The Effects of High Intensity Short Rest Resistance Exercise on Muscle Damage Markers in Men and Women

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Abstract

Heavens, KR, Szivak, TK, Hooper, DR, Dunn-Lewis, C, Comstock, BA, Flanagan, SD, Looney, DP, Kupchak, BR, Maresh, CM, Volek, JS, and Kraemer, WJ. The effects of high intensity short rest resistance exercise on muscle damage markers in men and women. *J Strength Cond Res* 28(4): 1041–1049, 2014–Within and between sexes, universal load prescription (as assigned in extreme conditioning programs) creates extreme ranges in individual training intensities. Exercise intensity has been proposed to be the main factor determining the degree of muscle damage. Thus, the purpose of this study was to examine markers of muscle damage in resistance-trained men ($n = 9$) and women ($n = 9$) from a high intensity (HI) short rest (SR) (HI/SR) resistance exercise protocol. The HI/SR consisted of a descending pyramid scheme starting at 10 repetitions, decreasing 1 repetition per set for the back squat, bench press, and deadlift, as fast as possible. Blood was drawn pre-exercise (pre), immediately postexercise (IP), 15 minutes postexercise (+15), 60 minutes postexercise (+60), and 24 hours postexercise (+24). Women demonstrated significant increases in interleukin 6 (IL-6; IP), creatine kinase (CK; +24), myoglobin (IP, +15, +60), and a greater relative increase when compared with men (+15, +60). Men demonstrated significant increases in myoglobin (IP, +15, +60, +24), IL-6 (IP, +15), CK (IP, +60, +24), and testosterone (IP, +15). There were significant sex interactions observed in CK (IP, +60, +24) and testosterone (IP, +15, +60, +24). Women completed the protocol faster (women: 34:04 ± 9:40 minutes, men: 39:22 ± 14:43 minutes), and at a slightly higher intensity (women: 70.1 ± 3.5%, men 68.8 ± 3.1%); however, men performed significantly more work (men: 14384.6 ± 1854.5 kg, women: 8774.7 ± 1612.7 kg). Overall, women demonstrated a faster inflammatory response with increased acute damage, whereas men demonstrated a greater prolonged damage response. Therefore, strength and conditioning professionals need to be aware of the level of stress imposed on individuals when creating such volitional high intensity metabolic type workouts and allow for adequate progression and recovery from such workouts.

Key Words metabolic stress, load prescription, myoglobin, creatine kinase, IL-6, testosterone, extreme conditioning

Introduction

Resistance training leads to changes in muscle fiber recruitment, size, and strength as a result of different factors including mechanical stress, neuromotor control, metabolic demands, and endocrine activities that ultimately regulate gene expression and protein synthesis (13,21,35). The magnitude of integration among these factors will determine the specific changes within the muscle fiber. Muscle growth is dependent upon the relationship between protein synthesis and breakdown (35). Mechanical deformation of muscle fibers as a result of muscle contraction, hormonal responses, immune responses, and cell signaling pathways leads to upstream signaling and eventually adaptation (35). These hormonal and immune responses differ in men and women (37,42) and are influenced by manipulation of the acute program variables (19,35).

As described in a previously published "sister article" (38), high intensity, short rest (HI/SR) resistance exercise is growing in popularity as a way to manipulate the program variables to increase metabolic work capacity (14). This training methodology is unique from other exercise programs in the way it incorporates resistance training (weight lifting, power lifting, and Olympic lifts), gymnastics style training (bodyweight exercises), and cardiovascular training completed in the shortest amount of time possible (14). This differs from high intensity interval training in the modes of training that are used and rest periods or lower intensity

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28(4)/1041–1049

Journal of Strength and Conditioning Research

intervals that are not incorporated in the program prescription. Each workout is a varied combination of said components, with a wide range of intensities, as load is prescribed as a universal weight or is based upon percentage of body weight (14). With this focus of time to completion and work performed, the effects of relative intensity and load prescription on structural muscle damage are unknown.

High intensity, short rest resistance exercise aims to increase the time under tension, which leads to an increased anabolic hormonal response and ultimately, muscle hypertrophy (13,21). In particular, the increased testosterone (T) response leads to increased protein synthesis and an anabolic state (13,21). Testosterone is a rapid signaling hormone and may be important in the priming of other mechanisms including the androgen receptor (AR) contributing, in part, to the increase in strength and muscle hypertrophy through resistance training (36). Moderate to heavy loads, large muscle mass activation, moderate to high repetitions, and short rest periods have been shown to enhance muscle AR content (36), elevate endogenous T (36), and stimulate an immune response (11,36) to promote anabolism and decrease catabolism, most likely due to higher metabolic demands and adrenergic response (21,35,36).

