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Creatine Supplementation: Practical Strategies and Considerations for Mixed Martial Arts

Short Review

Tony Ricci[1], Scott C. Forbes[2], Darren G. Candow[3]

[1]*Department of Athletic Training and Exercise Science, Long Island University, Brooklyn, New York, United States*
[2]*Department of Physical Education, Brandon University, Brandon, Manitoba, Canada*
[3]*Faculty of Kinesiology & Health Studies, University of Regina, Regina, Saskatchewan, Canada*

Abstract
Mixed martial arts (MMA) is an intermittent sport that is physically and cognitively demanding. Nutritional strategies to support training, competition, and weight-cutting are important to optimize performance. One purported ergogenic aid that may have beneficial effects for MMA is creatine monohydrate. The purpose of this narrative review is to (1) discuss how creatine supplementation impacts MMA performance; (2) outline the effect of creatine supplementation on body composition and highlight specific strategies while cutting weight; (3) discuss how creatine can be used after weigh-ins to enhance re-hydration and glycogen re-synthesis; (4) evaluate the potential cognitive benefits of creatine supplementation; and (5) discuss practical real life strategies and considerations when considering creatine supplementation.

Key Words: Brain Health, Supplements, Performance, Creatine Monohydrate, Combat

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Corresponding author: Tony Ricci, tony@fightshape.net

Introduction

Mixed martial arts (MMA) is a combative sport that that has increased in popularity since the creation of the Ultimate Fighting Championship (UFC) [1]. MMA involves techniques from various martial art disciplines, including boxing, kickboxing, Brazilian jiu-jitsu, karate, judo, muay thai, wrestling, and others [2,3]. MMA fights range from three (regular bouts) to five (competition bout) five-minute rounds with one-minute rest between rounds [3]. Depending on total fight time (~15-25 min), the physiological demands are mainly supported by oxidative phosphorylation [4,5]; however, due to the intermittent nature and the explosive actions required, anaerobic pathways are also important [3,5,6]. For example, MMA is characterized by a combination of explosive bursts of high intensity short duration actions such as striking and grappling interspersed by lower intensity actions [3,5]. These short-term high intensity explosive actions are often implicated in the success of a match [3,6]. Beyond the muscular and metabolic demands, MMA also requires tactical strategies and thus a high level of cognitive activity and function [7]. MMA athletes must be able to quickly process information, react to opponents, make strategic decisions (i.e. executive function), and have a well-adapted short and long term memory [7]. To support the physical and cognitive demands of MMA, it is imperative that athletes have proper nutritional support strategies [8,9].

One dietary supplement that is purported to enhance MMA performance is creatine monohydrate [10]. Creatine (N-aminoiminomethyl-N-methyl glycine) is a naturally occurring nitrogen containing compound found primarily in red meat, fish, and poultry [11-13]. Creatine has been shown to influence both muscle [10,14] and brain function [15]. The purpose of this brief review is to discuss the nuances of creatine supplementation for MMA athletes. Specifically, this review will (1) discuss how creatine impacts MMA performance; (2) outline the effect of creatine on body composition and highlight specific strategies while cutting weight; (3) discuss how creatine can be used after weigh-ins to enhance re-hydration and glycogen re-synthesis; (4) evaluate the potential cognitive benefits of creatine supplementation; and (5) discuss practical real life strategies and considerations when considering creatine supplementation.

