The Effect of Creatine Loading on Neuromuscular Fatigue in Women

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[1]*Department of Exercise and Sport Science, University of North Carolina Chapel Hill, Chapel Hill, NC;* [2]*Sport and Exercise Science, University of Central Florida, Orlando, FL;* [3]*Department of Kinesiology, California State University–San Bernardino, San Bernardino, CA; and* [4]*Department of Nutrition and Health Sciences, University of Nebraska-Lincoln, Lincoln, NE*

ABSTRACT

SMITH-RYAN, A. E., E. D. RYAN, D. H. FUKUDA, P. B. COSTA, J. T. CRAMER, and J. R. STOUT. The Effect of Creatine Loading on Neuromuscular Fatigue in Women. *Med. Sci. Sports Exerc.*, Vol. 46, No. 5, pp. 990–997, 2014. **Purpose**: This study aimed to examine the effects of intermittent isometric fatigue on maximal voluntary contraction (MVC) strength, percent voluntary activation (%VA), peak twitch force (PTF), peak rate of force development (PRFD), half relaxation time (HRT), and maximal compound action potential (M-wave) amplitude of the soleus and medial gastrocnemius muscles before and after creatine (Cr) loading. **Methods**: Using a double-blinded, placebo-controlled, randomized design, 12 women were assigned to a Cr ($n = 6$; mean age ± SD = 23.3 ± 3.0 yr) or placebo (PL; $n = 6$; mean age ± SD = 21.3 ± 1.6 yr) group. Participants supplemented four times daily for 5 d with 5 g of Cr + 10 g of fructose or 10 g of fructose. At baseline and after testing, an isometric MVC and the twitch interpolation procedure were used before and after a 4-min isometric fatigue protocol of the plantarflexor muscles, which consisted of six intermittent duty cycles per minute (7-s contraction, 3-s relaxation) at 70% MVC. **Results**: There were no interactions between the Cr and PL groups ($P > 0.05$) for any dependent variable. The fatigue protocol reduced voluntary strength (−17.8%, $P < 0.001$) and %VA (−3.7%, $P = 0.005$). Baseline PTF ($P < 0.005$) and PRFD ($P < 0.001$) values were less than those of all respective time points, but PTF value decreased from 3 min to 4 min and after testing ($P < 0.005$). HRT increased from baseline to minutes 1 and 2 and then returned to baseline at minutes 3 and 4 and after testing. The M-wave did not change ($P > 0.05$). **Conclusions**: Five days of Cr loading did not influence isometric force, %VA, evoked twitch properties, or the central and peripheral aspects of fatigue measured in this study. **Key Words:** ERGOGENIC AID, SEX, PHOSPHOCREATINE, CONTRACTILE PROPERTIES, MUSCLE FATIGUE, EMG

Creatine (Cr) is synthesized endogenously from arginine, glycine, and methionine within the human liver and pancreas as well as obtained through the exogenous consumption of poultry, meat, and fish (31). Creatine loading has been shown to increase phosphocreatine (PCr) stores, which aids in the rapid production and regeneration of adenosine triphosphate (ATP), and has been shown to elicit improvements in high-intensity anaerobic activities (15). Cr monohydrate supplementation has also been shown to increase maximal force and power output during short, intense bouts of exercise (5). Despite the extensive body of Cr literature supporting its use as an ergogenic aid (5,27,41), the exact mechanisms of action are not completely understood. Rawson et al. (32) have suggested that the ergogenic effects of Cr are a result of a number of factors including metabolic adaptations, protein turnover, hormonal alterations, stabilization of lipid membranes, and molecular modifications. The primary factor believed to be responsible for the ergogenic actions of Cr is linked with an improvement in energy resynthesis and may act on the Ca^{2+} adenosine triphosphatase (ATPase) pump, thereby augmenting cross-bridge recycling (30) as well as potentially serving as an endogenous metabolic buffer helping to maintain pH (15).

The twitch interpolation technique has been used to characterize voluntary muscle activation. This technique is commonly used to examine central fatigue, and as recently reported by Gandevia et al. (12), the increased superimposed twitch after fatiguing exercise reflects the "… low volitional drive to high-threshold motor units, which stop firing or are discharging at low frequencies" (p. 1373). Furthermore, evoked twitch properties, such as peak twitch force (PTF), peak rate of force development (PRFD), half relaxation time (HRT), and M-wave, are often assessed to determine the extent of fatigue-induced peripheral skeletal muscle and activation alterations, respectively (17).

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Submitted for publication May 2013.
Accepted for publication October 2013.

0195-9131/14/4605-0990/0
MEDICINE & SCIENCE IN SPORTS & EXERCISE®

DOI: 10.1249/MSS.0000000000000194

While numerous studies have evaluated the metabolic consequences of Cr supplementation, only a few have assessed its influence on neuromuscular fatigue (3,21,38,39). Acute Cr ingestion has been shown to delay neuromuscular fatigue during exercise. Stout et al. (39) and Smith et al. (38) have reported that Cr supplementation delayed neuromuscular fatigue during cycle ergometry using surface EMG in women. These previous authors used global assessments of fatigue, evaluating the physical working capacity at fatigue threshold (PWC_{FT}) and EMG fatigue threshold (EMG_{FT}), providing a general estimate of a workload that is sustainable without inducing a rise in EMG amplitude. During a fatiguing exercise, EMG activity is thought to increase as a result of either additional motor unit recruitment or an increase in the firing frequency of active motor units (23). Physiologically, peripheral fatigue mechanisms (drop in pH, energy depletion) are the primary cause of an increase in EMG amplitude (28). Delaying peripheral fatigue would result in higher PWC_{FT} and EMG_{FT} values, as previously reported with Cr intake.

