Published in final edited form as:

J Strength Cond Res. 2016 May ; 30(5): 1438–1446. doi:10.1519/JSC.0000000000001223.

Effects of coffee and caffeine anhydrous intake during creatine loading

Eric T. Trexler[1,2], **Abbie E. Smith-Ryan**[1,2], **Erica J. Roelofs**[1], **Katie R. Hirsch**[1], **Adam M. Persky**[3], and **Meredith G. Mock**[1]

[1]Applied Physiology Laboratory, Department of Exercise and Sport Science, University of North Carolina, Chapel Hill, NC, USA

[2]Human Movement Sciences, Department of Allied Health Sciences, University of North Carolina, Chapel Hill, NC, USA

[3]School of Pharmacy, Division of Pharmacotherapy and Experimental Therapeutics, University of North Carolina, Chapel Hill, NC, USA

Abstract

The purpose of this study was to determine the effect of 5 d of creatine (CRE) loading alone or in combination with caffeine anhydrous (CAF) or coffee (COF) on upper and lower body strength and sprint performance. Physically active males (n=54; Mean ± SD; Age = 20.1 ± 2.1 yrs; Weight = 78.8 ± 8.8 kg) completed baseline testing, consisting of one-repetition maximum (1RM) and repetitions to fatigue (RTF) with 80% 1RM for bench press (BP) and leg press (LP), followed by a repeated sprint test of five, 10 s sprints separated by 60 s rest on a cycle ergometer to determine peak power (PP) and total power (TP). At least 72 hr later, subjects were randomly assigned to supplement with CRE (5 g creatine monohydrate, 4 times*d^{-1}; n=14), CRE+CAF (CRE + 300 mg*d^{-1} of CAF; n=13), CRE+COF (CRE + 8.9 g COF, yielding 303 mg caffeine; n=13), or placebo (PLA; n=14) for 5 d. Serum creatinine (CRN) was measured prior to and following supplementation and on day six, participants repeated pre-testing procedures. Strength measures were improved in all groups ($p<0.05$), with no significant time × treatment interactions. No significant interaction or main effects were observed for PP. For TP, a time × sprint interaction was observed ($p<0.05$), with no significant interactions between treatment groups. A time × treatment interaction was observed for serum CRN values ($p<0.05$) that showed increases in all groups except PLA. Four subjects reported mild gastrointestinal discomfort with CRE+CAF, with no side effects reported in other groups. These findings suggest that neither CRE alone, nor in combination with CAF or COF, significantly affected performance compared to PLA.

Keywords

Phosphocreatine; repeated sprint; strength; one-rep maximum; ergogenic aid

Corresponding Author: Abbie E. Smith-Ryan, PhD, CSCS*D, Department of Exercise and Sport Science, University of North Carolina-Chapel Hill, 312 Woollen, CB #8700, Chapel Hill, NC 27599, Office: 919-962-2574, Fax: 919-962-6325, abbsmith@email.unc.edu.

Introduction

Creatine (CRE) and caffeine (CAF) supplements are commonly used by athletes to improve performance. Surveys conducted in 2004 and 2005 revealed that 37% of Division I collegiate athletes had used CRE supplements (13), and 89% of triathletes intended to use CAF either before or during their upcoming race (10). Creatine supplementation has been shown to increase muscle phosphocreatine (PCr) storage (18), which increases adenosine triphosphate (ATP) availability and improves exercise performance (6). During intense exercise there is an elevated demand for ATP which allows for sustained crossbridge cycling and force output. The rapid provision of ATP is facilitated by stored PCr, which phosphorylates adenosine diphosphate in the creatine kinase reaction; creatine is cycled through this reaction from phosphocreatine to CRE. To date, hundreds of studies have investigated the effects of CRE supplementation on exercise performance, with the majority of studies demonstrating an ergogenic effect on strength and sprint performance lasting less than 30 seconds (5, 21, 23, 30, 40, 41, 43).

While CRE is primarily effective for enhancing short-term bouts of high intensity and intermittent exercise (5, 30, 41), CAF has been shown to have ergogenic effects for both anaerobic (7, 32, 42) and endurance exercise performance (8, 20). While the primary ergogenic mechanism of CAF is antagonism of adenosine receptors, it may affect performance by a number of both central and peripheral mechanisms (1, 11, 14, 22, 27). In previous literature, CAF doses ranging from 3-6 $mg*kg^{-1}$ of body mass have been consistently shown to improve endurance performance (8, 14, 20). Evidence also suggests that CAF improves strength (3, 44) and sprint (32, 42, 44) performance, particularly in trained subjects (7).

Creatine and CAF do not display pharmacokinetic interactions when ingested together (37), and are thought to improve performance via independent mechanisms, which has prompted interest in the potential for combined supplementation. Previous studies have reported performance improvements from CRE mixed into caffeinated tea or coffee (COF) (4, 9), and a number of multi-ingredient supplements containing CRE+CAF, among other ingredients, have been shown to improve outcomes for strength, power, and body composition (15, 28, 33). Research has also indicated that acute CAF supplementation (a single dose, consumed 60 min prior to an exercise bout) after CRE loading may improve performance more than CRE loading alone (24, 25). However, the scarce research directly investigating combined supplementation has indicated that 3-4 d of CAF supplementation (consumed for multiple consecutive days during CRE loading) may blunt the ergogenic effect of CRE loading (17, 19, 38). This apparent incompatibility could potentially be explained by CRE and CAF imposing opposite effects on muscle relaxation time (19), or by gastrointestinal distress caused by concurrent ingestion of both ingredients (17, 31). It is currently unclear if these discrepant findings may relate to differences in the dose or source of caffeine consumed. Further research is warranted to determine if 5 d of daily COF or CAF consumption blunt the ergogenic effect of CRE loading, as both CRE and CAF are commonly used by recreational and competitive athletes prior to training and competition. Results of such research may assist athletes and practitioners in maximizing the potential benefits of both CRE loading and CAF supplementation. Therefore, the purpose of the current study was to

determine the effect of 5 d of CRE loading alone or in combination with CAF or COF on upper and lower body strength and sprint performance in physically active males.