1. Creatine and MMA Performance

Creatine is a nitrogen containing compound endogenously derived (1-2 g·day^{-1}) from reactions involving glycine, arginine and methionine in the liver and kidney [13]. In parallel, creatine is metabolized and excreted (i.e. creatinine) at a rate of ~2 g·day^{-1} [11]. Exogenous dietary creatine is found in food and is also readily available as a commercial dietary supplement. Approximately ninety-five percent of creatine is stored in skeletal muscle with the remainder found in other tissues (e.g., brain), of which 60-70% is phosphorylated (i.e. phosphocreatine [PCr]) and the remainder is free creatine (Cr). Phosphocreatine rapidly re-synthesizes adenosine diphosphate (ADP) to maintain adenosine triphosphate (ATP) during high intensity exercise, such as grappling or striking [4]. Elevated PCr stores by exogenous creatine supplementation may increase exercise training intensity and capacity leading to greater muscular adaptations [10]. Importantly, the responsiveness to creatine supplementation seems to depend on initial intramuscular PCr content, muscle fiber type composition and habitual dietary creatine ingestion [16]. Beyond increasing PCr, there are several other potential mechanisms that may alter adaptation and performance over time [13]. Creatine appears to increases muscle glycogen storage and myocellular water retention due to increased intracellular osmolarity, [17]. Increased cell swelling may influence satellite cell differentiation, activity, and content; insulin growth factor-1 (IGF-1) [18], muscle protein kinetics (protein kinases downstream in the mammalian target of rapamycin pathway; leucine oxidation, 3-methylhistidine excretion) and inflammation and oxidative stress [19]. Creatine plays a role in shuttling intracellular energy from sites of ATP synthesis (i.e. mitochondria) to subcellular sites of ATP utilization (ATPases) [10], thereby supporting oxidative metabolism.

From an applied sports performance perspective, creatine supplementation has been shown to increase single and repetitive high intensity sprints, muscular endurance, and augment training adaptations (e.g., increases in muscle mass and strength) [10,20,21]. In addition, creatine supplementation enhances glycogen re-synthesis [22], anaerobic exercise capacity [23], and aerobic exercise capacity via greater shuttling of ATP from the mitochondria [10]. Despite several meta-analyses examining creatine and exercise adaptive responses in aging adults [20,24,25], there are limited reviews and meta-analyses in younger adults [21,26,27] and no meta-analysis has focused solely on athletes. Almost two decades ago, Branch [21] conducted a systematic review that included 96 peer reviewed studies and concluded that creatine supplementation was effective at improving repetitive high intensity exercise (≤ 30 seconds in duration). Furthermore, creatine was more effective for upper body exercises which may have important implications for specific skill development and requirements involved in MMA. According to the UFC performance institute [28] average strike rates per minute increased from 4.17 in 2004 to 8.5 in 2017 and striking accounts for 72% of the top 5 performance indicators across weight classes. It is not uncommon for a winning round in MMA matches to be determined within the final 30-45 seconds via the total number and significance of strikes thrown. As such, creatine supplementation, in theory, can augment the capacity for the MMA athlete to administer repetitive upper body bouts at high intensities in the form of striking/punches, influencing the outcome of the fight. They did not find any differences between genders or training status [21]. In 2015, Lanhers et al. [27] included 60 studies (using a more rigorous inclusion criteria) with a total of 1297 participants and reported that creatine supplementation was an effective ergogenic aid for augmenting lower-body strength and performance in activities lasting less than 3 minutes. More recently, Lanhers and colleagues extended their previous findings to conclude that creatine supplementation was effective for increasing upper limb strength (53 included studies; 1138 participants) [26].

To date, there are no creatine supplementation studies focused specifically on MMA, however, there is limited research investigating the effects of creatine in other combative sports. However, due to the varying nature of different combat sports and the differences in the physiological demands (reviewed elsewhere [5,6]) caution is required. Manjarrez-Montes de Oca [29] assessed male taekwondo participants (N=10) in a cross-over study that consisted of creatine (50 mg/kg/day) or placebo for 6 weeks with a 6-week washout period. Creatine did not enhance lower body anaerobic power (Wingate Test) compared to placebo [29]. Similarly, in wrestlers (N=20), creatine supplementation (0.3 g/kg/day) for 5 days did not alter peak power, mean power, or fatigue index in a repetitive upper body muscle anaerobic power test used to mimic wrestling matches [30]. In contrast, Kocak and Karli [31] examined active international level wrestlers (N=20) with 20 g·day^{-1} of creatine or placebo for 5 days. Kocak and Karli found no change over time in the placebo condition while the creatine group's average power and peak power significantly increased over time [31]. Overall, the limited body of literature suggests that creatine supplementation has no beneficial effect on laboratory tests involving combative sport athletes.