To achieve hypertrophy of the muscle fiber, an increased duration and intensity of exercise is necessary (19,21,35). This increase in duration and intensity leads to an increase in neuroendocrine and metabolic factors (26). These neuroendocrine factors play a role in the recruitment of leukocytes, macrophages, proinflammatory and anti-inflammatory cytokines, and muscle damage markers (23,26). Rest interval length has been shown to influence this neuroendocrine response when other resistance exercise factors have been kept constant (26). Short rest, high intensity training has consistently been shown to increase the amount of muscle damage (17), which also increases the neuroendocrine response and recruitment of said markers (26).

Damage to muscle fibers can occur during intense exercise bouts, which can include the disruption of the sarcolemma, swelling or disruption of the sarcotubular system, distortion of the contractile components of myofibrils, cytoskeletal damage, extracellular matrix changes, and release of cellular proteins (5,6). Indicators of muscle damage can include localized inflammation, a reduction in muscle strength and range of motion, and an increased amount of muscle proteins within the blood (5,6,8). Myoglobin, the oxygen binding protein in muscle, is released into the bloodstream in increasing amounts upon muscle damage (5). This damage can have a negative effect on the ability of the muscle cell to adapt to new stimulus, rebuild and repair muscle fibers, and synthesize satellite cells (36,40).

Creatine kinase (CK) and myoglobin are well known for their role in muscle disruption, where CK peaks around 24–72 hours (4,7,9), and myoglobin with a much shorter (hours) response (5,24). Creatine kinase is attached to the M protein of the muscle fiber (22), and myoglobin is the oxygen-binding protein found in muscle (5,7,22), which permeate the cell membrane after mechanical damage and are released into circulation. Myoglobin is about half the size of CK (22), which makes it easier to permeate the membrane; however, there is controversy over which marker is a better indicator of the degree of damage. Although there is a differing length of response between the 2 markers, likely due to the differing structural size and placement (22), we targeted these responses in the first 24-hour period, as it is likely that in a practical setting, another bout of exercise would be performed after this time period leading to compounding damage. Interleukin 6 (IL-6) has been demonstrated to be released by muscle tissue (11) in response to inflammatory action. There are many factors which influence the degree of release, including body mass index, body fat percentage, exercise intensity, exercise choice, and duration (11).

There is a sex difference in the hormonal response to resistance exercise (42). Young women typically show small or no changes in the elevation in plasma T values which may be attributed to plasma volume reductions, adrenergic stimulation, lactate-stimulated secretion, and the lack of Leydig cells (21). Leydig cells are proposed to be responsible for acute increases in T after resistance exercise in men (40). Basal concentrations of T in women are related to the magnitude of strength development induced by training and are dependent upon the state of the muscle tissue (21).

Muscle damage has also shown an attenuated response in women compared with men (13,18). When muscle damage is similar between men and women, women demonstrate an attenuated inflammatory response (13). Women demonstrate a greater initial response to infiltration of inflammatory cell populations, but women exhibit an attenuated long-term response (13). The inflammatory response is important in the regeneration of new muscle cells as it will signal to neutrophils and macrophages to remove the damaged debris (13). Local responses to tissue damage in women may be influenced by estrogen (42), which is thought to have a protective mechanism based on the chemoattractant neuroendocrine signals from the muscle and an increase in muscle cell membrane stability (42). Muscle damage markers such as CK have been shown to be decreased in response to exercise in women (42). Administration of estradiol has been shown to attenuate leukocyte activity after injury and the postexercise CK response in animals (18,42). Therefore, a short rest, high intensity exercise protocol may create extensive damage to the muscle fiber, but demonstrate different responses in men and women.

As part of a larger investigation (16,38), we chose to examine the impact of a consistent relative intensity (75% 1 repetition maximum [RM]), specific to individual ability, rather than universal load prescription due to safety, in a HI/SR protocol on markers of muscle damage, inflammation, and T response in men and women. Due to greater muscle fiber cross-sectional area (2,27,33), men have the potential to perform more work, leading to an increase in structural

Table 1. Subject anthropometrics and 1 repetition maximum strength.*

Subjects	Age (y)	Weight (kg)	Height (cm)	Body fat (%)	Back squat 1RM (kg)†	Bench press 1RM (kg)†	Deadlift 1RM (kg)†
Men	23.6 ± 3.5	77.8 ± 8.8	172.4 ± 4	9.3 ± 3.3	130.3 ± 15	97 ± 20.4	146.5 ± 27
Women	22.9 ± 2	68.6 ± 10.4	168.6 ± 9.4	13.6 ± 3.3	81 ± 15.2	50.5 ± 12.2	92.4 ± 19

*Data are presented as mean ± *SD*.
†1RM = 1 repetition maximum.

disruption. It was hypothesized that men would demonstrate a greater degree of muscle damage in comparison to women. As HI/SR exercise programs increase in popularity, these findings have applications for safe and effective exercise prescription to reduce muscle damage and injury, as HI/SR protocols are often implemented in sequential training days, compounding damage and increasing the likelihood of future injury. Therefore, the purpose of this study was to examine differences in markers of muscle tissue damage, inflammation, and T response to a HI/SR resistance exercise protocol between resistance-trained men and women.