While these previous investigations suggest an improvement in neuromuscular function, they are more focused on global assessments of fatigue. Further work is necessary to examine the central-versus-peripheral aspects of fatigue using more controlled testing models. Bazzucchi et al. (3) demonstrated a positive effect of Cr on evoked twitch properties (peak torque and time-to-reach peak torque) and the torque–angular velocity curve of the forearm flexors, suggesting an improvement in neuromuscular function and improved contractile efficiency. van Leemputte et al. (40) reported a beneficial effect of Cr supplementation on muscle relaxation time. Rawson et al. (33) also demonstrated an improvement in fatigue resistance during repeated bouts of high-intensity isokinetic concentric leg-extension muscle actions after a low dose (1.7–2.9 $g \cdot d^{-1}$) Cr supplementation. In contrast, Jakobi et al. (21) is the only previous study to attempt to discriminate between central and peripheral effects of Cr supplementation by measuring twitch properties and percent voluntary activation of the forearm flexors before, and after a controlled isometric fatigue model and reported no ergogenic effects of Cr.

To date, we are aware of only one previous study that has evaluated the influence of Cr supplementation on neuromuscular properties before and after fatiguing exercise in the forearm flexors (21). Furthermore, few neuromuscular evaluations have been done in women (38,39), and no studies have evaluated central and peripheral contributions of fatigue, with Cr intake, in women. Therefore, the purpose of the present study was to use a controlled intermittent isometric fatigue protocol to examine the effects of Cr loading on maximal voluntary contraction (MVC) strength, percent voluntary activation (%VA), and the time course of fatigue on PTF, PRFD, HRT, and M-wave amplitude of the soleus (SOL) and medial gastrocnemius (MG) muscles in women.

METHODS

Participants. Twelve women (mean ± SD; age = 22.3 ± 2.5 yr, stature = 166.9 ± 5.5 cm, body mass = 64.8 ± 12.4 kg) volunteered to participate in this study that was approved by the university's institutional review board for the protection of human subjects. Participants signed an informed consent form and completed a health and exercise status questionnaire to confirm that they were healthy and had no current or ongoing neuromuscular diseases or musculoskeletal injuries. Because of their reported levels of aerobic exercise, resistance training, and recreational sports (1–4 $h \cdot wk^{-1}$), participants were classified as moderately active and recreationally trained. Participants were also screened for previous and current supplementation use (e.g., creatine, β-alanine) and were excluded if consumption had occurred within 3 months before testing.

Experimental design. Participants visited the laboratory on three separate occasions separated by 2–7 d to complete a familiarization trial and two experimental trials. At baseline and after supplementation, MVC, %VA, PTF, PRFD, HRT, and M-wave amplitude of the SOL and MG were measured before and after a 4-min fatiguing protocol. Twitch properties during the fatigue bout were also evaluated at each min (Fig. 1). All experimental trials were performed at the same time of the day (±2 h).

Supplementation protocol. After pretreatment testing, participants were randomly assigned to either a placebo (PL; 10 g of flavored fructose powder per packet; $n = 6$) or A creatine (Cr; 5 g dicreatine citrate plus 10 g of flavored fructose powder per packet; $n = 6$) (Creatine Edge; FSI Nutrition Inc., Omaha, NE) group. Both treatments were effervescent powders, packaged to be identical in taste and appearance and were dissolved in 8–12 oz of water. Each group ingested one packet four times per day at regular intervals (every 3–4 h) for 5 d (total of 20 $g \cdot d^{-1}$). Compliance was measured with the return of empty packets. Cr content of the product was confirmed using Fourier Transform Infrared Spectroscopy.

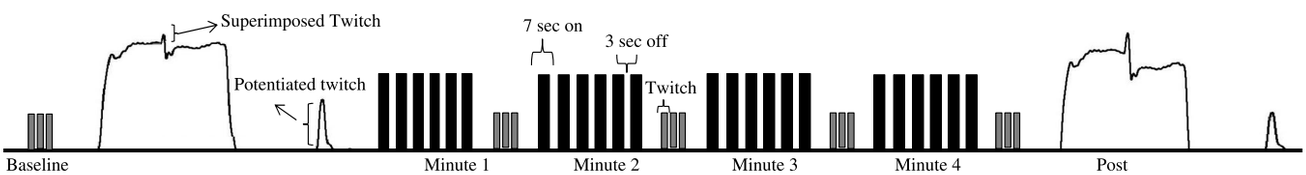

FIGURE 1—A schematic representation of the neuromuscular assessments that occurred during each experimental visit for each participant before (week 1), and after (week 2) supplementation. For the fatigue protocol, single twitches are represented as *small gray bars* and duty cycles are represented as *tall black bars*.