2. Creatine and body composition and practical strategies while cutting weight

Creatine, in combination with strengthening exercises, is well known to enhance lean body mass gains over time [20]. Chilibeck et al. [20] conducted the most comprehensive review comparing lean body mass gains with creatine in combination with resistance training compared to placebo. Creatine supplementation during resistance training led to significantly more lean body mass accretion (mean difference: 1.37 kg) compared to placebo and resistance training in aging adults. Branch [21] reported that creatine increased lean body mass (2.2 ± 0.7%) while placebo had no effect over time (0.6 ± 0.2%). Increasing lean body mass is due to an increase in the balance of muscle protein synthesis relative to muscle protein breakdown[32]. It has been proposed that creatine supplementation may result in greater lean body mass over time by decreasing muscle protein breakdown and by influencing variables involved in muscle hypertrophy (i.e. satellite cells, IGF-1, myostatin, protein kinases) [13,33]. Creatine may also be involved in adipose tissue energetics [34]. Kazak et al. [35,36] crossed mice that led to off-springs that lacked the creatine transporter in fat tissue. This resulted in lower creatine and phosphocreatine levels, lower whole-body energy expenditure, and decreased oxidative metabolism in beige and brown adipose tissue. In humans, there was a negative correlation between mRNA expression of the creatine transporter and body mass index (BMI). Earnest et al. [37] provided participants with 5 g·day^{-1} of creatine in hypercholesteremic participants. Creatine supplementation reduced plasma triglyceride levels by ~20% after 4 to 8 weeks. A recent meta-analysis in aging adults found a non-significant decrease in fat mass (0.5 kg) with creatine compared to placebo in aging adults [34]. Overall, results across studies suggest that creatine has the potential to influence properties of muscle and adipose tissue biology which may be of benefit for elite MMA athletes. However, the effects of creatine supplementation on measures of lipolysis in MMA fighters during weight maintenance or weight cutting is unknown.

An increase in muscle mass, combined with a decrease in fat mass, may or may not be desirable in a weight classification sport such as MMA. Body mass typically increases by 1.2 ± 0.3% following creatine supplementation [21]. Importantly, total body water is increased due to the increase in osmolarity following creatine supplementation. As such, total body water typically increases 1.8 ± 0.3% following creatine supplementation compared to placebo (-0.2 ± 1.0%) [21]. A potential practical strategy includes initiating creatine supplementation at least 10-12 weeks prior to weigh-in. This is the time frame when body mass is relatively stable before the athlete will undergo substantive fluctuations in body mass due to increased training volume and a reduction in total calories [9]. Typically, most athletes implement a creatine loading phase (20 g·day^{-1} for 5-7 days) during the initial stages of a supplementation protocol. [38]. The MMA athlete and coach should record body mass increases at the initiation and completion of creatine loading (i.e. before starting supplementation and after the loading phase). Subsequently, a maintenance dose of 3-5 g·day^{-1} will preserve the typical 20-40% increase in intramuscular creatine stores [39]. After one week on the creatine maintenance dose, body mass should again be recorded to acquire a total increase in body mass from creatine supplementation associated with both the loading and maintenance dose. When the MMA athlete records dosing and the associated body mass gain; this can be accounted for in the weight cutting process. If necessary, the athlete can slowly titrate the dosing as they approach their weigh-in. Whether creatine ingestion must be completely withdrawn in the weeks preceding the weigh-in is highly contingent upon the athlete's remaining body mass loss requirement. As noted, total body water with creatine supplementation is ~1.8 ± 0.3%. For well-conditioned MMA athletes, this water is usually released and refunded easily in the weight-cutting and refueling practices. Additionally, if fat mass is not significantly impacted affected by creatine supplementation [34], this still may result in a contribution to the MMA athlete's body mass loss efforts. Accordingly, chronic dosing of creatine may benefit MMA fighters and the short duration of titrating the dose is not likely to impact long term performance benefits as research has shown that once creatine stores in the muscle are elevated, it generally takes 4–6 weeks for creatine stores to return to baseline [10,40,41].