Methods

Experimental Approach to the Problem

This study was conducted as part of a larger investigation (16,38) over a total of 6 visits, including a familiarization (visit 1), fitness test (visit 2), 1RM tests (visits 3 and 4), HI/SR protocol (visit 5), and a recovery visit (visit 6). The night before each testing session and the morning of testing, subjects were instructed to drink 2 cups of water to ensure proper hydration. Baseline testing consisted of a fitness test (2 minutes of push-ups, 2 minutes of sit-ups, and a 2-mile run) and 1RM tests for the back squat, bench press, and deadlift. Testing visits were spaced a minimum of 48 hours apart, with a minimum of 72 hours between visit 4 (1RM testing) and 5 (HI/SR protocol), to ensure that subjects were adequately rested before the acute protocol. The HI/SR protocol was performed in a descending pyramid routine at an intensity of 75% 1RM for each exercise, with verbal encouragement to finish as fast as possible. Subjects were also asked to refrain from ingestion of caffeine, alcohol, drugs, or anti-inflammatory medications for 24 hours before the HI/SR protocol. The recovery visit occurred 24 hours after the completion of the HI/SR exercise bout. Blood samples were obtained at pre-exercise (pre), immediate postexercise (IP), 15 minutes postexercise (+15), 60 minutes postexercise (+60), and 24 hours postexercise (+24) after the acute testing visit. Collection was terminated at +24 hours due to the fact that a subsequent HI/SR exercise bout would be conducted 24–48 hours after in a typical commercial exercise program.

Subjects

This study was approved by the University of Connecticut Institutional Review Board for use of human subjects in research. After subjects were instructed of the procedures, risks, and benefits of participation, each subject signed an informed consent document. Upon voluntary participation, subjects completed a medical history questionnaire, and each subject was cleared to participate by a university physician. Eighteen resistance-trained subjects (9 men, 9 women) participated in this study. As described previously (38), subjects had a minimum of 6 months resistance training experience (minimum 2 times per week), and performing the exercises included in the HI/SR protocol was a requirement for participation. Based on a self-reported physical activity questionnaire, subjects selected for inclusion in the study averaged participation in resistance exercise 3–4 times per week, with some type of cardiovascular training 2–3 times per week. Subjects were not enrolled in the study if they reported experience with a HI/SR training program.

Procedures

Acute Testing Visit. On visit 5, subjects reported to the laboratory in the morning and then consumed a standardized breakfast (approximately 320–350 calories) with a protein to fat to carbohydrate ratio of 20:35:45 (protein, fat, carbohydrate as percentage). Subjects were seated and rested for 90 minutes at which point an indwelling catheter was inserted into the antecubital vein. A baseline blood sample was drawn 15 minutes after insertion into the vein. After performing the standardized warm-up, subjects began the HI/SR protocol. The first set of the HI/SR protocol consisted of 10 repetitions of each of the 3 barbell exercises, back squat, bench press, and deadlift, respectively, in a descending pyramid fashion. Each progressive set decreased by 1 repetition, finishing with the final set of 1 repetition. Load was set at 75% of the subject's 1RM for each exercise. If the subject was unable to maintain the prescribed number of repetitions at the given load (determined by unsafe lifting technique or the need to rack the bar during the set), the weight was

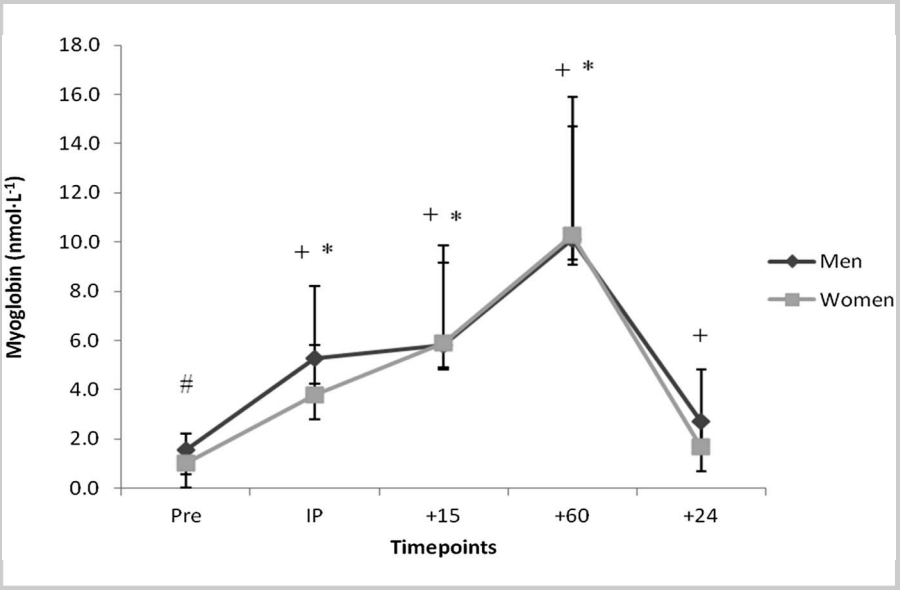

Figure 1. Myoglobin concentrations (mean) in resistance-trained men and women at pre-exercise (pre), immediately postexercise (IP), 15 minutes postexercise (+15), 60 minutes postexercise (+60), and 24 hours postexercise (+24) time points. *$p \leq 0.05$ from corresponding pre-exercise values in women; +$p \leq 0.05$ from corresponding pre-exercise values in men; #$p \leq 0.05$ from corresponding male values.