Familiarization trial. At 2–3 d before the experimental trials, each participant underwent a familiarization trial where they practiced the MVC and %VA assessments to ensure tolerability of the procedures and to minimize potential learning effects. Participants were also familiarized with the fatigue protocol, completing 2 min of the protocol.

Muscle force assessments. All MVCs were performed at an ankle joint angle of 81.7° (neutral = 90° between the foot and the leg) with a leg flexion angle of 0° below the horizontal plane on a custom-built apparatus equipped with a load cell (range 0–500 lb, model LC402; Omegadyne, Stamford, CT) connected to a calibrated Biodex System 3 dynamometer (Biodex Medical Systems, Inc. Shirley, NY; Fig. 2). Each participant was seated with restraining straps over the pelvis and thigh, with the lateral malleolus of the fibula aligned with input axis of the dynamometer in accordance with the manufacturer's instructions (Biodex Pro Manual, Applications/Operations, Biodex Medical Systems, Inc.). The foot was secured in a heel cup attached to a footplate with toe and ankle straps over the metatarsals and malleoli. To determine peak force (N) and %VA, each participant performed two 5-s isometric MVCs. Two minutes of rest was allowed between each MVC. The participants were instructed to give a maximal effort, and strong verbal encouragement was provided by the investigators. The MVC that yielded the highest force value was used for all future analyses. Previous test–retest reliability statistics from this laboratory has reported intraclass correlation coefficients of 0.94 and 0.84 for MVC strength and %VA, respectively, with no reported differences between testing days ($P > 0.05$) (6,37).

%VA. The twitch interpolation technique was used to determine %VA as previously described (37). Transcutaneous electrical stimuli were delivered to the tibial nerve using a high-voltage (maximum voltage = 400 V) constant-current stimulator (Digitimer DS7AH, Herthfordshire, UK). The stimuli were applied via bipolar surface electrodes that were placed in the popliteal space. Single-square-wave stimuli were administered to the tibial nerve at a low current (amperage = 20–50 mA) to determine optimal probe location on the visual inspection of the M-wave of the SOL muscle monitored on an external computer. Once the location was determined and marked, the maximal M-wave was achieved with incremental amperage increases (20 mA) until a plateau in the peak-to-peak (p-p) M-wave was observed, despite amperage increases. When a plateau was reached, 20% was added to the amperage that yielded the highest p-p M-wave to ensure a supramaximal stimulus. In accordance with the twitch interpolation procedure (1), a supramaximal doublet (delivered successively at 100 Hz) was administered 350–500 ms into the MVC plateau (superimposed twitch) and then again 3–5 s after the MVC trial at rest (potentiated twitch). %VA was calculated with the following equation:

$$\%\mathrm{VA} = \left[1 - \left(\frac{\text{superimposed twitch}}{\text{potentiated twitch}}\right)\right] \times 100$$

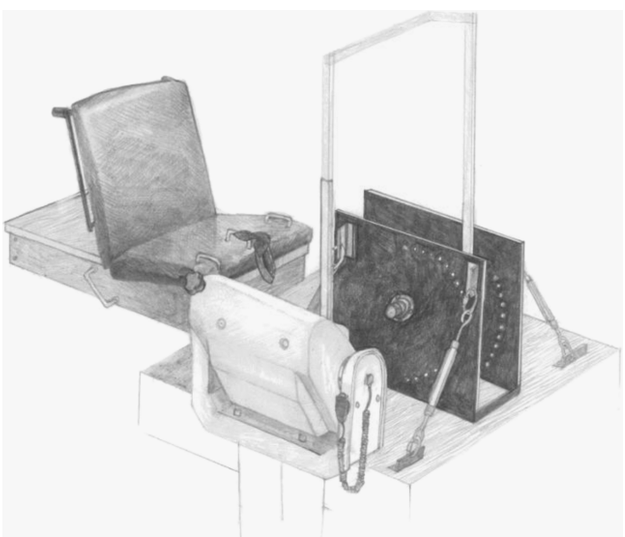

FIGURE 2—Custom-built apparatus equipped with a load cell designed for the twitch interpolation procedure, fatiguing protocol, and evoked twitch assessments.

Surface EMG. Preamplified bipolar, active surface electrodes (TSD150B; Biopac Systems Inc., Santa Barbara, CA; nominal gain = 350, bandwidth = 12–500 Hz), with a fixed center-to-center interelectrode distance of 20 mm, were placed on the SOL and MG muscles (18). For the SOL, the electrodes were placed along the longitudinal axis of the tibia at 66% of the distance between the medial condyle of the femur and the medial malleolus. The electrodes for the MG were placed on the most prominent bulge of the muscle. A single pregelled disposable electrode (Ag–Ag Cl, Quinton Quick Prep; Quinton Instruments Co., Bothell, WA) was placed on the spinous process of the seventh cervical vertebrae to serve as a reference electrode. To reduce interelectrode impedance and to increase the signal-to-noise ratio, local areas of the skin were shaved and cleaned with isopropyl alcohol before placement of the electrodes.

