting creatine is a consistent finding in the literature (reviewed in BRANCH, 2003; RAWSON & VOLEK, 2003), and creatine supplementation is widely practiced by athletes (reviewed in RAWSON & CLARKSON, 2003). More recently, the potential benefits of creatine supplementation have been studied in patient populations and in older adults. Muscle mass decreases about 1 to 2% per year after the age of fifty (HUGHES et al., 2002; SEHL & YATES, 2001), and is accompanied by decreased strength, power, and ability to perform daily tasks, which can lead to functional disability. Age-related sarcopenia (decreased muscle mass) and dynapenia (decreased strength) affect a large number of older adults (13-24% of adults age ≤ 70 yr; > 50% of adults age > 80 yr) (BAUMGARTNER et al., 1998), which makes the development of treatments to slow or reverse these processes essential. Physical activity, specifically progressive resistance training, is a well known therapy for sarcopenia and dynapenia (reviewed in JOHNSTON et al., 2008). However, nutritional therapies to combat aging have been less effective. Creatine supplementation represents an inexpensive, safe, and effective dietary strategy to slow or reverse age-associated changes in muscle morphology and function. The purpose of this review is to 1.) provide an overview of the effects of creatine supplementation on skeletal muscle, 2.) discuss the implications of aging on skeletal muscle morphology and energy metabolism, and 3.) examine the effects of creatine supplementation on muscle function and body composition in older adults.

BACKGROUND

Role of Creatine in Energy Metabolism

Creatine, methyl-guanidino acetic acid, is a naturally occurring nitrogen-containing compound that is synthesized in the kidneys, liver, and pancreas (WYSS & KADDURAH-DAOUK, 2000). Creatine is also ingested through the diet, with the highest concentrations found in meat (about 3 to 4 grams/kg). Approximately 95% of total body creatine is found in skeletal muscle, where it is stored in the form of phosphocreatine (≈60%) and free creatine (≈40%) (HARRIS et al., 1974; HARRIS et al., 1992). Creatine acts as a temporal energy buffer during times of high energy demand by facilitating the maintenance of adenosine triphosphate (ATP). Through the creatine-phosphocreatine shuttle, creatine plays a role in energy transfer between the sites of ATP synthesis (i.e. the mitochondrion) and the sites of ATP utilization (i.e. myofibrils) (BESSMAN & GEIGER, 1981).

Creatine Supplementation

About a 20% increase in intramuscular creatine and phosphocreatine levels can be achieved via low-dose longer-term (about 2 to 3 g/d for 4 to 6 wk) or high-dose shorter-term (20 g/d for 5 d) oral creatine supplementation (HARRIS et al., 1992; HULTMAN et al., 1996). In young adults, increased muscle creatine subsequent to supplementation improves muscle function through several mechanisms, including: increased pre-exercise phosphocreatine (GREENHAFF et al., 1994), faster phosphocreatine resynthesis (GREENHAFF et al., 1994), increased expression of growth factors (DELDICQUE et al., 2008; DELDICQUE et al., 2005; SAFDAR et al., 2008; WILLOUGHBY & ROSENE, 2003), and reduced muscle damage and inflammation (BASSIT et al., 2008; SANTOS et al., 2004). In young adults, creatine supplementation without exercise training increases body mass and enhances fatigue resistance particularly during high-intensity exercise (BRANCH, 2003). When combined with resistance training, creatine supplementation increases strength and fat free mass, and enhances fatigue resistance in young adults more than resistance training alone (RAWSON & VOLEK , 2003).