Methods

EXPERIMENTAL APPROACH TO THE PROBLEM

The current randomized, partially blinded study consisted of two laboratory visits, with a 5 d supplementation period preceding the second visit. Baseline testing included serum creatinine levels, one-rep maximum (1RM) and repetitions to fatigue (RTF) for leg press (LP) and bench press (BP), and a repeated sprint protocol to determine peak power (PP) and total work (TW) output. At least 72 hr after baseline testing, participants began supplementation with either CRE monohydrate (CRE; 20 $g*d^{-1}$; n=14), CRE and caffeine anhydrous (CRE+CAF; 20 $g*d^{-1}$ CRE and 300 $mg*d^{-1}$ of CAF; n=13), CRE and COF (CRE+COF; 20 $g*d^{-1}$ creatine and 8.9 $g*d^{-1}$ of instant coffee yielding 303 mg of CAF; n=13), or placebo (PLA; n=14). Participants supplemented for 5 d and returned to the laboratory on day six for serum creatinine analysis and exercise testing.

SUBJECTS

Fifty-four males aged 18-35 yrs (Mean ± SD; Age = 20.1 ± 2.1 yrs; Height = 177.3 ± 5.6 cm; Body mass = 78.8 ± 8.8 kg) who had been resistance training for ≥30 $min*d^{-1}$, 3 $d*wk^{-1}$ for at least 3 mo completed the current study. Fifty-six participants enrolled in the study; two dropped out for personal reasons after baseline testing but prior to the onset of supplementation. Exclusion criteria included supplementation with CRE or beta-alanine in the 3 mo prior to the study, habitual CAF intake of over 800 $mg*d^{-1}$, or a history of adverse reactions to caffeine. Participants were also excluded if they were not willing to abstain from substances known to significantly influence the cytochrome P450 1A2 isozyme that metabolizes caffeine (i.e., tobacco products, antidepressant drugs) for the duration of the study. Average habitual CAF intake for participants was 32.9 ± 59.6 $mg*d^{-1}$ (range = 0 – 214 $mg*d^{-1}$). Participants were instructed to abstain from CAF intake within 48 hr of baseline testing, and to avoid strenuous exercise within 24 hr of all testing sessions. Aside from these restrictions, participants were encouraged to maintain their normal training and dietary habits, and to replicate similar food intake before visits to the laboratory. Each participant completed a 3 d dietary log at baseline that was analyzed using The Food Processor software (ESHA Research, Salem, OR, USA) to evaluate habitual dietary intakes. Laboratory visits occurred at a similar time of day (± 2 hr). All methodology was approved by the University's Biomedical Institutional Review Board, and all participants signed an informed consent prior to participation.

PROCEDURES

Serum Creatinine—Prior to exercise at each laboratory visit, a 3.5 mL sample of blood was obtained from a vein in the antecubital region of the arm using a BD Vacutainer Serum Separator Tube (Becton, Dickinson and Company, Franklin Lakes, NJ, USA). Blood samples were immediately stored in a refrigerator, then transported to an independent laboratory (Core Laboratory, McLendon Clinical Labs, UNC Hospitals, Chapel Hill, NC) for serum creatinine analysis no more than 12 hr after sample collection.

One Repetition Maximum & Repetitions to Fatigue—One-repetition maximum for LP and BP were determined using free weights (York Barbell Co., York, PA, USA) and a spotter. Before testing, participants were allowed time for a brief warm up and technique familiarization. The first warm up set consisted of 8-10 repetitions performed with a load estimated to be 50% of 1RM. After 1-2 min of rest, participants performed a second warm up set consisting of 80% of the anticipated 1RM, lifted for 4-6 repetitions. Participants were allowed 2 min of rest, after which participants completed their first 1RM attempt. For all subsequent sets, the load was adjusted and a single repetition was performed until the 1RM was identified, with 2-3 min of rest provided between attempts.

Following the final 1RM attempt for a given lift, participants rested for three min, after which the RTF test was completed. This test consisted of lifting 80% of the 1RM load for as many repetitions as possible, until failure was reached. Testing was supervised by trained laboratory personnel, and failure was defined as the point at which a full repetition could no longer be completed with appropriate technique. Verbal encouragement was provided for all strength testing. For the second laboratory visit, participants used the same load (80% of baseline 1RM) for the RTF test, regardless of any changes in 1RM. In all testing sessions, leg press 1RM and RTF testing preceded the bench press. Reliability calculations from our laboratory have indicated an intraclass correlation coefficient ($ICC_{2,1}$) of 0.97 and 0.99 for LP and BP 1RM, respectively, in resistance trained males (n=11) with at least 48 hr between tests. The standard error of measurement (SEM) for LP and BP 1RM are 7.4 kg and 1.9 kg, respectively.

Repeated Sprint Protocol—Ten min after the conclusion of strength testing, participants completed a repeated sprint test consisting of five, 10 s sprints on a Monark friction-braked cycle ergometer (Ergomedic 894 E; Monark, Stockholm, Sweden). Participants completed a self-paced, 5 min warm up with a standardized load of 0.5 kg. After the warm up, participants completed the sprint protocol adapted from Wiroth et al. (43), completing five maximal sprints lasting 10 s each, with a load of 95 $g*kg^{-1}$ of body mass applied to the weight basket. Each sprint was followed by a passive rest period of 60 s. Participants remained in a seated position for the duration of each sprint, and verbal encouragement was provided by lab personnel. For each sprint, PP and TW were evaluated using the default software (Monark ATS Software; Monark, Stockholm, Sweden). For this sprint protocol, reliability calculations from our laboratory have indicated an ICC of 0.96 and SEM of 19.7 watts for average PP in resistance trained males (n=12) with at least 48 hr between tests.

Supplementation—Participants were randomly assigned to a treatment group for five continuous days of supplementation, using a computer generated allocation sequence (Random Allocation Software, Isfahan, Iran). One group (CRE; n=14) consumed a loading dose (20 $g*d^{-1}$, split between 4 servings) of creatine monohydrate (Micronized Creatine Powder; Optimum Nutrition, Aurora, IL, USA) mixed with noncaloric flavoring (Crystal Light; Kraft Foods, Northfield, IL, USA). A second group (CRE+CAF; n=13) followed the same creatine loading protocol, but with 300 mg of caffeine anhydrous (CAF; Smart Powders, Graham, NC, USA) added to the first dose of each day. A third group (CRE+COF; n=13) followed the creatine loading protocol, but mixed each day's first dose of creatine into

a caffeine-matched serving (8.9 g) of instant coffee (COF; Nescafé House Blend; Nestle, Vevey, Switzerland). The final group (PLA; n=14) consumed a flavored, noncaloric placebo beverage (3.8 g Crystal Light), ingested four times daily. Participants were instructed to consume their respective supplement at regular intervals throughout the day. It was suggested to mix the supplement with 300 mL of water, but participants were permitted to deviate from this suggestion, if necessary, to satisfy individual taste preferences. All participants weighed between 60-100 kg, to ensure that 300 mg CAF doses were between 3-5 $mg*kg^{-1}$ of bodyweight. The current study may be considered partially blinded, as COF has a distinct taste. However, laboratory personnel were blinded to the groups, and participants did not know if the coffee-flavored beverage contained caffeine. Previous research has used a similar instant coffee product and verified a caffeine concentration of 3.4 g caffeine/100 g of instant coffee (20). As such, caffeine content was approximately matched between CRE+CAF and CRE+COF treatment arms (300 mg and 303 mg, respectively), which equates to an average caffeine dose of approximately 3.8 $mg*kg^{-1}$ in the current sample.