Signal processing. The EMG (μV) and force (N) signals were recorded simultaneously with a Biopac data acquisition system (MP150WSW; Biopac Systems, Inc.) during each isometric MVC and evoked twitch assessment. The force signal from the load cell and the EMG signals recorded from the SOL and MG were sampled at 2 kHz. All signals were stored on a personal computer (Dell Inspiron 8200; Dell, Inc., Round Rock, TX) and processed offline using custom-written software (LabVIEW v. 8.5; National Instruments, Austin, TX). The EMG signals were digitally filtered (zero-phase-shift, fourth-order Butterworth filter) with a pass band of 10–500 Hz. The force signal was smoothed with a zero-phase-shift 100-pt moving average. Isometric MVC force was calculated as the average force value that occurred during the 0.25-s epoch taken immediately before the superimposed twitch. Peak twitch force was calculated as the highest mean of 20 consecutive data points that occurred at the apex of the evoked twitch. Peak rate of force

development was calculated as the highest slope value for any 20 consecutive data points from the onset of force production to PTF from the evoked twitch. HRT was calculated as the time it took the twitch to relax to 50% of its PTF. The M-waves for the SOL and MG were calculated as the root mean square (RMS) amplitude values as recommended by Arabadzhiev et al. (2).

Isometric fatiguing protocol. For the fatiguing protocol, participants were required to track their force production on a computer monitor placed in front of them, which displayed their real-time digitized force signal. A preprogrammed template was displayed on the screen at 70% of their MVC. The participants were required to track this line for 7 s followed by a 3-s rest. Each participant completed this protocol for a total of 4 min (four sets of six intermittent isometric contractions), adapted from the procedures described by Russ et al. (36) and Jakobi et al. (21). Before and after the fatiguing protocol and at the end of each minute, three consecutive single-square-wave stimulations (200 μs in duration) were delivered to examine twitch and maximum compound action potential (M-wave) properties. During the fatiguing protocol, RPE were also recorded at the end of each minute.

Statistical analyses. Separate three-way mixed-factorial ANOVA [time (pre vs post) × day (week 1 vs week 2) × treatment (Cr vs Pl)] were used to analyze MVC force, %VA, and [time (baseline vs 1 min vs 2 min vs 3 min vs 4 min vs post) × day (week 1 vs week 2) × treatment (Cr vs PL)] for PTF, PRFD, HRT, and M-wave properties for the SOL and MG. A similar three-way mixed-factorial ANOVA was used to analyze RPE (excluding an acute preassessment). Body mass was evaluated using a two-way mixed-factorial ANOVA [day (week 1 vs week 2) × treatment (Cr vs PL)]. When appropriate, follow-up analyses were performed using one-way repeated-measures ANOVA with Bonferroni corrections. An α of $P \leq 0.05$ was used to determine statistical significance. Partial eta-squared (η_p^2) values were also reported to reflect the magnitude of the change. All analyses were completed using SPSS version 19.0 (SPSS, Inc., Chicago, IL).

RESULTS

Body mass. For body mass, there was no two-way interaction ($P = 0.397$, $\eta_p^2 = 0.072$), no main effect for day ($P = 0.617$, $\eta_p^2 = 0.026$), and no main effect for treatment ($P = 0.069$, $\eta_p^2 = 0.293$). The Cr group gained an average of 0.43 kg (baseline mean ± SD = 67.2 ± 7.0 kg) and PL group lost 0.11 kg (baseline = 58.6 ± 10.7 kg), indicating that there was a nonsignificant increase in body mass after supplementation. Tables 1 and 2 contain the mean ± SD values for MVC force and %VA, and PTF, PRFD, HRT, M-wave RMS amplitude, and RPE, respectively.

Central fatigue. In general, the fatiguing exercise resulted in a significant reduction in MVC force and %VA (Fig. 3) but were unaffected by Cr supplementation.

MVC force. As expected, MVC force decreased after a bout of fatiguing contractions (Fig. 3A). There was no significant three-way (time × day × treatment, $P = 0.578$, $\eta_p^2 = 0.032$) or two-way interactions ($P = 0.065$–0.972, $\eta_p^2 = 0.001$–0.003) and no main effect for day ($P = 0.221$, $\eta_p^2 = 0.145$) or treatment ($P = 0.068$, $\eta_p^2 = 0.295$). Individual baseline MVC values before and after supplementation are presented in Figure 4. There was a main effect for time ($P < 0.001$, $\eta_p^2 = 0.828$) (Table 1).

%VA. There was no three-way ($P = 0.775$, $\eta_p^2 = 0.009$) or two-way ($P = 0.064$–0.997, $\eta_p^2 = 0.001$–0.303) interactions and no main effect for day ($P = 0.805$, $\eta_p^2 = 0.006$) or treatment ($P = 0.878$, $\eta_p^2 = 0.002$). There was a main effect for time ($P = 0.005$, $\eta_p^2 = 0.558$) (Table 1). %VA was greater before the fatigue bout (Fig. 3B).

Peripheral fatigue. There were minor to no change in evoked twitch properties during and after the fatigue bout and after Cr supplementation.

PTF. There was no significant three-way ($P = 0.507$, $\eta_p^2 = 0.080$) or two-way ($P = 0.090$–0.998, $\eta_p^2 = 0.006$–0.201) interactions and no main effect for day ($P = 0.678$, $\eta_p^2 = 0.015$) or treatment ($P = 0.560$, $\eta_p^2 = 0.040$). There was a main effect for time ($P < 0.001$, $\eta_p^2 = 0.704$). Baseline PTF value was less than PTF values at 1 min, 2 min, 3 min, 4 min, and after testing ($P < 0.001$). PTF values at 3 min were also significantly greater than PTF values at 4 min ($P = 0.005$) and after testing ($P = 0.012$).