decreased by 5% 1RM for the next set. Each subject was instructed to complete the number of sets and repetitions as quickly as possible, with minimal rest in between sets and exercises. Any rest taken was voluntary, as no rest intervals were included, and verbal encouragement was given throughout the protocol to promote minimal rest. Two stopwatches were started as soon as the subject unracked the barbell from the squat rack, commencing the protocol, and were stopped once the subject reached full hip extension on the final repetition of the final set in the deadlift exercise. Subjects were then seated and the IP blood sample was drawn. Subjects remained seated for 60 minutes to obtain 2 more blood samples, during which time water was allowed ad libitum; however, food was not permitted until after the 60 minutes blood draw.

Recovery Visit. Subjects reported to the Human Performance Laboratory in the morning, 24 hours later. Before arrival, subjects ate a breakfast similar in calorie content (320–350 calories) and nutritional profile ratio (20:35:45; protein, fat, and carbohydrate as percentage) to the breakfast provided in visit 5. Participants were asked to refrain from exercise between the HI/SR and the recovery visit. Hydration was confirmed, and the +24 hour blood sample was obtained.

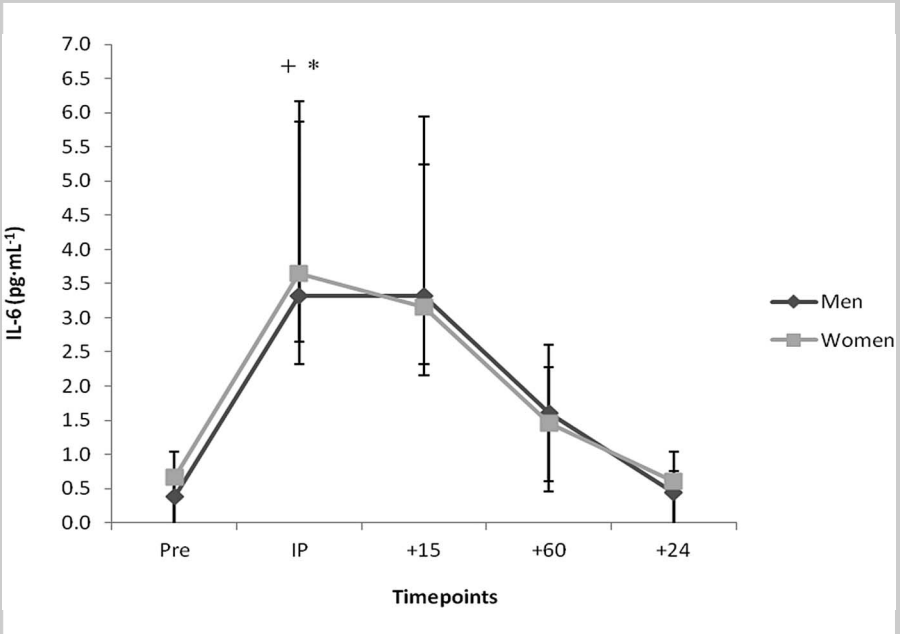

Figure 2. Interleukin-6 (IL-6) (pg·mL^{-1}) (mean ± *SD*) in resistance-trained men and women at pre-exercise (pre), immediately postexercise (IP), 15 minutes postexercise (+15), 60 minutes postexercise (+60), and 24 hours postexercise (+24) time points. *$p \leq 0.05$ from corresponding pre-exercise values.

Blood Collection. Blood samples were obtained at 5 different time points: pre, IP, +15, +60, and +24. An indwelling cannula (catheter) was inserted into the antecubital vein 15 minutes before the pre-exercise time point. The cannula was kept open with saline solution, and as a result, 3 ml of blood was extracted before each blood draw obtained to avoid dilution of the sample. Each sample consisted of ~22 ml of blood, with a total of about 120 ml collected throughout the protocol. Resulting serum was spun, aliquoted, and stored at −80° C for subsequent analyses.