Throughout supplementation, subjects were instructed to maintain their normal diet and exercise habits, but to abstain from any extraneous CAF consumption. To ensure compliance, participants were required to document their supplement intake in a written log. Analysis of supplement logs indicated compliance rates of 99% or greater in all groups. After 5 d of supplementation, participants reported for the second exercise testing session on day six. To avoid an acute ergogenic effect of COF or CAF intake, there was no supplementation on day six, regardless of treatment group.

STATISTICAL ANALYSES

Data are expressed as mean ± standard deviation with the exception of Figure 1 and Figure 2, which depict 95% confidence intervals. A series of one-way ANOVAs were used to evaluate baseline differences between groups for dietary intakes, strength outcomes, sprint outcomes, and serum creatinine values. Strength changes were evaluated using a series of two-way (2 × 4; time × treatment) repeated measures ANOVAs. Peak power and TW achieved during each sprint, along with average PP and TW, were compared using mixed factorial ANOVAs (2 × 5 × 4; time × sprint × treatment) with Bonferroni *post hoc* comparisons. Serum creatinine and body weight values were compared using mixed factorial ANOVAs (2 × 4; time × treatment). In the event of a significant interaction, Bonferroni post hoc comparisons were completed using specialized syntax to identify the source of the interaction.

For serum creatinine values and all performance outcomes, 95% confidence intervals (CI) were calculated for change scores from baseline to post-testing (mean ± 1.96 × SEM). A change was considered significantly significant ($p \leq 0.05$) if zero did not fall within the 95% confidence interval. Microsoft Excel (Version 2011, Microsoft Corporation; The Microsoft Network, LLC, Richmond, WA, USA) was used to calculate and plot 95% confidence intervals. All other statistical analyses were performed using SPSS software, (Version 20.0; IBM, Armonk, NY, USA), with the level of significance set *a priori* at $\alpha \leq 0.05$.

Results

Descriptive characteristics and dietary intakes are listed by group in Table 1. There were no significant differences ($p>0.05$) between groups for anthropometric measures, macronutrient intakes, or CAF intake at baseline.

Strength outcomes

For all strength outcomes, there were no significant interaction effects or main effects for treatment (all $p>0.05$). However, significant main effects for time were observed for BP 1RM ($p<0.05$; mean Δ= 2.5% increase; Table 2), BP RTF ($p<0.05$; mean Δ= 0.9 repetition increase), LP 1RM ($p<0.05$; mean Δ= 6.4% increase; Table 2), and LP RTF ($p<0.05$; mean Δ= 4.2 repetition increase).

Analysis of 95% confidence intervals for change scores indicated that all groups significantly improved BP and LP 1RM from baseline to post-testing (Table 2). For LP RTF, 95% CIs demonstrated significant increases in repetitions for PLA [CI: 2.9, 7.0 repetitions], CRE+COF [1.5, 5.6], CRE+CAF [2.0, 6.8], and CRE [1.1, 6.8]. For BP RTF, 95% CIs indicated significant increases in repetitions for PLA [CI: 0.6, 2.4 repetitions], CRE+CAF [0.2, 1.2], and CRE [0.4, 1.4], but not for CRE+COF [−0.6, 1.1].

Sprint outcomes

Peak power and TW for each sprint are presented in Table 3. For PP, the time × sprint × treatment interaction was not significant ($p>0.05$). Similarly, there were no significant time × sprint ($p=0.13$), sprint × treatment ($p>0.05$), or time × treatment ($p>0.05$) interactions. A significant main effect was observed for sprint ($p<0.05$), but not for time or treatment (both $p>0.05$). *Post hoc* comparisons of marginal means revealed that PP dropped significantly between all five sprints (all $p<0.05$).

For TW, the time × sprint × treatment interaction was not significant ($p>0.05$), but a significant time × sprint interaction was observed ($p<0.05$). There were no significant differences between pre- and post-test values for TW for any sprint; *post hoc* comparisons showed significant reductions in TW between all five sprints for pre-testing ($p<0.05$), while the TW drop between sprints 4 and 5 were not significant in post-testing ($p>0.05$). Sprint × treatment and time × treatment interactions were not significant (both $p>0.05$). A significant main effect was observed for sprint ($p<0.05$), but not for time or treatment (both $p>0.05$).

Analysis of 95% confidence intervals for change scores revealed no statistically significant changes in PP or TW for any sprint, or in average PP or TW, in any treatment group (Table 3). Confidence intervals for changes in average TW are presented in Figure 1.

Serum creatinine values

A significant time × treatment interaction was observed for serum creatinine (CRN) values ($p<0.05$). Bonferroni post hoc comparisons revealed a significant difference between PLA and CRE+COF after supplementation ($p<0.05$), with no other significant differences between groups. Post hoc comparisons identified significant increases from pre- to post-testing in CRE+COF and CRE+CAF ($p<0.05$), but not in CRE ($p=0.09$) or PLA ($p>0.10$).

Analysis of 95% confidence intervals for change scores revealed a significant increase in serum CRN values for CRE [CI: 0.01, 0.15 mg/dL], CRE+COF [0.05, 0.35], and CRE+CAF [0.06, 0.25], but not for PLA (Figure 2).

Reported side effects

Four participants (30.8%) given CRE+CAF reported mild gastrointestinal (GI) disturbance, which was not reported in any other group. For changes in body weight, there was no significant time × treatment interaction, with no main effects for time or treatment (all $p>0.05$). Weight was slightly reduced in PLA (−0.2 ± 1.0 kg) and CRE+COF (−0.2 ± 1.2 kg), with small increases observed in CRE+CAF (0.5 ± 0.7 kg) and CRE (0.1 ± 0.7 kg).