PRFD. There was no significant three-way ($P = 0.407$, $\eta_p^2 = 0.094$) or two-way ($P = 0.116$–0.999, $\eta_p^2 = 0.004$–0.158) interactions and no main effect for day ($P = 0.688$, $\eta_p^2 = 0.017$) or treatment ($P = 0.574$, $\eta_p^2 = 0.048$). There was a significant main effect for time ($P < 0.001$, $\eta_p^2 = 0.727$). Baseline PRFD values were significantly ($P < 0.001$) less than those at all other time points.

HRT. There was no significant three-way ($P = 0.731$, $\eta_p^2 = 0.053$) or two-way ($P = 0.728$–0.997, $\eta_p^2 = 0.001$–0.053) interactions and no main effect for day ($P = 0.130$, $\eta_p^2 = 0.214$) or treatment ($P = 0.948$, $\eta_p^2 = 0.001$). There was a main effect for time ($P = 0.001$, $\eta_p^2 = 0.422$). The HRT values at 1 min were significantly greater than those at 4 min ($P = 0.037$) and after testing ($P = 0.015$). HRT values at 2 min were greater than those at 3 min ($P = 0.024$), 4 min ($P = 0.029$), and after testing ($P = 0.022$).

TABLE 1. Pretreatment and posttreatment mean ± SD values for the strength assessments, maximal voluntary contraction (MVC) force, and percent voluntary activation (%VA).

	MVC Force	%VA
Creatine		
Pretreatment baseline	343.4 ± 39.5*	91.6 ± 8.2*
Pretreatment post fatigue	288.7 ± 41.4	88.4 ± 11.1
Posttreatment baseline	347.0 ± 23.7*	97.0 ± 4.9*
Posttreatment post fatigue	269.1 ± 46.2	86.3 ± 13.3
Placebo		
Pretreatment baseline	301.3 ± 50.6*	93.5 ± 9.4*
Pretreatment post fatigue	242.2 ± 28.6	89.3 ± 7.3
Posttreatment baseline	298.3 ± 65.1*	93.6 ± 9.3*
Posttreatment post fatigue	247.6 ± 48.0	83.8 ± 13.2

*Values are significantly greater than postfatigue strength assessment ($P < 0.001$).

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TABLE 2. Mean ± SD values at baseline, 1 min, 2 min, 3 min, 4 min, and post-fatigue for the dependent variables for both treatment groups at week 1 and week 2.

		PTF (N)		PRFD (N·s^{-1})		HRT (ms)		RMS SOL (μV)		RMS MG (μV)		RPE	
	Time	Wk 1	Wk 2	Wk 1	Wk 2	Wk 1	Wk 2	Wk 1	Wk 2	Wk 1	Wk 2	Wk 1	Wk 2
Cr	Baseline	53.6 ± 12.4*	52.4 ± 11.2*	663.0 ± 141.4*	669.8 ± 132.4*	95.0 ± 17.9	88.9 ± 18.4	916.5± 218.6	882.7 ± 235.8	382.9 ± 145.5	431.8 ± 161.3	—	—
	1 min	77.8 ± 11.1	77.9 ± 14.3	1002.4 ± 131.5	1021.4 ± 171.2	98.5 ± 13.3**	92.6 ± 12.6**	1048.3 ± 340.1	888.2 ± 256.6	367.6 ± 151.7	454.5 ± 235.3	11.0 ± 1.7	10.1 ± 2.0
	2 min	76.3 ± 10.6	76.3 ± 13.3	1004.2 ± 117.8	1024.6 ± 150.8	96.8 ± 20.3***	95.3 ± 13.8***	899.7 ± 337.1	901.2 ± 258.7	360.7 ± 157.3	447.8 ± 220.8	13.0 ± 1.5****	11.6 ± 2.4****
	3 min	77.7 ± 12.4**	76.6 ± 16.4**	1028.6 ± 118.3	1059.2 ± 196.9	89.9 ±15.4	88.0 ± 13.6	1032.8 ± 224.6	883.6 ± 260.3	384.7 ± 153.9	423.8 ± 180.6	12.3 ± 4.8****	13.7 ± 2.6****
	4 min	71.8 ± 13.3	69.1 ± 17.2	975.2 ± 129.2	979.2 ± 223.5	87.0 ± 12.8	84.7 ± 9.8	1029.6 ± 210.4	888.4 ± 261.9	363.9 ± 127.0	416.8 ± 192.9	15.4 ± 1.9	15.7 ± 2.6
	Post	69.2 ± 15.8	66.1 ± 19.4	943.7 ± 164.3	944.4 ± 251.2	84.3 ± 8.7	83.1 ± 9.3	899.4 ± 267.4	892.9 ± 275.9	339.4 ± 104.8	400.7 ± 176.1	16.6 ± 2.5*	17.4 ± 2.6*****
PL	Baseline	49.6 ± 13.5*	44.5± 11.2*	637.2 ± 173.9*	575.6 ± 128.8*	90.9 ± 9.5	86.7 ±9.2	728.8 ± 248.8	623.6 ± 147.8	579.45 ± 198.9	580.6 ± 143.9	—	—
	1 min	70.2 ± 18.3	74.6 ± 17.4	918.1 ± 232.5	994.7 ± 235.9	99.1 ±17.7**	96.6 ± 17.1**	762.2 ± 235.8	649.4 ± 166.0	578.7 ± 260.9	576.9 ± 120.1	10.8 ± 1.2	10.3 ± 1.0
	2 min	70.3 ± 17.8	72.1 ± 20.2	935.0 ± 208.0	963.9 ± 245.5	99.5 ± 18.4***	95.2 ± 14.5***	767.6 ± 264.4	677.2 ± 164.8	586.5 ± 250.0	604.1 ± 109.4	12.8 ± 1.6****	13.2 ± 1.5****
	3 min	70.6 ± 19.1**	70.4 ± 19.0**	953.6 ± 219.9	959.0 ± 223.5	90.3 ± 13.3	85.6 ± 9.1	963.3 ± 463.8	891.0 ± 478.9	593.4 ± 238.2	599.1 ± 117.9	15.3 ± 2.6****	15.5 ± 1.4****
	4 min	66.7 ± 20.3	65.3 ± 17.6	918.7 ± 242.3	896.9 ± 200.7	85.2 ± 13.4	85.4 ± 9.9	956.8 ± 479.2	875.3 ± 441.5	608.2 ± 235.7	583.9 ± 79.8	16.7 ± 2.7	17.2 ± 2.1
	Post	64.0 ± 21.0	62.3 ± 18.6	887.0 ± 251.0	865.5 ± 216.9	83.9 ± 8.5	80.6 ± 13.3	1096.6 ± 496.6	901.0 ± 379.9	594.0 ± 213.1	574.8 ± 98.6	18.0 ± 2.5*	18.2 ± 2.2*****