Consequences of Aging on Skeletal Muscle

Sarcopenia in the elderly is characterized by the loss of skeletal muscle mass and strength, which may be attributed to a myriad of causes including: selective loss and atrophy of type II fibers (LEXELL, 1995; LEXELL et al., 1983), decreased number of motor units (DOHERTY et al., 1993), and decreased levels of anabolic hormones (i.e. testosterone, growth hormone) (IRANMANESH et al., 1991; SZULC et al., 2004). Type II fibers contain ≈20% greater phosphocreatine than type I fibers (SAHLIN et al., 1997), and the loss and atrophy of type II fibers may result in subsequent decreased phosphocreatine in older adults (CAMPBELL et al., 1999; MCCULLY et al., 1991; MOLLER et al., 1980). In addition to reduced muscle fiber number and size, aged muscle is more susceptible to damage and has impaired regenerative capacity, partly due to decreased satellite cell number/proliferation and molecular changes within the skeletal muscle environment (JEJURIKAR & KUZON, 2003). Recently, creatine supplementation has been shown to augment the increase in satellite cell number in response to resistance training in young subjects (OLSEN et al., 2006) and increase expression of certain genes and proteins involved in muscle hypertrophy both at rest and following resistance exercise/training (DELDICQUE et al., 2008; DELDICQUE et al., 2005; SAFDAR et al., 2008; WILLOUGHBY & ROSENE, 2003). Creatine supplementation has the potential to promote a more favorable environment for muscle growth in aged muscle, which has diminished capacity for muscle regeneration and growth.

CREATINE SUPPLEMENTATION IN OLDER ADULTS

Muscle Creatine and Phosphocreatine

It has been reported that muscle creatine decreases with age (CAMPBELL et al., 1999; MCCULLY et al., 1991; MOLLER et al., 1980), although this has not been shown in every case (RAWSON et al., 2002). Muscle creatine may naturally decrease as part of the aging process, or this decrease may be related to low levels of physical activity (MACDOUGALL et al., 1977) or decreased dietary creatine intake (BURKE et al., 2003). While it could be debated if muscle creatine is reduced in older adults, creatine supplementation increases muscle creatine in older muscle to a similar extent as in young muscle.

Rawson et al. (2002) reported a 7% increase in muscle phosphocreatine in older men (70 yr) following creatine ingestion (20 g/d for 5 d). In this study, young adults had a greater increase in muscle phosphocreatine with supplementation (35%); however, baseline muscle phosphocreatine was higher in the older relative to the young subjects (RAWSON et al., 2002). The magnitude of the increase in muscle creatine in response to creatine ingestion is largely determined by baseline muscle creatine (HARRIS et al., 1992; HULTMAN et al., 1996; RAWSON et al., 2002). In longer term studies where creatine ingestion was combined with exercise training, Brose et al. (2003) reported increased muscle total creatine (30% men; 17% women) in older adults (70 yr) following supplementation (5 g/d for 14 wk). Similarly, Eijnde et al. (2003) reported increased muscle total creatine (5%) and free creatine (21%) following supplementation (5 g/d for 6 mo). Thus, the increase in muscle creatine in older adults ranges from 5 to 30%. This range is similar to what was noted in early creatine supplementation studies of young adults, and represents the typical variability in muscle creatine uptake when creatine is not ingested with carbohydrate.

Fatigue Resistance

Early studies by Rawson et al. (1999) and Rawson & Clarkson (2000) demonstrated improved fatigue resistance (3 to 9%) during repeated bouts of isokinetic knee extensions in creatine supplemented older men (66 yr). Subsequently, Wiroth et al. (2001) reported that five days of creatine supplementation (15 g/d) increased work done (+4.1%) by older men (70 yr) during five 10 second maximal sprints on a cycle ergometer separated by 60 seconds of passive recovery. Using a similar maximal cycling test (5 x 10 s sprints; 2 min recovery) as a performance outcome, Gotshalk and colleagues (2002; 2008) demonstrated greater increases in lower body mean power output (+11%) in creatine supplemented older men (65 yr) and in lower body (+7.7%) and upper body (+8.5%) mean power output in creatine supplemented older women (63 yr) than placebo supplemented participants following seven days of supplementation (0.3 g/kg/d). In support of these findings, Stout et al. (2007) reported significant increases in physical working capacity at fatigue threshold (+15.6%) during an incremental, discontinuous cycle ergometry protocol following 2 weeks of creatine supplementation (20 g/d for 7 d, followed by 10 g/d for 7 d) in older men and women (75 yr).