Discussion

Previous research has suggested that 3-4 d of CAF intake blunts the ergogenic effect of CRE loading (17, 19, 38). In contrast, studies have demonstrated the efficacy of CRE supplementation when mixed into caffeinated tea or COF (4, 9). Because many pre-workout supplement formulations include both CRE and CAF (15, 28, 33), further research on the potential interaction is needed. While previous studies on CRE+CAF supplementation have employed unique exercise tests consisting of electrical stimulation (19) or isokinetic knee extension (17, 38), the current study used dynamic exercise tests relating more closely to the training of many resistance trained individuals. Strength outcomes were improved in all groups, except for a non-significant improvement in BP RTF for CRE+COF. For sprint outcomes, no group interactions were observed for PP or TW. Although not statistically significant, average TW was reduced in PLA, but not in CRE+CAF, CRE+COF, or CRE (Figure 1). Confidence intervals indicated that serum creatinine values were elevated in all treatment groups, except PLA.

In the current study, upper and lower body strength measurements improved in all treatment groups, with the exception of BP RTF for CRE+COF, which did not change. A meta-analysis published in 2003 (5), including interventions of varying duration, indicated that CRE supplementation led to significant improvements in 1RM and RTF. Creatine loading interventions (5-7 d) have demonstrated increases in muscle PCr storage (16), while changes in strength have been mixed. Although CRE loading has been shown to increase indices of maximal strength (21, 40) and RTF (21, 41), Zuniga et al. (45) found no effect of CRE loading on 1RM for leg extension or BP in untrained men. Izquierdo et al. (21) documented improvements in half-squat 1RM, half-squat RTF, and BP RTF in trained handball players, while BP 1RM did not improve. Volek et al. (40) reported improvements in BP 1RM with one week of CRE loading in resistance trained males, but no change in squat 1RM or BP RTF. In the current study, CRE did not improve strength outcomes more than PLA, with or without the addition of COF or CAF. Single-rep strength performance is not likely limited by the phosphagen energy system, which may explain the results observed for 1RM. For RTF, null findings could possibly be explained by the presence of non-responders in the sample, as up to 30% of individuals may not see performance benefits from CRE (16, 35). It is also possible that day to day variability in performance may be too large in moderately trained subjects, or subjects performing testing that does not mimic their normal training

habits, to detect the modest benefits of CRE supplementation. As such, more sensitive measures of strength (i.e. maximal voluntary contraction) may be needed to consistently detect strength improvements from short-term CRE loading, and future studies should employ exercise tests that closely resemble the regular training of a highly trained sample. Previous research has also shown that longer CRE supplementation protocols lasting 10-12 weeks, with concurrent resistance training, have yielded greater improvements in strength outcomes compared to short-term loading (39, 40), suggesting that a longer duration of supplementation may be necessary to detect an ergogenic effect in moderately trained subjects.

For sprint outcomes, no significant changes in PP or TW were observed for any group. It was hypothesized that CRE would improve sprint performance, as CRE is thought to be particularly effective for repetitive high-intensity bouts lasting ≤30 seconds (5). A number of previous studies have shown CRE supplementation to improve performance on both single (34) and repeated (4, 9, 30, 34, 36) sprint tests, with samples ranging from recreationally active (30) to elite-level athletes (36). However, McKenna et al. (26) demonstrated that CRE did not improve performance on a repeated sprint test consisting of five ten-second sprints with variable rest periods in recreationally active subjects. Finn et al. (12) also reported no benefit of CRE on a protocol consisting of four 20-second sprints with 20 seconds of rest between sprints in trained triathletes. Using a sprint protocol similar to that of the current study, Wiroth et al. (43) found CRE to improve performance in both young and old sedentary participants, but not in well-trained participants. It is not clear if the lack of improvement in the current study is a result of the sprint protocol employed, or characteristics of the sample. Despite the non-significant statistical results, it does appear that average TW declined in PLA, but was maintained in all groups consuming CRE (Figure 1). This may have practical significance, as it suggests a modest benefit of CRE loading for individuals who are reliant on repetitive, intermittent bursts of high-intensity activity. Similarly to strength outcomes, the inclusion of CAF or COF with CRE did not appear to negatively affect sprint performance.

While no pharmacokinetic interaction has been observed between CRE and CAF (37), Vandenberghe et al. (38) demonstrated that CAF blunted the ergogenic effect of CRE loading. Subsequent research suggested that opposing effects on muscle relaxation time may explain this interaction (19). Results of Vandenberghe et al. (38) may have been influenced by an insufficient washout period (three weeks), or CAF withdrawal, as the final CAF dose was ingested at least 20 hr before post-testing. In a published abstract, Harris et al. (17) sought to replicate the findings of Vandenberghe et al. (38), but employed a six week washout period and included post-test sessions both two and 24 hr after CAF cessation. While CAF appeared to blunt the ergogenic effect of CRE, the authors (17) suggested that this effect was explained by GI discomfort with CRE+CAF, which was reported in four out of ten subjects completing the study. Gastrointestinal discomfort was also noted in another recent study involving CRE+CAF supplementation (31), in which three out of seven subjects reported symptoms. In agreement with past studies, GI discomfort was reported in four of thirteen participants in the CRE+CAF group in the current study. While mild GI distress has been reported anecdotally with CRE supplementation (29), it was not reported by any participants in PLA, CRE, or CRE+COF. Future studies should seek to determine if

individuals engaged in strength or sprint training can successfully combine CRE and CAF by employing supplement timing strategies to mitigate GI distress and CAF withdrawal before exercise.

In agreement with previous research (29), serum CRN values in the present study were significantly elevated in all groups supplementing with CRE (Figure 2). High serum CRN is an indirect indicator of impaired kidney function, but values can be influenced by a number of factors including age, sex, lean mass, diet, physical activity, and creatine supplementation (2, 29). Changes in serum CRN were greater in CRE+COF and CRE+CAF compared to CRE, but differences were not statistically significant. Supplement logs indicated a compliance rate of ≥99%, as supported by changes in serum CRN. In individuals supplementing with CRE, high serum CRN levels should be interpreted with caution, as increased creatine breakdown may increase serum CRN in the absence of impaired kidney function (29). Creatine is osmotically active, and CRE loading generally results in a weight gain of 1-2 kg in men due to water retention (29). Despite excellent compliance, the current study did not find a significant time × treatment interaction for body weight, with no group increasing by more than 0.5 kg. It is unknown if this lack of weight gain may relate to the high protein intake reported by participants, which is generally associated with greater dietary creatine intake, inadequate hydration, or other factors. Elevated serum CRN and lack of weight gain could potentially be indicative of poor muscle CRE uptake, although these values are often variable and influenced by a number of factors. While Syrotuik et al. (35) found that creatine non- and quasi-responders gained less weight and had greater increases in urinary CRN compared to responders after CRE loading, differences were non-significant and varied between individuals. As such, these values may not be valid indicators for identifying CRE non-responders.