Biochemical Analyses

Serum and EDTA vacutainers were used for the blood collection. Blood samples were analyzed in our laboratory using biochemical assays for T, myoglobin, and IL-6 at pre, IP, +15, +60, and +24 hours, and CK at pre, IP, +60, and +24 hours. Plasma myoglobin was analyzed by ELISA (CALBiotech, Spring Valley, CA, USA), with sensitivity of 0.30 nmol·L^{-1}, intra-assay coefficient of variation (CV) of 3.9% and interassay CV of 6.2%. The assay wavelength was read at 450 nm on a Molecular Devices VERSAmax tunable microplate reader. Serum T was analyzed by ELISA (CALBiotech), with sensitivity of 0.8 nmol·L^{-1}, intra-assay CV of 4.7% and interassay CV of 7.5%. The assay wavelength was read at 450 nm on a Molecular Devices VERSAmax tunable microplate reader. Serum IL-6 was analyzed by ELISA (Invitrogen, Grand Island, NY, USA), with sensitivity of 0.104 pg·mL^{-1}, intraassay CV of 7.1%, and interassay CV of 9.8%. The assay wavelength was read at 450 nm on a Molecular Devices VERSAmax tunable microplate reader. The serum creatine kinase-SL assay (SEKISUI, Charlottetown, Canada #326-30) was performed on human serum samples with modifications. The assay wavelength was read at 340 nm on a Thermo Scientific Biomate 3 Spectrophotometer. The CV was 2.3%.

Statistical Analyses

Data are presented as mean ± *SD*. All variables met the requirement for linear statistics. Testosterone, myoglobin, IL-6, and CK were analyzed with a 2 × 5 repeated measures analysis of variance with sex as a between subjects factor and time as the repeated measure. A Fisher Least Significant Difference (LSD) Post Hoc test was used to analyze differences at specific time points, sex differences, and a sex by time interaction. Significance was set at $p \leq 0.05$.

Results

The primary findings of this study were the significant increases in myoglobin for both men and women in comparison to pre-exercise values. Myoglobin demonstrated a similar absolute increase in both sexes; however, when put into relative terms, women demonstrated a greater increase. Creatine kinase was significant at all time points for men; however, only significant for women at the +24 time point. Interleukin 6 was significantly increased in men and women at IP; however, there were no sex interactions. Significant sex interactions were seen in T at all time points; however, significant increases from baseline were only seen in men at IP and +15. Men performed significantly more work in terms of absolute load; however, average working intensity was not significantly different between sexes.

Myoglobin

In both men and women, myoglobin concentrations increased similarly at corresponding time points. The only difference observed between sexes was at pre, where men demonstrated significantly higher concentrations compared with women. Men demonstrated significant increases in comparison to pre-exercise values at all time points, whereas women only demonstrated significant increases at IP, +15, and +60. Figure 1 illustrates the increase in myoglobin over all time points. When accounted for by fat free mass, women demonstrated a greater relative increase than men at +15 and +60 time points.

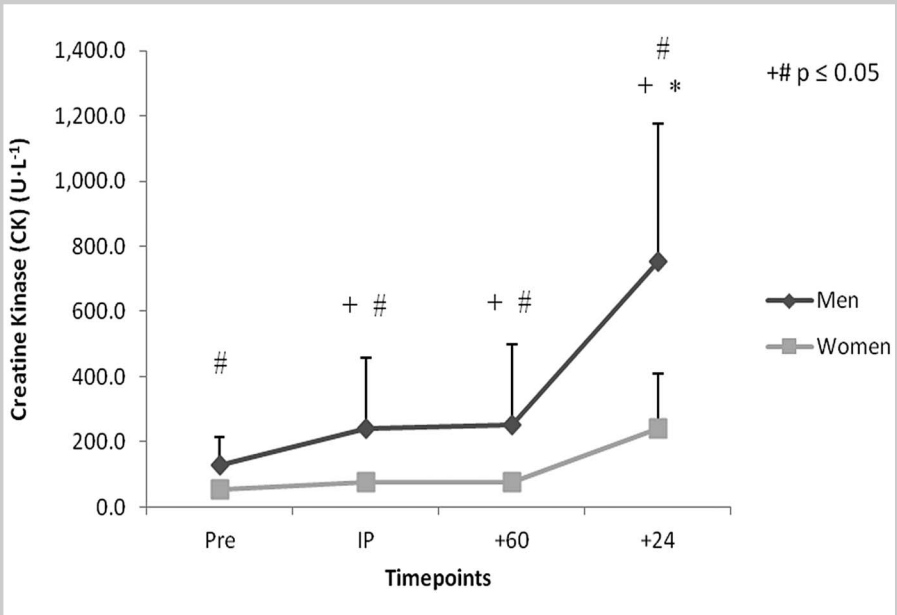

Figure 3. Creatine kinase (CK) concentrations in resistance-trained men and women (mean ± *SD*) at pre-exercise (pre), immediately postexercise (IP), 60 minutes postexercise (+60), and 24 hours postexercise (+24) time points. *$p \leq 0.05$ from corresponding pre-exercise values in women. +$p \leq 0.05$ from corresponding pre-exercise values in men; #$p \leq 0.05$ from corresponding male values.