3. Creatine and glycogen re-synthesis

Following cutting body mass and achieving a successful weigh-in there are two major goals, rehydration and replenishing glycogen stores [9]. Creatine supplementation can impact both of these goals [10]. Robinson et al. [42] examined the effect of glycogen-depleting exercise on subsequent muscle total creatine accumulation and glycogen re-synthesis during post-exercise periods with carbohydrate or a mixture containing creatine and carbohydrates. Fourteen subjects performed unilateral single leg cycling exercise to exhaustion. Muscle biopsies were taken from both the exercise and non-exercised legs immediately after exercise, after 6 hours, and after 5 days of recovery. Total muscle creatine content was increased after 5 days following creatine and carbohydrate intake. Greater creatine accumulation was achieved in the exercised limb, suggesting that exercise may enhance creatine uptake. Similarly, glycogen was increased above non-exercise concentrations in the exercise limbs of both groups after 5 days, but importantly glycogen concentration was greater in the creatine and carbohydrate group compared to the carbohydrate only group, suggesting that creatine augments glycogen super-compensation in exercised muscle. More recently, Roberts et al. [22] examined the time-course of creatine induced carbohydrate super compensation. In a well-designed study, healthy males (N=14) performed cycling at 70% VO_2peak to exhaustion. During the next 6 days, creatine (20 g·day^{-1}) or placebo was provided with a high carbohydrate diet (37.5 kcal/kg/day, >80% calories as carbohydrate). After 1 day (24 hours) of creatine supplementation, muscle total creatine content, free creatine, and PCr were significantly elevated relative to placebo. Muscle glycogen content was augmented above placebo after 1 day of supplementation. These findings have important implications for fighters, since both PCr content and glycogen are important substrates during fighting and weigh ins may occur the day before a fight.

To date, there has only been one very small study that investigated the effects of creatine supplementation during recovery from rapid body mass reduction on metabolism and muscle performance in fighters (well-trained wrestlers) [43]. Oopik et al. [43] examined well-trained wrestlers (N=5) in a placebo controlled cross over study. The results suggest that creatine supplementation with glucose ingestion during the 17 hours of recovery from rapid body mass loss did not accelerate the restoration of body mass but improved recovery of physical performance in maximal intensity efforts. Future research should investigate the mechanistic effects of creatine, alone and in combination with macronutrients, on glycogen metabolism and body mass homeostasis.

4. Creatine, Cognition, and mTBI

Cognitive function plays a key role in MMA performance [7]. The brain is highly metabolically active (~20% of total energy expenditure and ~2% of total body mass), and brain creatine is important for energy production [44]. The brain requires constant energy to maintain electrical membrane potentials, action potential propagation, and peripheral and central nervous system signaling [45-47]. In theory, increasing brain creatine (free creatine and PCr) would support cognitive function in athletes [46]. During an MMA match, brain energetics (ATP turnover) would increase and PCr may be important to facilitate energy matched ATP regeneration, supporting cognitive function and enhancing neural activity [48]. From a cognitive performance perspective, there are six studies that have examined creatine supplementation on cognition in younger adults at rest [48-53] and four studies that have examined creatine under cognitive "stress" [47,54-56]. The results are mixed with some showing a positive effect on a least one cognitive outcome variable [48,50,51,53] while others showed no effect [49,52]. When the brain is stressed, either by hypoxia [47], sleep deprivation [54,55], or mental fatigue [56] the benefits of creatine to support cognitive function become more consistent. Lastly, there are three sport specific studies (as shown in table 1), one in rugby players [57] and two in soccer players [58,59] that investigated the impact of creatine on cognitive based motor skills (i.e. passing or shooting accuracy). Cook et al. [57] concluded that 1 day of creatine supplementation (50 or 100 mg/kg) was able to attenuate sleep deprived (3-5 hours of sleep in the night proceeding) reduction in cognitive function. The two soccer studies examining shooting accuracy did not find any benefit of creatine supplementation compared to placebo. These results support previous research using standardized laboratory computer based cognitive tests, suggesting that creatine was more effective in stressed situations. However, in theory, MMA athletes may have sleep problems prior to a big fight and the stress associated with combat sports may be the ideal environment to implement creatine supplementation.