Limitations of the current study must be noted. While the 5 d CRE loading protocol has been shown to increase muscle creatine stores (16), more pronounced performance effects would likely be observed with a longer supplementation period accompanied by progressive resistance training. Despite the recruitment of physically active participants with weight training experience, strength improvements in the PLA group may indicate a learning effect or placebo effect for 1RM and RTF, but not for sprint outcomes. Although 1RM and RTF are highly applicable to the training of athletes, more sensitive indices of strength may be favorable for future studies on short-term creatine loading. It is also important to note that subjects in the current study were physically active, but not competitive athletes. Finally, the current study did not directly measure muscle creatine content, and therefore cannot rule out the presence of nonresponders in the sample. Future research should investigate the effects of COF and CAF with a longer period of CRE supplementation combined with progressive resistance training, and seek to determine if supplement timing and dosing strategies can be employed to obtain the ergogenic benefits associated with CRE and CAF without experiencing GI discomfort.

Practical Applications

Creatine loading did not improve strength or sprint outcomes to a greater extent than placebo, and the addition of 300 mg of CAF in the form of anhydrous powder or instant

COF had no statistically significant effects on performance in physically active men. While differences were not statistically significant, reductions in TW output were attenuated to a similar extent by CRE, CRE+CAF, and CRE+COF, compared to PLA. Results support previous research indicating that GI discomfort is observed with combined CRE+CAF supplementation, while this was not observed with CRE+COF. In physically active men, longer periods of CRE supplementation combined with progressive training may be required to see significant improvements in the outcomes measured, as groups consuming CRE did not outperform PLA to a significant degree. Athletes and resistance trained individuals supplementing with CRE may be advised to consider the source, dose, and timing of any CAF consumed to avoid GI discomfort.

Acknowledgements

This study was funded by the National Strength and Conditioning Association Foundation. The project described was also supported by the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant *1KL2TR001109*. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

References

1. Allen DG, Westerblad H. The effects of caffeine on intracellular calcium, force and the rate of relaxation of mouse skeletal muscle. J Physiol. 1995; 487(Pt 2):331–342. [PubMed: 8558467]
2. Baxmann AC, Ahmed MS, Marques NC, Menon VB, Pereira AB, Kirsztajn GM, Heilberg IP. Influence of muscle mass and physical activity on serum and urinary creatinine and serum cystatin C. Clin J Am Soc Nephrol. 2008; 3:348–354. [PubMed: 18235143]
3. Beck TW, Housh TJ, Schmidt RJ, Johnson GO, Housh DJ, Coburn JW, Malek MH. The acute effects of a caffeine-containing supplement on strength, muscular endurance, and anaerobic capabilities. J Strength Cond Res. 2006; 20:506–510. [PubMed: 16937961]
4. Birch R, Noble D, Greenhaff PL. The influence of dietary creatine supplementation on performance during repeated bouts of maximal isokinetic cycling in man. Eur J Appl Physiol Occup Physiol. 1994; 69:268–276. [PubMed: 8001541]
5. Branch JD. Effect of creatine supplementation on body composition and performance: a meta-analysis. Int J Sport Nutr Exerc Metab. 2003; 13:198–226. [PubMed: 12945830]
6. Buford TW, Kreider RB, Stout JR, Greenwood M, Campbell B, Spano M, Ziegenfuss T, Lopez H, Landis J, Antonio J. International Society of Sports Nutrition position stand: creatine supplementation and exercise. J Int Soc Sports Nutr. 2007; 4:6. [PubMed: 17908288]
7. Collomp K, Ahmaidi S, Chatard JC, Audran M, Prefaut C. Benefits of caffeine ingestion on sprint performance in trained and untrained swimmers. Eur J Appl Physiol Occup Physiol. 1992; 64:377–380. [PubMed: 1592065]
8. Costill DL, Dalsky GP, Fink WJ. Effects of caffeine ingestion on metabolism and exercise performance. Med Sci Sports. 1978; 10:155–158. [PubMed: 723503]
9. Dentkowski A, Opaszwoski B, Blachnio D, Polanowski B. Effect of creatine supplementation on the performance in supramaximal, intermittent exercise. Biol Sport. 1997; 14:291–298.
10. Desbrow B, Leveritt M. Awareness and use of caffeine by athletes competing at the 2005 Ironman Triathlon World Championships. Int J Sport Nutr Exerc Metab. 2006; 16:545–558. [PubMed: 17240785]
11. Duncan MJ, Stanley M, Parkhouse N, Cook K, Smith M. Acute caffeine ingestion enhances strength performance and reduces perceived exertion and muscle pain perception during resistance exercise. Eur J Sport Sci. 2013; 13:392–399. [PubMed: 23834545]
12. Finn JP, Ebert TR, Withers RT, Carey MF, Mackay M, Phillips JW, Febbraio MA. Effect of creatine supplementation on metabolism and performance in humans during intermittent sprint cycling. Eur J Appl Physiol. 2001; 84:238–243. [PubMed: 11320642]

13. Froiland K, Koszewski W, Hingst J, Kopecky L. Nutritional supplement use among college athletes and their sources of information. Int J Sport Nutr Exerc Metab. 2004; 14:104–120. [PubMed: 15129934]

14. Goldstein ER, Ziegenfuss T, Kalman D, Kreider R, Campbell B, Wilborn C, Taylor L, Willoughby D, Stout J, Graves BS, Wildman R, Ivy JL, Spano M, Smith AE, Antonio J. International society of sports nutrition position stand: caffeine and performance. J Int Soc Sports Nutr. 2010; 7:5. [PubMed: 20205813]

15. Gonzalez AM, Walsh AL, Ratamess NA, Kang J, Hoffman JR. Effect of a preworkout energy supplement on acute multi-joint resistance exercise. J Sports Sci Med. 2011; 10:261–266. [PubMed: 24149870]

16. Greenhaff PL, Bodin K, Soderlund K, Hultman E. Effect of oral creatine supplementation on skeletal muscle phosphocreatine resynthesis. Am J Physiol. 1994; 266:E725–730. [PubMed: 8203511]

17. Harris RC, Sale C, Delves SK. Modification of the ergogenic effects of creatine loading by caffeine. Med Sci Sports Exerc. 2005; 37:S348–S349.