Interleukin 6

As shown in Figure 2, there were no observed sex differences in IL-6 at any time point. Men demonstrated a significant increase at IP and +15, whereas women only demonstrated a significant increase at IP.

Creatine Kinase

As shown in Figure 3, in comparison to pre-exercise values, there were significant increases in CK at all time points for men. The only significant increase from baseline for women was shown at +24. In

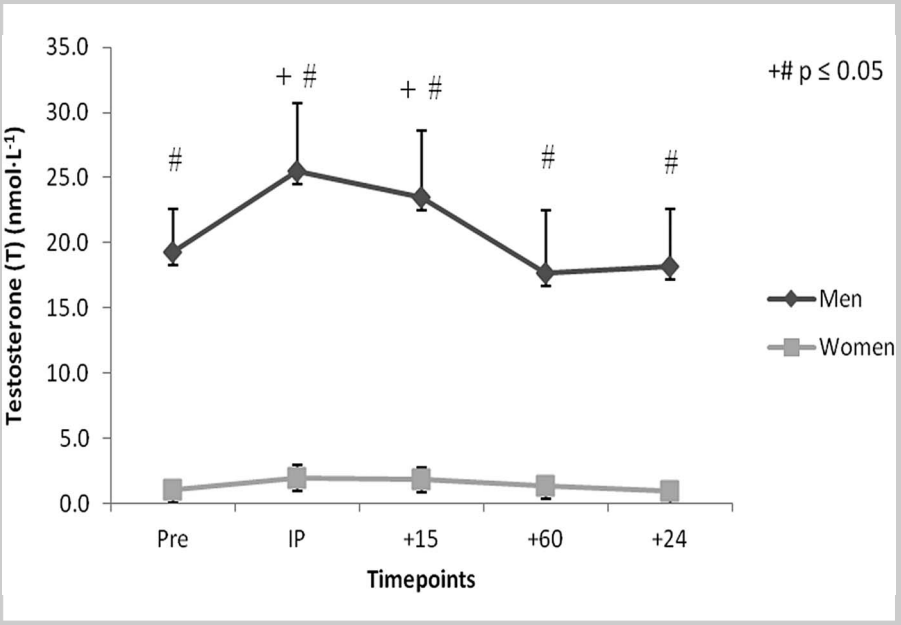

Figure 4. Serum testosterone (T) concentrations (mean ± *SD*) in resistance-trained men and women at pre-exercise (pre), immediately postexercise (IP), 15 minutes postexercise (+15), 60 minutes postexercise (+60), and 24 hours postexercise (+24) time points. *$p \leq 0.05$ from corresponding pre-exercise values in women; +$p \leq 0.05$ from corresponding pre-exercise values in men; #$p \leq 0.05$ from corresponding male values.

comparison to women, average concentrations for men were significantly increased at all time points.

Testosterone

As shown in Figure 4, T was significantly increased for men at IP and +15 in comparison to pre-exercise values. There were no significant increases observed in women. At peak average concentration (IP), men demonstrated values 18 times greater than corresponding values for women.

Stress Markers

Lactate and cortisol were also analyzed as measures of the stress of the exercise protocol. As previously reported (38), lactate concentration peaked at IP in both men (17.3 mmol·L^{-1}) and women (13.8 mmol·L^{-1}). Significant increases in lactate were seen at IP, +15, and +60 in both men and women, with a significant sex interaction at IP and +15 (mean ± *SD* men: 14.2 ± 2.3 mmol·L^{-1}, women: 9.1 ± 2.2 mmol·L.$^{-1}$). Cortisol peaked at +15 in both men (1860.2 nmol·L^{-1}) and women (1831.7 nmol·L^{-1}). Results showed significant increases in cortisol at IP, +15, and +60 in both men and women, with no significant sex interactions (mean ± *SD* men: 1247.4 ± 364 nmol·L^{-1}, women: 985.2 ± 438.1 nmol·L^{-1}) (38).

Total Work Performed

All participants completed 55 repetitions of each exercise, totaling 165 repetitions for the entire protocol. No participant maintained 75% 1RM for every exercise for the duration of the protocol. Women's mean back squat and deadlift 1RM were about 63% of men's and about 52% for bench press. Men performed significantly more work than women (mean ± *SD*: 14384.6 ± 1854.5kg; 8774.7 ± 1,612.7 kg, respectively). However, as reported elsewhere (38), women maintained a slightly higher relative intensity (averaged through all 10 sets and 3 exercises) throughout the protocol (mean ± *SD*: men: 68.8 ± 3.1%, women: 70.1 ± 3.5%). Women also on average completed the protocol faster than men (mean ± *SD*: men: 39:22 ± 14:43 minutes, women: 34:04 ± 9:40 minutes).

Discussion

The purpose of this study was to investigate the differences in muscle damage between men and women in response to a HI/SR resistance training protocol with a prescribed individual intensity based on repetition maximum. Consistent with our hypothesis, men demonstrated greater muscle damage than women. Although women completed the protocol faster, men performed significantly more work, leading to the increase in muscle damage.