Table 1. Creatine on skill related sport skills

Author	Dose	Duration	Tests	Stressor	Sport Specific Skill

Cook et al 2011	50 or 100 mg/kg	1 day	Repeated rugby passing skill task	Sleep Deprivation: 3-5 hours the night preceding	↑
Cox et al 2002	20 g/day	6 days	Soccer shooting accuracy	None	↔
Hamid et al 2012	20 g/day	7 days	Soccer shooting accuracy	None	↔

Lastly, but importantly following cumulative head impacts and concussions (mild traumatic brain injury), brain creatine levels are reduced [60,61]. Creatine is a potential nutritional supplement that might reduce the severity of, or enhance recovery from mild traumatic brain injury (mTBI; [46]. In an animal model creatine supplementation prior to a traumatic brain injury decreased damage by as much as 50% [62]. In humans, there are two studies in children with TBI [63,64] that show improvements in cognition, communication, self-care, personality, and reductions in headaches, dizziness, and fatigue. Again, caution is warranted when translating these findings to athletes, however creatine may be an important supplement to support and protect the brain of fighters.

5. Practical Strategies

When considering creatine supplementation, there are several factors that are important [13], including type, dose, co-ingestion, timing, safety, and responders versus non-responders (summarized in table 2). For extensive reviews examining several factors, we refer the reader to Candow et al. [13] and Kreider et al. [10]. This section will focus on specific practical strategies to implement creatine supplementation in MMA.

There are several forms of creatine (e.g., creatine monohydrate, citrate, maleate, fumarate, tartrate, pyruvate, creatine esters), however, the most common form is creatine monohydrate. Importantly, most of the performance studies have used creatine monohydrate [10] and to date, there is no clear performance advantage of any other form of creatine. Creatine monohydrate is very well absorbed and can be dissolved into water (based primarily on water temperature). In one liter of water 6 grams of creatine can be dissolved at 4 degrees Celsius, 14 grams at 20 degrees Celsius [65]. Furthermore, creatine monohydrate is very stable and appears to show no signs of deterioration even at elevated temperatures [65], unless creatine is mixed in an aqueous solution. In a typical meat-eating diet that contains 1-2 $g \cdot day^{-1}$ of creatine, muscle creatine supplementation can increase total creatine in the muscle ~20% [10,39]. Hultman et al. [39] was one of the first to examine the impact of creatine supplementation loading on muscle creatine concentrations. In 31 health male participants, supplementing with 20 $g \cdot day^{-1}$ for 6 days was able to saturate muscle concentrations (~20% increase) and participants were able to maintain this increase with 2 $g \cdot day^{-1}$ for 30 days thereafter. Once creatine supplementation was ceased, total creatine concentration declined and returned to pre-supplementation values within 30 days. A similar but more gradual increase in total creatine concentration was found after 28 days of supplementation with a lower dose (3 $g \cdot day^{-1}$) [39]. Therefore, a dosing strategy may depend on the short vs. long term goal of the fighter. Importantly, there is no dose response study examining the uptake of creatine into the brain and it has been suggested that a higher dose (e.g. 20 $g \cdot day^{-1}$) may be required for cognitive benefits [46]. Although, not clear in the literature, some studies suggest that larger athletes may require larger doses of creatine (5-10 $g \cdot day^{-1}$) in order to maintain creatine stores [10,38]. Candow and colleagues have utilized a relative dosing strategy of 0.1 g/kg/day for long term studies in aging adults and found positive effects on muscle biology [66]. Creatine is transported into cells through a creatine transporter that is both sodium and insulin dependent [67]. Thus, ingesting creatine with a carbohydrate or a combination of carbohydrate and protein mix (that causes an insulin spike) have been reported to enhance creatine uptake and retention [68]. Furthermore, it has been hypothesized that combining high doses of caffeine (> 5mg/kg) and creatine may be counterproductive due to competing mechanistic pathways [69], however, from an applied perspective short term studies are inconsistent [69-71] and long term (> 4 weeks) co-ingestion studies are lacking. From a timing perspective, there appears to be a small advantage to ingesting creatine after exercise [14]. There have been three studies that have investigated the impact of creatine before compared to after and when included into a small meta-analysis, it appears to favor creatine after exercise for muscle hypertrophy but not for strength gains [14]. Importantly, no timing study has examined creatine uptake into the muscle and thus caution is warranted, and from a practical perspective the best time to take creatine (pending no or minimal gastrointestinal distress) is when the athlete will remember to take it. With regards to safety of creatine supplementation, there have been hundreds of studies over the last century examining creatine. Very few side effects have been reported in the literature [10,72]. The international society for Sport nutrition concluded that creatine is extremely safe [10] and has also been shown to be safe in adolescent athletes [73]. There appears to be no evidence that creatine impacts kidney function in health adults [73,74]. Lastly, it is important to highlight that individuals respond differently to creatine [16]. Syrotuik and Bell [16] found that those with lower levels of muscle creatine content (e.g., vegetarians) prior to supplementation and individuals with more fast twitch muscle fibers responded more favorably to creatine supplementation. In theory, creatine may impact muscles that contain more fast twitch fibers (e.g., triceps) more so than muscles that contain more slow twitch fibers.