* Significantly lower value than any other time point ($P < 0.001$).
** Significantly greater value than at 4 min and after testing ($P < 0.001$).
*** Significantly greater value than at 3 min, 4 min, and after testing ($P = 0.022–0.024$).
**** Significantly lower value than at 4 min and after testing ($P < 0.001$).
***** Significantly greater value than any other time point ($P < 0.001$).

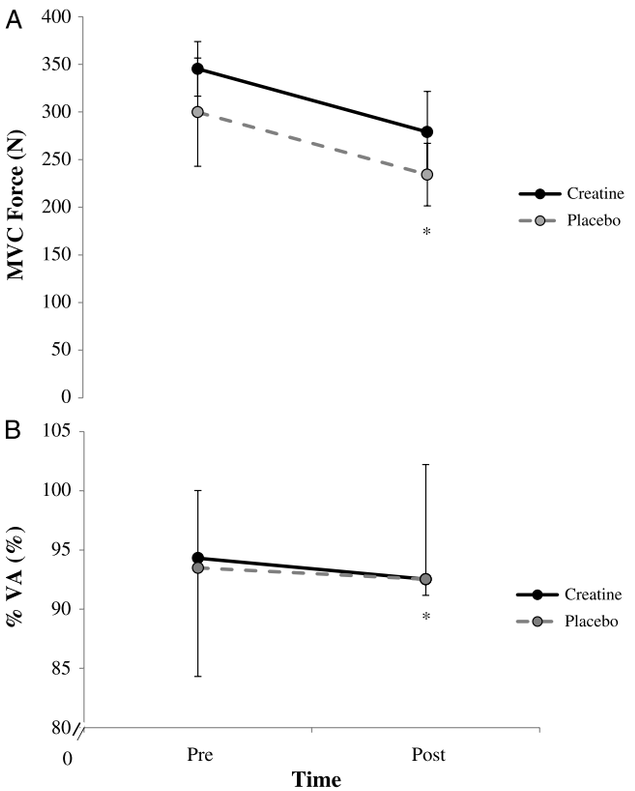

FIGURE 3—The marginal means (collapsed across day) for maximal voluntary contraction (MVC) force (A) and percent voluntary activation (%VA) (B) for the creatine (*black*) and placebo (*gray*) groups before and after the fatiguing protocol. *Significantly lower value than at baseline. Mean ± SD. $P < 0.05$.

M-wave. For the soleus (SOL RMS), there was no significant three-way ($P = 0.089$, $\eta_p^2 = 0.169$) or two-way ($P = 0.196$–$P = 0.827$, $\eta_p^2 = 0.041$–0.133) interactions and no main effects for time ($P = 0.196$, $\eta_p^2 = 0.133$), day ($P = 0.510$, $\eta_p^2 = 0.045$), or treatment ($P = 0.135$, $\eta_p^2 = 0.209$).

For the medial gastrocnemius (MG RMS), there was no significant three-way ($P = 0.849$, $\eta_p^2 = 0.038$) or two-way ($P = 0.380$–0.663, $\eta_p^2 = 0.061$–0.078) interactions and no main effects for time ($P = 0.663$, $\eta_p^2 = 0.061$), day ($P = 0.430$, $\eta_p^2 = 0.063$), or treatment ($P = 0.067$, $\eta_p^2 = 0.297$).