18. Harris RC, Soderlund K, Hultman E. Elevation of creatine in resting and exercised muscle of normal subjects by creatine supplementation. Clin Sci (Lond. 1992; 83:367–374. [PubMed: 1327657]

19. Hespel P, Op't Eijnde B, Van Leemputte M. Opposite actions of caffeine and creatine on muscle relaxation time in humans. J Appl Physiol. 2002; 92:513–518. [PubMed: 11796658]

20. Hodgson AB, Randell RK, Jeukendrup AE. The metabolic and performance effects of caffeine compared to coffee during endurance exercise. PLoS One. 2013; 8:e59561. [PubMed: 23573201]

21. Izquierdo M, Ibanez J, Gonzalez-Badillo JJ, Gorostiaga EM. Effects of creatine supplementation on muscle power, endurance, and sprint performance. Med Sci Sports Exerc. 2002; 34:332–343. [PubMed: 11828245]

22. Kalmar JM, Cafarelli E. Effects of caffeine on neuromuscular function. J Appl Physiol. 1999; 87:801–808. [PubMed: 10444642]

23. Kreider RB. Effects of creatine supplementation on performance and training adaptations. Mol Cell Biochem. 2003; 244:89–94. [PubMed: 12701815]

24. Lee CL, Lin JC, Cheng CF. Effect of caffeine ingestion after creatine supplementation on intermittent high-intensity sprint performance. Eur J Appl Physiol. 2011; 111:1669–1677. [PubMed: 21207054]

25. Lee CL, Lin JC, Cheng CF. Effect of creatine plus caffeine supplements on time to exhaustion during an incremental maximum exercise. European Journal of Sport Science. 2011; 12:338–346.

26. McKenna MJ, Morton J, Selig SE, Snow RJ. Creatine supplementation increases muscle total creatine but not maximal intermittent exercise performance. J Appl Physiol. 1999; 87:2244–2252. [PubMed: 10601174]

27. Mohr T, Van Soeren M, Graham TE, Kjaer M. Caffeine ingestion and metabolic responses of tetraplegic humans during electrical cycling. J Appl Physiol. 1998; 85:979–985. [PubMed: 9729573]

28. Ormsbee MJ, Mandler WK, Thomas DD, Ward EG, Kinsey AW, Simonavice E, Panton LB, Kim JS. The effects of six weeks of supplementation with multi-ingredient performance supplements and resistance training on anabolic hormones, body composition, strength, and power in resistance-trained men. J Int Soc Sports Nutr. 2012; 9:49. [PubMed: 23153110]

29. Persky AM, Brazeau GA. Clinical pharmacology of the dietary supplement creatine monohydrate. Pharmacol Rev. 2001; 53:161–176. [PubMed: 11356982]

30. Preen D, Dawson B, Goodman C, Lawrence S, Beilby J, Ching S. Effect of creatine loading on long-term sprint exercise performance and metabolism. Med Sci Sports Exerc. 2001; 33:814–821. [PubMed: 11323554]

31. Quesada T, Gillum T. Effect of acute creatine supplementation and subsequent caffeine ingestion on ventilatory anaerobic threshold. J Exerc Physiol Online. 2013; 16:112–120.

32. Schneiker KT, Bishop D, Dawson B, Hackett LP. Effects of caffeine on prolonged intermittent-sprint ability in team-sport athletes. Med Sci Sports Exerc. 2006; 38:578–585. [PubMed: 16540848]

33. Shelmadine B, Cooke M, Buford T, Hudson G, Redd L, Leutholtz B, Willoughby DS. Effects of 28 days of resistance exercise and consuming a commercially available pre-workout supplement, NO-Shotgun(R), on body composition, muscle strength and mass, markers of satellite cell activation, and clinical safety markers in males. J Int Soc Sports Nutr. 2009; 6:16. [PubMed: 19656392]
34. Skare OC, Skadberg, Wisnes AR. Creatine supplementation improves sprint performance in male sprinters. Scand J Med Sci Sports. 2001; 11:96–102. [PubMed: 11252467]
35. Syrotuik DG, Bell GJ. Acute creatine monohydrate supplementation: a descriptive physiological profile of responders vs. nonresponders. J Strength Cond Res. 2004; 18:610–617. [PubMed: 15320650]
36. Theodorou AS, Cooke CB, King RF, Hood C, Denison T, Wainwright BG, Havenetidis K. The effect of longer-term creatine supplementation on elite swimming performance after an acute creatine loading. J Sports Sci. 1999; 17:853–859. [PubMed: 10585165]
37. Vanakoski J, Kosunen V, Meririnne E, Seppala T. Creatine and caffeine in anaerobic and aerobic exercise: effects on physical performance and pharmacokinetic considerations. Int J Clin Pharmacol Ther. 1998; 36:258–262. [PubMed: 9629989]
38. Vandenberghe K, Gillis N, Van Leemputte M, Van Hecke P, Vanstapel F, Hespel P. Caffeine counteracts the ergogenic action of muscle creatine loading. J Appl Physiol. 1996; 80:452–457. [PubMed: 8929583]
39. Vandenberghe K, Goris M, Hecke P, Van Leemputte M, Vangerven L, Hespel P. Long-term creatine intake is beneficial to muscle performance during resistance training. J Appl Physiol. 1997; 83:2055–2063. [PubMed: 9390981]
40. Volek JS, Duncan ND, Mazzetti SA, Staron RS, Putukian M, Gomez AL, Pearson DR, Fink WJ, Kraemer WJ. Performance and muscle fiber adaptations to creatine supplementation and heavy resistance training. Med Sci Sports Exerc. 1999; 31:1147–1156. [PubMed: 10449017]
41. Volek JS, Kraemer WJ, Bush JA, Boetes M, Incledon T, Clark KL, Lynch JM. Creatine supplementation enhances muscular performance during high-intensity resistance exercise. J Am Diet Assoc. 1997; 97:765–770. [PubMed: 9216554]
42. Wiles JD, Coleman D, Tegerdine M, Swaine IL. The effects of caffeine ingestion on performance time, speed and power during a laboratory-based 1 km cycling time-trial. J Sports Sci. 2006; 24:1165–1171. [PubMed: 17035165]
43. Wiroth JB, Bermon S, Andrei S, Dalloz E, Hebuterne X, Dolisi C. Effects of oral creatine supplementation on maximal pedalling performance in older adults. Eur J Appl Physiol. 2001; 84:533–539. [PubMed: 11482548]
44. Woolf K, Bidwell WK, Carlson AG. The effect of caffeine as an ergogenic aid in anaerobic exercise. Int J Sport Nutr Exerc Metab. 2008; 18:412–429. [PubMed: 18708685]
45. Zuniga JM, Housh TJ, Camic CL, Hendrix CR, Mielke M, Johnson GO, Housh DJ, Schmidt RJ. The effects of creatine monohydrate loading on anaerobic performance and one-repetition maximum strength. J Strength Cond Res. 2012; 26:1651–1656. [PubMed: 21921817]