Table 2: Practical considerations and potential benefits

Summary	
Type	Creatine Monohydrate
Timing	Close proximity to training. Ingesting creatine after training may provide a small greater increase in muscle mass vs. ceatine before training sessions.
Dose	Muscle: Loading Phase: 20 g/day (0.3 g/kg/day) for 5-7 days followed by 3-5 g/day thereafter (maintenance phase). Alternative dosing strategy: 0.1 g/kg/day. Brain: Higher doses (i.e., 20 g/day) may be required.
Co-Ingestion	Mix with water and ingest with a carbohydrate or a carbohydrate and protein source. Potentially high doses of caffeine (>5 mg/kg) may be counterproductive.
Considerations	Weight Cutting: Record body mass before and after loading phase and maintenance phases in preparation for weight cutting. Responders tend to have lower baseline muscle creatine levels and have more fast twitch muscle fibers.
Potential Benefits	↑ performance, improved body composition (↑ muscle mass, ↓ fat mass ?), ↑ rehydration, ↑ glycogen re-synthesis, neuroprotective, attenuates cognitive decline during sleep deprivation and mental fatigue.
Safety	There is substantial amount of evidence demonstrating the safety of creatine monohydrate.

Conclusion

Overall, there is substantial amount of laboratory based performance studies to suggest that creatine enhances short term high intensity exercise, thus creatine may be ergogenic for MMA athletes. With regards to sport specific fighting literature, there appears to be both positive and null effects reported, however, most of these studies were under powered. Despite an increase in water retention and an increase in body mass, when strategically planned, creatine can augment exercise induced gains in muscle and potentially aid in the reduction in fat mass, which may benefit the athlete during weight cutting. Creatine co-ingested with carbohydrates may also be beneficial following weigh-ins to enhance both rehydration and glycogen re-synthesis. More recently, creatine has shown positive impacts, although highly variable, on cognitive performance and in theory may protect or enhance recovery following mild traumatic brain injury. Overall, creatine is a safe supplement with strong scientific rationale for MMA athletes, however, future research is warranted.

Media-Friendly Summary

Mixed martial arts is both physically and cognitively demanding. Creatine supplementation, when strategically planned, may improve MMA performance, body composition, enhance recovery, aid in rehydration, enhance storage of carbohydrates into the muscle, protect the brain, and improve cognition. This review outlines the scientific evidence and provides practical recommendations.

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