Two groups reported enhanced fatigue resistance following creatine supplementation plus resistance training compared with placebo supplementation plus resistance training (CHRUSCH et al., 2001; TARNOPOLSKY et al., 2007). Chrusch et al. (2001) reported greater increases in leg press endurance (3 sets of pre-training 80% 1RM separated by 60 s rest; creatine group vs. placebo group) (+47 vs. +32 reps), knee extension endurance (+21 vs. +14 reps), and average isokinetic knee extension/flexion power (3 sets of 10 reps separated by 60 s rest; +27 vs. +18 Watts) in creatine supplemented (0.3 g/kg/d for 5 d; 0.07 g/kg/d 12 wk) older men (70 yr) following a twelve week resistance training intervention. Similar to these findings, Tarnopolsky et al. (2007) reported greater improvements in chest press (maximal number of reps performed at pre-training 1RM; creatine vs. placebo) (men +21 vs. +16 reps; women +31 vs. +17 reps) and arm flexion (men +20 vs. +15 reps, women +24 vs. +14 reps) muscular endurance in creatine supplemented (5 g/d for 24 wk) older men and women (70 yr) when compared to six months of resistance training plus placebo ingestion. Collectively, these studies indicate that creatine supplementation with or without the addition of resistance training enhances fatigue resistance in older adults.

Strength/Power

The studies by Chrusch et al. (2001) and Tarnopolsky et al. (2007) described previously also demonstrated significant increases in maximal strength following creatine supplementation combined with resistance training compared to placebo supplementation plus resistance training. Chrusch et al. (2001) reported greater increases in leg press 1RM (creatine vs. placebo group) (+50.1 vs. +31.3 kg) and knee extension 1RM (+14.9 vs. +10.7 kg). Tarnopolsky et al. (2007) reported greater increases in isokinetic knee extension strength in creatine supplemented older men and women. Similar to these findings, Brose et al. (2003) demonstrated greater increases in isometric knee extension strength (+46.2% vs. 22.5%) in older men (69 yr) and women (71 yr), and a greater increase in isometric dorsi-flexion strength (+17.8% vs. 5.6%) in older men following 14 weeks of creatine supplementation combined with progressive resistance training.

Reportedly, creatine supplementation increases maximal strength/power in older individuals without concurrent resistance training. Gotshalk et al. (2002) demonstrated greater increases in 1RM bench press (+4.1 kg) and leg press (+16.1 kg), lower body peak power (+10%), and maximal isometric knee extension and flexion (+9 to 15%) in older men supplemented with creatine than those supplemented with placebo. In addition, Gotshalk et al. (2008) reported greater increases in 1RM bench press (+1.7 kg) and leg press (+5.2

kg) in older women supplemented with creatine compared to those ingesting the placebo. Wiroth et al. (2001) demonstrated a greater improvement in maximal power (+3.7%) during repeated cycle ergometer sprints in older sedentary men, and Stout et al. (2007) demonstrated a greater improvement in maximal isometric grip strength (6.7%) in older men and women following creatine supplementation when compared to placebo supplemented participants. Data from these studies show that creatine supplementation has the potential to increase maximal strength and power in older individuals, which may in turn lead to increased functional capacity and decreased risk of injury.

Fat Free Mass

Data from Chrusch et al. (2001), Tarnopolsky et al. (2007), and Brose et al. (2003) show greater increases in FFM (creatine vs. placebo groups) (+3.3 vs. +1.3 kg, +2.1 vs. +0.9 kg, +1.7 vs. +0.4 kg, respectively) following creatine supplementation (BROSE et al., 2003; CHRUSCH et al., 2001) or creatine and conjugated linoleic acid supplementation (TARNOPOLSKY et al., 2007) plus resistance training when compared to placebo groups. Furthermore, Chrusch et al. (2001) and Brose et al. (2003) demonstrated greater increases in total body mass (+3 kg vs. no change, +1.2 vs. -0.2 kg, respectively), while Tarnopolsky et al. (2007) demonstrated a significantly greater reduction in fat mass (-1.9 vs. -0.4 kg) following supplementation. In addition, Candow et al. (2008) demonstrated greater increases in body mass (+0.6 vs. -0.7 kg) and muscle thickness (10.4% vs. 5.5%) in creatine supplemented (0.1g/kg/d, 3d/wk) older men (66 yr) when compared to placebo supplemented participants following 10 weeks of progressive resistance training. These studies show that combining creatine supplementation with resistance training may be more effective on improving body composition than resistance training alone in older individuals.