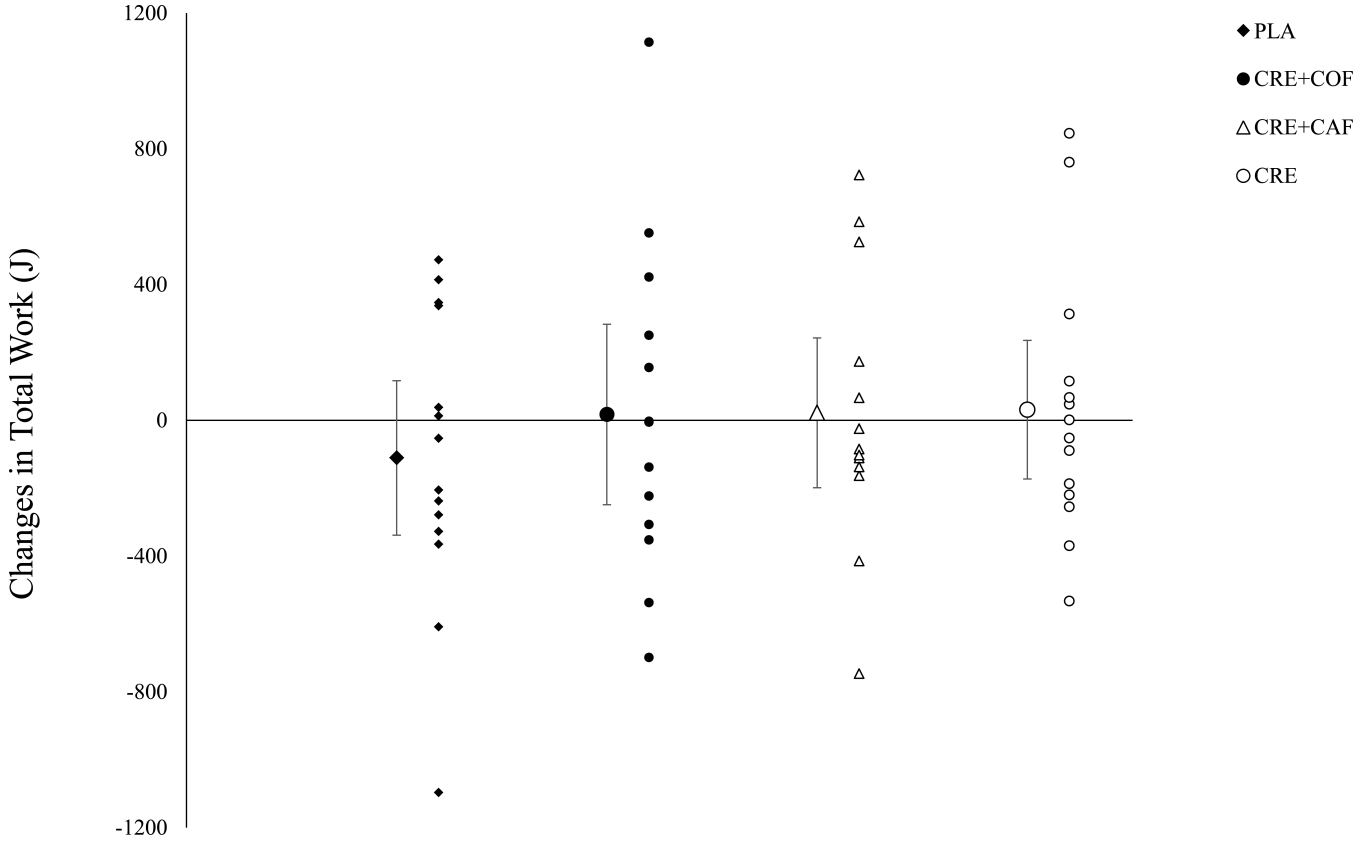

Figure 1.
Mean (± 1.96 × SEM) and individual changes in average total work (TW; joules) after supplementation.