No participant was successfully able to maintain 75% 1RM for all 165 repetitions performed during this protocol. On average, women's lower body strength was approximately 63% of men's, and their upper body strength was approximately 52% of men's, based on 1RM. Although women performed at a slightly higher average relative intensity than men, men performed 64% more work than women, and when accounted for by fat free mass, men performed 38% more work than women. Consistently, women completed the protocol 5 minutes and 18 seconds (15.6%) faster than men. Based on these results, men were subjected to greater loads, but women were subjected to a greater cardiovascular stress, further supporting the difference in the CK and myoglobin responses.

This type of HI/SR exercise elicits a multitude of cellular and hormonal responses. The metabolic stress activates many signaling cascades, thereby mobilizing inflammation factors, growth factors, hormones, and various muscle proteins (35). Inflammatory cytokines signal immune and hormonal responses, leading to muscle hypertrophy (31,35), given muscle damage is not excessive. The hormonal response in terms of muscle hypertrophy (testosterone) is

known to be greater in men than women (21), which is consistent with our findings at every time point. Although there was an increase of almost twice the resting concentration in women, it was not significant, also consistent with previous findings (30,39,40). In both men and women, the greatest increase in T was IP, consistent with cell signaling processes (35). This blunted response of T may be due to the dramatically increased concentration of cortisol (a catabolic hormone) (22), as reported by Szivak et al. (38). Cortisol increased similarly to other metabolically demanding protocols (15,20). The domination of cortisol would lead to greater catabolic functions and inhibit anabolic actions, such as protein repair (22).

Interleukin 6 is known as an "inflammation responsive" (31) cytokine as it is involved in inflammatory processes but is indirectly anti-inflammatory. Men and women demonstrated a similar increase (women experienced a slightly higher peak), with the greatest concentration at IP, consistent with other reports (10). Hormones, sex, body composition, and exercise intensity have been reported to play a role in IL-6 concentrations (11); however, according to Fischer (10), duration is the most important factor. Most investigations with IL-6 demonstrate a significant increase in response to aerobic exercise, and limited increases with resistance exercise. Although this was a demanding exercise bout with high intensity, in comparison to other studies investigating IL-6, the total time under tension was short. Interleukin 6 has been shown to have the greatest systemic concentrations with consistent longer duration exercise such as running (10). This suggests that a short immediate inflammatory response is associated with this type of exercise protocol in resistance-trained subjects in both men and women. Although there was a similar response in men and women, women demonstrated greater increases at IP, whereas men peaked at +15. The response associated with this type of training seems to peak shortly after cessation of exercise; however, there seem to be high and low responders associated with this cytokine. As previously mentioned, body composition may play a role in this as it is also released in small amounts from adipose tissue as well (11). There was no association with the IL-6 response and the total work performed for total time.

Although there was only a short response in inflammation, as previously reported, serum cortisol and plasma lactate measures demonstrated the stress associated with this protocol (38). Greater peak lactate values have been reported by Kraemer et al. (20), albeit at a greater relative intensity. The peak lactate recorded in our study was still among the highest seen in similar high intensity exercise (1,29,41). These measures indicate a great amount of stress experienced by this exercise program, leading to an increase in muscle damage.

Creatine kinase is an intramuscular protein released in circulation when damage occurs and is cleared from the blood by the reticuloendothelial system (25). Creatine kinase is a well-known marker but arguably qualitative (24) as there are high and low responders. CK is known to be associated with damage from mechanical stimuli, with many factors affecting the concentration in the blood. Men demonstrated a greater amount of intramuscular damage than women after the IP time point. In both men and women, the peak concentration was at +24 hours, which is consistent with other studies which investigated rest interval length, intensity, and volume (23,26,32). Women have consistently demonstrated lower basal and postexercise CK concentrations in comparison to men, which is also true in our study (3,4,13,18). This may be attributed to the greater muscle mass in men, therefore, more fibers may be mechanically damaged and release such proteins. Although the intensity was based on individual ability, men performed significantly more work, leading to greater potential for structural damage. Due to the fact that CK normally peaks at about 24–72 hours after an intense training bout (4,7,9,12,28), the peak CK response in the current study may have been missed without a 48 or 72 hours post blood draw; however, we were attempting to capture the +24 hours response considering the sequential nature of HI/SR protocols, with another bout of exercise typically performed 24 hours after the initial bout, leading to compounding damage.

Estrogen has been proposed to exhibit a protective role in tissue damage and local inflammatory responses to cellular stress by maintaining membrane stability (3,4,18,42). Bär et al. (3) investigated this with ovariectimized rats in response to strenuous exercise. The absence of the production of estrogen resulted in a CK response similar to the male rats (an acute significant increase), whereas the ovariectimized rats that received estrogen treatment experienced a CK response similar to the female rats (no significant acute increase). Wolf et al. (42) reported no significant changes in estradiol receptors expressed after exercise or between sexes when matched for similar estradiol concentrations, proposing the sex interaction may be due to differing hormonal signaling cascades. It remains to be seen whether the lower CK values in women are due to membrane stability or if the muscle fibers are truly less damaged (18).