RPE. There was no three-way ($P = 0.842$, $\eta_p^2 = 0.031$) or two-way ($P = 0.268$–0.725, $\eta_p^2 = 0.012$–0.109) interactions for RPE and no main effects for day ($P = 0.506$, $\eta_p^2 = 0.041$) or treatment ($P = 0.264$, $\eta_p^2 = 0.112$). There was a main effect for time ($P < 0.001$, $\eta_p^2 = 0.838$). Pairwise comparisons indicated that RPE was significantly lower at 1 min than at all other time points (2 min, 3 min, 4 min, and after testing; $P < 0.001$). RPE values at 2 and 3 min were significantly less than those at 4 min and after testing ($P < 0.001$). RPE values after testing were significantly greater than those at all other time points ($P < 0.001$).

DISCUSSION

The model used in the current study was designed to examine the influence of Cr loading on both central and peripheral

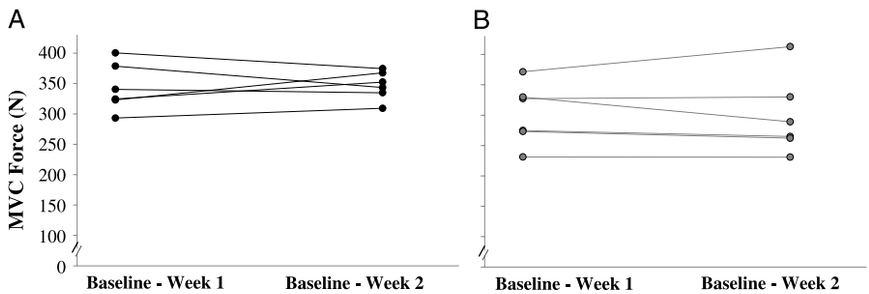

FIGURE 4—Individual values for maximal voluntary contraction (MVC) strength before supplementation at baseline (week 1) and after supplementation at baseline (week 2) for creatine (A) and placebo (B) treatment groups.

aspects of neuromuscular fatigue in young women. The primary findings of the present study demonstrated that an acute bout of fatiguing muscle actions (4 min of 70% duty cycles at 70% of MVC) resulted in a significant reduction in MVC force and %VA (Fig. 3) and minor or no change in evoked twitch properties (Table 2) among recreationally active young women. These findings are supported by Russ et al. (34) and by Jakobi et al. (21). Furthermore, 5 d of Cr supplementation did not influence any of these variables during and after the acute bout of fatiguing intermittent isometric muscle actions.

The ergogenicity of Cr supplementation is often attributed to its physiological role in energy resynthesis. Muscle relaxation during intermittent contractions accounts for a substantial amount of energy consumption (4). Concomitantly, PCr is reduced during fatiguing contractions, potentially altering muscle relaxation through cross-bridge recycling (43). As a result of intense contractions, the breakdown of PCr also yields an accumulation of inorganic phosphate (P_i). Previous studies suggest that P_i may enter the sarcoplasmic reticulum during fatigue, reducing calcium release resulting in a decline in muscle force (44). Decrements in neuromuscular performance are generally affected by both central and peripheral characteristics.

Central fatigue. A fatigue-induced reduction in force-generating capacity has been reported to occur at any point along the transmission path from the CNS to the intramuscular contractile components (25). Determining the influence of the CNS on fatigue, or the extent of voluntary activation, is commonly quantified from the force during an MVC in comparison to a superimposed electrically evoked twitch (17). In the present study, the PL and Cr groups experienced a similar decline in MVC force and % VA after the 4 min of isometric duty cycles (Table 1 and Fig. 3) before and after Cr supplementation at similar perceived exertions (Table 2). Previous authors (9,17) have suggested that a reduction in voluntary activation may be a result of insufficient neural drive to the muscle, a lack of full motor unit recruitment, and/or insufficient discharge rates. Our results are in agreement with the findings from Jakobi et al. (21) who reported that Cr supplementation had no effect on MVC force and %VA reductions after an intermittent isometric fatiguing protocol in the forearm flexors of young men. Although the present study did not evaluate sex differences, previous literature has suggested that men may have a greater decline in central activation than women (34). Interestingly, however, the current results in women were similar to the decreases in %VA observed in men by Jakobi et al. (21). In addition, chronic MVC force and %VA values were not augmented by Cr supplementation (Table 1). The lack of effect of Cr loading on MVC force is consistent with previous studies (7,21,40) using similar isometric protocols. In contrast, Bazzucchi et al. (3) demonstrated improvements in maximal isokinetic strength at the fastest velocities ($180°\cdot s^{-1}$ and $240°\cdot s^{-1}$) in the elbow flexors, which may have been attributed to fiber type–specific improvements from Cr supplementation. It may be that these conflicting results were due to the static-versus-dynamic nature of strength testing, the muscle group evaluated, as well as the primary sex used, which future studies should consider when examining these issues.