Several investigators have found increases in fat free mass in older adults ingesting creatine without resistance training. Gotshalk and colleagues (2002; 2008) reported significantly greater increases in FFM (+2.2 kg men; +0.5 kg women) and body mass (+1.9 kg men; +0.5 kg women) following creatine supplementation in older adults. Rawson & Clarkson (2000) reported a significant increase in body mass (+0.5 kg) in older men following 5 days of creatine supplementation (20g/d), but no change in FFM. Similarly, Jakobi et al. (2001) determined that the same dose and duration of creatine supplementation (20g/d for 5 days) resulted in a significant increase in body mass (+1.0 kg) in older men (72 yr). Collectively, these studies demonstrate the utility of creatine ingestion as a standalone or adjuvant therapy to resistance exercise to combat sarcopenia.

Activities of Daily Living

Several groups have found beneficial effects of creatine supplementation on performance of activities of daily living in older adults (CANETE et al., 2006; GOTSHALK et al., 2008; GOTSHALK et al., 2002), but this has not been shown in each case (BROSE et al., 2003; TARNOPOLSKY et al., 2007). Gotshalk et al. (2002; 2008) found reductions in time to complete sit-stand and tandem gait tests in older men (6 to 9% reduction) and women (5 to 7% reduction) following creatine supplementation. Similar to these findings, Canete et al. (2006) demonstrated a reduction in time to complete the sit to stand test (12% reduction) in older women (67 yr) following 7 days of creatine supplementation (0.3 g/d). These studies demonstrate that acute creatine supplementation has the potential to enhance quality of living in older adults by increasing performance of daily tasks.

Other Potential Benefits

The most commonly reported benefits of creatine supplementation in older adults are related to improved muscle function and increased fat free mass. However, creatine supplementation may also improve bone health and cognitive processing, which may reduce morbidity in older adults. For instance, Chilibeck et al. (2005) reported increased bone mineral content and Candow et al. (2008) demonstrated decreased bone resorption in creatine supplemented older men engaged in resistance training compared with resistance training alone. An additive effect of creatine on bone health beyond the benefits of resistance exercise has not been shown in every case (BROSE et al., 2003; TARNOPOLSKY et al., 2007). The potential for creatine to improve bone health is of great importance given the prevalence of osteoporosis and risk of fractures older adults. An additional benefit of creatine supplementation in older individuals is improved cognitive function. Recently, McMorris et al. (2007) demonstrated improvements on cognitive tasks in older adults (76 yr) supplemented with creatine (20g/d for 7d) compared to those supplemented with placebo.