Myoglobin is considered to be a more sensitive marker of muscle damage, as it rises immediately after muscle damage (5,8,24,43). It differs from CK in that it is cleared by the kidneys (25). Myoglobin traditionally demonstrates an immediate increase after exercise, returning to basal concentrations shortly thereafter (4,5,7,24). However, in the present study, men demonstrated a significant increase at all time points in comparison to pre-exercise values, including +24, indicating a prolonged response. Women were consistent with previously established values (5,8,24,43), as significant increases were demonstrated at all time points except +24. The only sex interaction was demonstrated at pre-exercise, where men demonstrated higher basal concentrations. An interesting finding of our study was the similarity in the magnitude of increase between men and women. At peak

myoglobin concentration, women were 10-fold greater than corresponding pre values, whereas men were only sixfold greater. When accounted for by kilogram of fat free mass, women demonstrated a greater relative response at +15 and +60. This may be due to the difference in clearance velocities between subjects (6,25).

Sorichter et al. (34) investigated CK and myoglobin responses to downhill running in men and women. Absolute values postexercise were significantly increased in men compared with women. This significant sex interaction was attributed to the greater muscle mass in men and greater membrane stability in women (34). This is in contrast to our study, as the only sex interaction for myoglobin was at the pre-exercise time point; however, our protocol included both concentric and eccentric muscle actions with an external load. The inconsistency associated with our results is that women demonstrated greater muscle damage when assessed by myoglobin, whereas men demonstrated greater damage when assessed by CK. These findings suggest muscle damage may be expressed differently between sexes due to different hormonal interactions and signaling pathways, when associated with a metabolically demanding exercise bout; however, more research is needed to investigate these differences.

As previously mentioned, program prescription associated with commercial extreme fitness programs, and more specifically load prescription is rather vague. Broad examples of programming have been provided (14); however, exact derivation is not explained, and examples include percentage of bodyweight and loads set at a certain weight but not based upon 1RM or relative intensity. Even with an individually based prescription employed, there was still a large variation between subjects. For example, in our resistance-trained females, myoglobin measured at the same time point for one subject was threefold higher than pre-exercise, while a different subject was 19-fold higher. Our minimum inclusion criteria included resistance training experience of 2 times per week for 6 months with no previous exposure to a metabolically demanding HI/SR protocol. This is representative of the training background of many people who begin commercial exercise programs, which when coupled with universally prescribed load, can lead to greater possibility for injury and extreme muscle damage. The diverse backgrounds and training history of each participant should be taken into consideration when programming training.

In summary, women demonstrated a faster inflammatory response with increased acute damage, whereas men demonstrated a greater prolonged damage response. The greater total work performed by men may be the overall contributor to the greater CK response and therefore structural damage even when prescription was based on individual ability. This prolonged damage response in men can contribute to compounding damage when intense exercise bouts are performed on consecutive days. This suggests that a HI/SR resistance exercise protocol elicits significant muscle damage in men and women; however, more research is needed to identify the mechanisms and signaling pathways between the vast sex differences in muscle damage markers. Due to these different endocrine responses between men and women, exercise intensity and load should be prescribed on an individual basis to avoid injury and extreme muscle damage.

Practical Applications

The results of this study demonstrate differences in the extent of muscle damage seen in men and women in response to an acute bout of HI/SR resistance exercise and expand upon data presented in a previously published sister paper (38) on the acute effects (cortisol, lactate) of an HI/SR protocol. Men demonstrate a greater prolonged response to damage, whereas women demonstrated a more acute response. This prolonged response can lead to compounding damage over consecutive exercise sessions, and can contribute to muscle injury. As demonstrated in this study, although this metabolically demanding protocol was an atypical exercise session for the subjects, prescription based on individual percentage of repetition maximum still resulted in a great amount of structural damage. Program intensity should be progressed appropriately for the individual as opposed to universal load prescription, which can potentially elicit extreme amounts of damage. Coaches and fitness professionals as well as participants should be aware of differences in individual performance capabilities and training history and should properly progress or scale training programs as needed. In doing so, coaches can ensure that the training intensity is properly scaled to the athlete's ability, thereby minimizing the risk of injury or excessive muscle damage. Furthermore, the muscle damage response observed in the present study points to the importance of appropriate recovery periods to allow for optimal tissue recovery, given the sequential nature of HI/SR protocols, which are typically conducted with few rest days in between exercise bouts.

Acknowledgments

The authors want to thank a dedicated group of subjects who made this study possible. This study does not reflect any official policy or endorsement by the National Strength and Conditioning Association, and this study was supported by internal laboratory funding.

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