Peripheral fatigue. Previous data have suggested that Cr loading may be effective in improving similar, brief, maximal, anaerobically reliant events (15) as well as improving recovery from intense contractions (14). Peripherally, the PCr system assists in maintaining intramuscular pH by acting as an immediate P_i and H^+ buffer, subsequently enhancing energy translocation and thereby maintaining contraction integrity (16,24). To date, the current study is only the second to evaluate the effects of Cr supplementation on stimulated contractile properties after a bout of fatiguing exercise in humans and the first to examine the plantar flexors. Our results demonstrated a potentiation in PTF from baseline to 3 min followed by a subsequent decrease in these values by the end of the 4-min protocol; PRFD also increased from baseline throughout the protocol. Based on previous findings by Russ et al. (34) demonstrating a sex difference in the loss of potentiation with fatigue, combined with current results, future studies should seek to evaluate specific sex differences with evoked and voluntary contractions with fatigue. Previous data have also reported contractile potentiation during the early phases of intermittent exercise (11,29); however, there was no effect of Cr supplementation on these contractile properties. Furthermore, the reduction in twitch force, with no change in peripheral activation, has been suggested to represent metabolic inhibition of the contractile process (26). In support of the current findings, Jakobi et al. (21) also demonstrated no influence of Cr loading on resting twitch properties in the

forearm flexor muscles. Similarly, HRT increased in the first and second minutes of the intermittent contractions (Table 2) and subsequently decreased over the remaining 2 min. Although previous fatigue-related studies often report a significant slowing (increase in HRT) in relaxation rate (10), these responses are often seen during low-frequency stimulated twitches (i.e., 50 Hz) versus single twitches as used in the current study. In line with the current study, Vollestad et al. (42) demonstrated a similar pattern when examining single-twitch HRT during high-intensity (60% MVC) intermittent contractions, suggesting that, initially, ATP replenishment may be dependent on anaerobic energy (lactate and P_i); and in the latter half of the protocol, substrate turnover is dependent on aerobic oxidation, limiting metabolite accumulation. When evaluating the effects of Cr loading on resting HRT, our results are similar to those reported by Bazzucchi et al. (3) and Jakobi et al. (21) who reported no significant effect of Cr supplementation; however, contrasting findings have been reported by Wakatsuki et al. (43) in the rat SOL muscle. In addition to the contractile properties, M-wave characteristics in the present study were not altered by the fatigue protocol or Cr supplementation (Table 2). It is possible that the current duty cycle fatiguing protocol disrupted the intramuscular metabolic milieu but did not have a significant influence on peripheral excitation that has been reported previously using similar duty cycle protocols (26,34). Therefore, the intermittent nature and longer duty cycles in the present study may have allowed for metabolites to diffuse toward the end of the protocol, diminishing any measurable peripheral contributions to fatigue. The present results and similar results reported by Jakobi et al. (21) may be limited by a small sample size (n = 6 per group).

Previous literature has suggested that women have a greater resistance to fatigue during intermittent submaximal isometric contractions (19,36). As a result of a greater reliance on aerobic metabolism and high proportion of Type I muscle fibers, there is a decrease in metabolite accumulation, thereby delaying peripheral fatigue (20,26,35). In parallel, the potential metabolic buffering properties of Cr may enhance this delay in peripheral fatigue. Two previous studies using more dynamic, global assessments of neuromuscular fatigue (38,39) have demonstrated positive effects of Cr loading in women. In contrast, the current study is the first to evaluate the effects of Cr loading on evoked twitched properties in women. Although our data did not demonstrate that Cr supplementation delayed evoked twitch and M-wave properties in women, additional research should explore sex-based differences with the use of Cr on contractile properties, as well as controlled dynamic activities.

Body mass comparisons. This study demonstrated nonsignificant changes in body mass (Cr: 0.43 ± 0.14 kg) after Cr supplementation. These findings are similar to those of other previous studies demonstrating similar nonsignificant changes in body mass in women (0.01–0.60 kg) (8,22). To date, Cr loading in women has not been shown to induce significant increases in body mass. Although muscle Cr levels were not directly measured, and is a limitation to this study, the supplementation regimen used in the current study has repeatedly been shown to effectively augment muscle Cr content after just 2 d of ingestion, compared to the 5 d implemented in the present study (15,16).

SUMMARY

The vast amount of Cr supplementation research has supported its use as an ergogenic aid for improvements in strength, performance, and body composition. For example, Gotshalk et al. (13) reported increases in bench press and leg press strength, fat-free mass, and tandem gait performance after 7 d of supplementation. Rawson et al. (33) also demonstrated improvements in fatigue resistance during dynamic knee extensor contractions. However, questions remain regarding its effect on neuromuscular properties and its use in women. While a few studies have suggested that Cr supplementation may delay neuromuscular fatigue (33,38,39), the methods used in the current protocol provide sensitive evaluations of both central and peripheral components of fatigue. Our findings are similar to those reported by Jakobi et al. (21) who reported that short-term Cr loading did not influence isometric force and %VA, stimulate twitch properties, or influence the central and peripheral aspects of fatigue. Collectively, these results demonstrate the need to evaluate the effects of dynamic-versus-isometric fatigue-induced protocols as well as potentially use larger sample sizes when determining the effect of Cr supplementation on neuromuscular function.

The authors would like to thank FSI Nutrition for donating and blinding the creatine and placebo used in the current study. The authors also thank Matthew LaFleur for the drawing of Figure 2. Product was donated by FSI Nutrition (Omaha, NE). There is no other funding to disclose. None of the authors have any conflicts of interest to declare and no company or entity will benefit from these results.

The results of the present study do no constitute endorsement by American College of Sports Medicine.

APPLIED SCIENCES

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