Equivocal Findings

While there are many reports of improved muscle function or increased fat free mass in older adults ingesting creatine (see Table 1), several studies have not found a benefit (BEMBEN et al., 2010; BERMON et al., 1998; CANDOW et al., 2008; EIJNDE et al., 2003; JAKOBI et al., 2001; WIROTH et al., 2001). Although it is unknown why some studies examining the effects of creatine supplementation on muscle function and body composition in older adults report no ergogenic effect, several factors may play a role, including: habitual physical activity level, dietary creatine intake, duration and intensity of performance outcomes, or design of the resistance training intervention. Physical activity and dietary creatine intake are rarely measured in creatine supplementation studies, but it is possible that very active or sedentary older adults may have marked differences in baseline muscle creatine, which would influence the response to supplementation. For example, Wiroth and colleagues (2001) found no effect of acute creatine supplementation on older trained cyclists, while there was a significant increase in cycle ergometer performance in sedentary older men. Similarly, those with low dietary creatine intake would be expected to respond differently to creatine supplements than those with normal or high dietary creatine ingestion. In some cases where creatine supplementation did not produce a measureable ergogenic effect in older adults, performance tests may have been too long in duration or too low in intensity to challenge the creatine-phosphocreatine energy system. For instance, Jakobi et al. (2001) found no effect of creatine supplementation in older adults using a low intensity (50% of MVC) fatigue protocol which lasted from four to forty two minutes in duration. In creatine supplementation plus resistance training studies, improved fatigue resistance or increased strength must be detectable over the variable improvement in fatigue resistance and strength from the resistance training protocol itself. This may be difficult to measure given the heterogeneity in muscle mass and function in older adults who are grouped solely on chronological age. Additional concerns include whether training volume is adjusted throughout the study (BEMBEN et al., 2010), because creatine supplementation causes spontaneous increases in training volume (VOLEK et al., 1999), and whether the outcome tests match the specificity of the training intervention (EIJNDE et al., 2003).

Table I - Beneficial effects of creatine supplementation on muscle function, activities of daily living, and fat free mass in older adults.

Effects of Creatine Supplementation	Strength of Support	References
↑ Fatigue resistance (creatine alone)	✓✓✓✓	RAWSON et al., 1999 RAWSON & CLARKSON, 2000 WIROTH et al., 2001 GOTSHALK et al., 2002 STOUT et al., 2007 GOTSHALK et al., 2008
↑ Fatigue resistance (creatine + RT)	✓✓✓✓	CHRUSCH et al., 2001 TARNOPOLSKY et al., 2007
↑ Strength/power (creatine alone)	✓✓✓	WIROTH et al., 2001 GOTSHALK et al., 2002 STOUT et al., 2007 GOTSHALK et al., 2008
↑ Strength/power (creatine + RT)	✓✓✓✓	CHRUSCH et al., 2001 BROSE et al., 2003 TARNOPOLSKY et al., 2007
↑ Performance of activities of daily living (creatine alone)	✓✓✓	GOTSHALK et al., 2002 CANETE et al., 2006 GOTSHALK et al., 2008
↑ FFM (creatine alone)	✓✓	GOTSHALK et al., 2002 GOTSHALK et al., 2008
↑ FFM (creatine + RT)	✓✓✓	CHRUSCH et al., 2001 BROSE et al., 2003 TARNOPOLSKY et al., 2007

RT = resistance training; FFM = fat free mass. ✓ = weak evidence; ✓✓✓✓✓ = strong evidence

Although an increase in performance of activities of daily living by older adults has been demonstrated following acute creatine supplementation (CANETE et al., 2006; GOTSHALK et al., 2008; GOTSHALK et al., 2002), the same benefit has not been found following supplementation plus resistance training. Brose et al. (2003) and Tarnopolsky et al. (2007) reported that creatine supplementation does not augment the increase in performance of functional tasks such as the 30 m walk, tandem gait walk, sit to stand, chair rise and walk, and stair climb beyond the improvements gained from resistance training alone. Potentially, the large variability in response to resistance training (HUBAL et al., 2005) makes detection of increased performance of activities of daily living difficult. This may explain why improved activities of daily living is a more consistent finding of acute creatine supplementation studies compared with longer-term creatine supplementation studies with a resistance training intervention.

CONCLUSION

There is evidence to support the beneficial effects of creatine supplementation on muscle function and body composition in older adults. These benefits may translate to improved quality of life as demonstrated in studies with performance of activities of daily living as outcomes. Creatine supplementation currently represents the only nutritional intervention that can improve both muscle and cognitive function, it is inexpensive, readily available, and in addition to a wealth of research on efficacy, has data which demonstrate an excellent safety profile (PERSKY & RAWSON, 2007). Future studies on creatine supplementation in older adults should explore benefits to bone and mental health, as these areas currently have the fewest number of published studies.

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