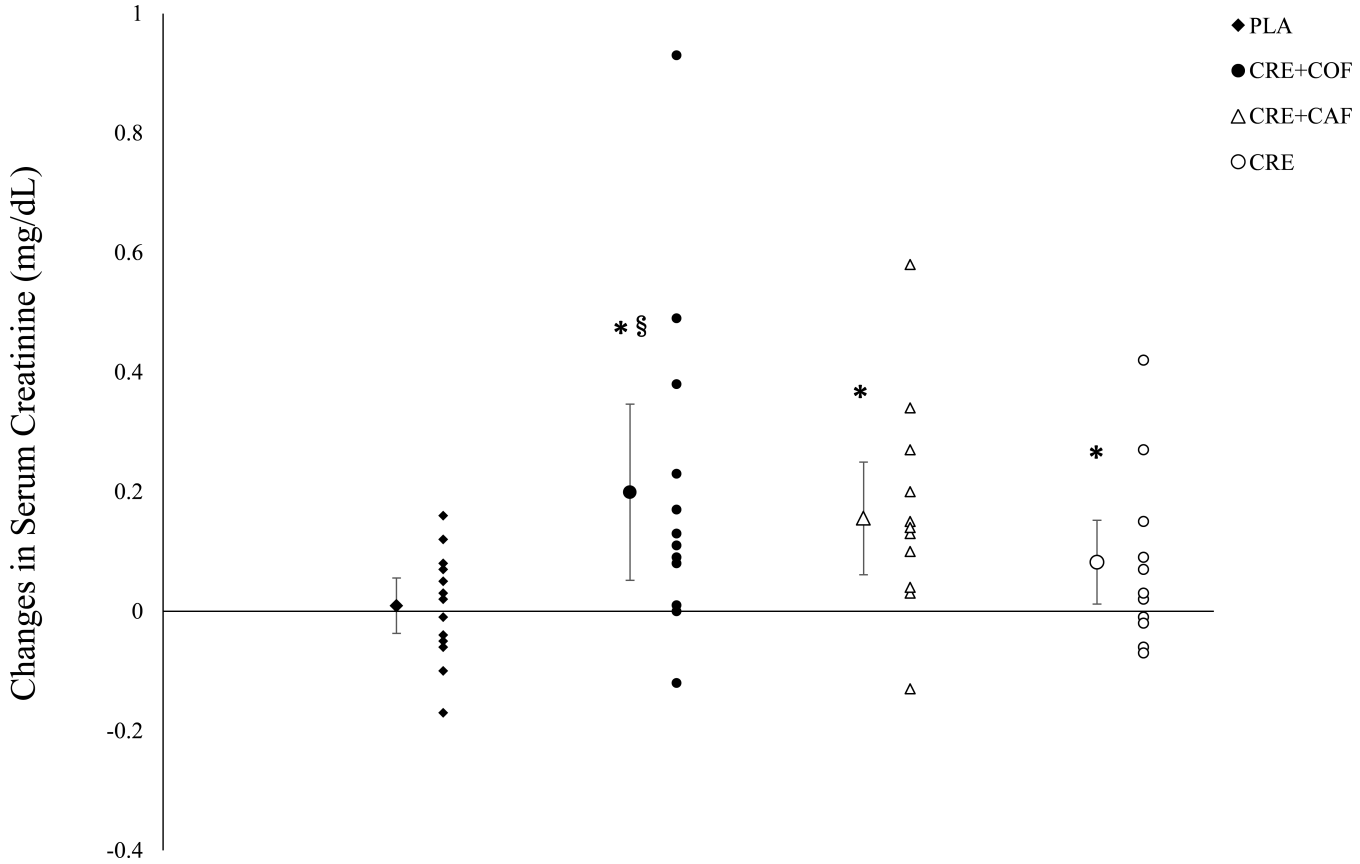

Figure 2.

Mean (± 1.96 × SEM) and individual changes in serum creatinine (mg/dL) after supplementation. *Significant change from baseline value, as determined by 95% confidence intervals ($p \leq 0.05$); § significantly greater than placebo ($p \leq 0.05$)

Table 1

Baseline characteristics and habitual dietary intakes by group.

	PLA (n=14)	CRE+COF (n=13)	CRE+CAF (n=13)	CRE (n=14)
Age (yrs)	19.9 ± 2.0	20.0 ± 1.3	20.2 ± 2.7	20.3 ± 2.3
Height (cm)	175.2 ± 7.0	177.6 ± 5.0	177.7 ± 5.3	178.7 ± 5.0
Weight (kg)	77.7 ± 9.2	77.9 ± 7.6	80.8 ± 10.6	78.7 ± 8.4
Calories (kcal)	2891.9 ± 941.9	2613.1 ± 680.1	2578.2 ± 378.7	2518.9 ± 372.7
CHO (g/day)	304.2 ± 103.4	307.3 ± 112.5	266.1 ± 74.4	288.7 ± 100.0
FAT (g/day)	126.3 ± 50.6	102.5 ± 28.0	106.2 ± 26.6	93.9 ± 23.5
PRO (g/day)	136.4 ± 43.8	124.2 ± 30.4	138.6 ± 35.2	131.9 ± 24.2
CAF (mg/day)	18.4 ± 57.5	12.1 ± 29.1	54.6 ± 76.0	46.4 ± 60.9

Values are mean ± SD

CHO = carbohydrate intake, PRO = protein intake, CAF = habitual caffeine intake

Table 2

Effects of supplementation on leg press and bench press 1RM (kg) for placebo (PLA), creatine + coffee (CRE + COF), creatine + caffeine (CRE + CAF), or creatine alone (CRE). Values are mean ± SD

	LP 1RM (kg)		BP 1RM (kg)	
Treatment	**Pre**	**Post**	**Pre**	**Post**
PLA	288.0 ± 73.2	308.9 ± 71.6*	89.6 ± 12.8	92.0 ± 13.3*
CRE+COF	289.0 ± 52.5	305.6 ± 52.0*	88.1 ± 15.6	90.2 ± 14.9*
CRE+CAF	299.6 ± 93.0	313.8 ± 97.0*	97.2 ± 20.9	99.3 ± 20.8*
CRE	288.0 ± 79.1	309.4 ± 76.0*	92.4 ± 21.7	95.0 ± 22.1*

*Significant change from baseline, as determined by 95% confidence intervals

Table 3

Absolute changes from baseline to post-supplementation in peak power (PP; watts) and total work (TW; joules).

Peak Power (W)						
Treatment	**Sprint 1**	**Sprint 2**	**Sprint 3**	**Sprint 4**	**Sprint 5**	**Average**
PLA	20.4 ± 93.9	−1.5 ± 76.4	−6.8 ± 77.0	−17.9 ± 57.8	−20.3 ± 128.0	−5.2 ± 45.0
CRE+COF	20.3 ± 72.0	−18.2 ± 78.2	−38.4 ± 83.1	4.0 ± 113.7	38.3 ± 105.0	1.2 ± 65.6
CRE+CAF	23.6 ± 105.3	20.1 ± 94.3	8.5 ± 73.1	−19.0 ± 74.8	2.1 ± 57.9	7.0 ± 59.0
CRE	3.8 ± 72.2	0.46 ± 69.3	−4.9 ± 60.8	−30.8 ± 71.4	16.9 ± 71.5	−2.9 ± 50.5

Total Work (J)						
Treatment	**Sprint 1**	**Sprint 2**	**Sprint 3**	**Sprint 4**	**Sprint 5**	**Average**
PLA	−43.7 ± 700.8	−169.4 ± 607.9	−208.4 ± 520.9	−169.8 ± 509.7	37.6 ± 843.7	−110.7 ± 434.3
CRE+COF	201.5 ± 612.1	−189.5 ± 682.0	−214.6 ± 639.0	2.4 ± 751.2	288.1 ± 633.6	17.6 ± 489.2
CRE+CAF	233.0 ± 615.5	−26.9 ± 522.4	18.3 ± 491.3	−112.2 ± 442.5	−1.2 ± 470.5	22.2 ± 405.5
CRE	80.1 ± 491.4	26.6 ± 476.7	−11.0 ± 366.8	−63.9 ± 585.8	126.3 ± 636.5	31.6 ± 389.9

Values are mean ± SD