THE EFFECTS OF RUNNING VOLUME IN TRAINING ON MUSCLE DAMAGE, MUSCLE SORENESS, AND RECOVERY AFTER A MARATHON: AN OBSERVATIONAL STUDY

A Manuscript Style Thesis Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Science – Human Performance

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College of Science and Health
Human Performance

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THE EFFECTS OF RUNNING VOLUME IN TRAINING ON MUSCLE DAMAGE, MUSCLE SORENESS, AND RECOVERY AFTER A MARATHON: AN OBSERVATIONAL STUDY

By Kevin J. Gries

We recommend acceptance of this thesis in partial fulfillment of the candidate's requirements for the degree of Master of Science – Human Performance.

The candidate has completed the oral defense of the thesis.

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ABSTRACT


The purpose of this investigation was to determine if running volume provides a protective effect to reduce muscle damage, muscle soreness (DOMS), and improve the perceived recovery status (PRS) after a marathon. Ten subjects’ training logs were collected including distance run each week and the longest weekly run. Before the marathon (PRE), a blood sample was given to determine serum creatine kinase (CK) levels. DOMS and PRS were determined using separate 0-10 Likert scales. These tests were then completed again one day (D1), three days (D3), and six days (D6) post-marathon. CK peaked D1 and remained elevated in post-marathon sessions. DOMS increased PRE to D1, and returned to baseline D3. PRS decreased significantly from PRE to D1 and did not return to PRE during testing period. Large effect sizes were found between PRE and all post-marathon sessions on CK, DOMS, and PRS data. No significant correlations were found when comparing long run or volume of training to peak and D6 values for CK, DOMS, and PRS. The data indicate that neither the volume of training, nor the length of longest run are related to the magnitude or recovery of muscle damage, DOMS, or PRS.
ACKNOWLEDGEMENTS

I would first like to thank my thesis chair, Dr. Glenn Wright. My interest in muscle physiology began to grow exponentially during Muscle Physiology class. Along with sparking my interest in muscle fiber analysis, he was also an incredible mentor for my thesis paper. Whether it was on the weekends or early mornings, I could ask him any question and he would respond very quickly. He also showed great patience when working through the project with me.

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INTRODUCTION

Muscle damage most notably occurs after unaccustomed eccentric exercise, which causes soreness within the muscle groups being used. The greatest amount of muscle damage has been found to occur one to three days after unaccustomed eccentric exercise (Vihko, Salminen, & Rantamaki, 1978). This delay is attributed to the slow rise and fall of proteolytic enzyme activity, which has been found to be elevated for three to five days after exhaustive exercise (Vihko et al., 1978). Due to the difficult nature of determining the amount of individual muscle damage, indirect markers, such as: lactate dehydrogenase, 3-methylhistidine, myoglobin, creatine kinase (CK) (Sorichter, Puschendorf, & Mair, 1999) and perceived delayed onset of muscle soreness (DOMS) (Clarkson & Hubal, 2002) are often used.

After unaccustomed exercise, the chief complaint within the individual is DOMS. Soreness typically peaks 24 to 48 hours following exercise and may last up to seven days (Clarkson & Hubal, 2002). During this period, the damaged muscle fibers may not be able to function correctly and cause a decrease in force, range of motion, and ultimately performance (Edwards, Hill, Jones, & Merton, 1977). However, after the damaged muscle fibers are healed, there appears to be a protective mechanism against further muscle damage called the repeated bout effect (Highman & Altland, 1963).

The repeated bout effect refers to adaptations within the muscle following a single bout of unaccustomed, usually eccentric, exercise that protects the muscle from further muscle damage with subsequent eccentric exercise and therefore a decrease in the
indirect markers of muscle damage (Highman & Altland, 1963). These adaptations include: more efficient neural recruitment patterns (Enoka, 1996; Moritani, Muramatsu, & Muro, 1988), increased strength of noncontractile connective tissue elements (Armstrong, Warren, & Warren, 1991), the removal of weak sarcomeres (Byrnes et al., 1985) and the longitudinal addition of sarcomeres (Fridén, Seger, Sjöström, & Ekblom, 1983). The muscular adaptations suggested by the repeated bout effect depend on the volume and intensity of the initial bout. Howatson, Van Someren, and Hortobagyi (2007) reported a greater attenuation of the indirect markers of muscle damage when volume was high and intensity was low in the initial exercise bout, compared to intensity being high and volume being low. On the contrary, Chen, Nosaka, and Sacco (2007) reported that as intensity increases and volume lessens, the greater attenuation of muscle damage occurred, suggesting intensity is a larger contributor than volume in the repeated bout effect. Due to the contrary studies, more research is needed.

During long distance running, there are a high degree of eccentric contractions to absorb the ground reaction force during each foot contact, causing the high magnitude of muscle damage. More specifically, marathons have been found to cause significant muscle damage as indicated by large increases in CK and DOMS (Hikida et al., 1983; Kobayashi, Takeuchi, Hosoi, Yoshizaki, & Loepky, 2005; Siegel, Silverman, & Holman, 1981).

Recommended training volume for optimal completion of the marathon ranges between 48 kilometers (Eyestone, 2014) and 206 kilometers per week (Billat, Demarle, Slawinski, Paiva & Koralsztein, 2001) based on the physiological adaptations observed during endurance training. However, to our knowledge the effects training volume has on
muscle damage and recovery status following a marathon has not been researched. It is likely that muscle damage and DOMS limits recovery and the ability to return to training in marathon runners. Therefore, the purpose of this study was to determine the relationship between volume of marathon training and muscle damage, perceived recovery status and the return to pre-marathon levels after running the marathon.
METHODS

Experimental Approach to the Problem

To determine the effects of running volume on the muscle damage and recovery after running a marathon, we compared indirect measures of muscle damage and perceived recovery status (PRS) to the longest training session and average weekly training volume during the 10 weeks prior to running a marathon. Serum CK and DOMS were used as indirect markers of muscle damage. Recovery status was determined using the PRS scale after the completion of a light exercise session. All data was collected at one day (D1), three days (D3), and six days (D6) following the marathon and compared the same variables measured pre-marathon (PRE), one to two days before the marathon.

Subjects

In total, 10 healthy subjects (6 females, 4 males) participated in the study. All subjects were recruited from the greater La Crosse, Wisconsin area who were in training for a certified Boston Qualifier marathon. Before the commencement of the study, ethical approval was contained by the University of Wisconsin-La Crosse IRB committee. All subjects were informed of the possible risks and provided written informed consent prior to participation of the study. Descriptive characteristics of the subjects are displayed in Table 1.
Table 1. Descriptive characteristics of the subject population (mean ± SD)

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Men (n=4)</th>
<th>Women (n=6)</th>
<th>All (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>25.8 ± 6.3</td>
<td>30.7 ± 7.9</td>
<td>28.7 ± 7.3</td>
</tr>
<tr>
<td>Height (meters)</td>
<td>180.1 ± 11.3</td>
<td>161.5 ± 4.3</td>
<td>1.69 ± 0.114</td>
</tr>
<tr>
<td>Mass (kg)</td>
<td>79.2 ± 11.4</td>
<td>58.4 ± 7.5</td>
<td>66.7 ± 13.7</td>
</tr>
<tr>
<td>Weekly volume (km)</td>
<td>42.8 ± 29.5</td>
<td>23.9 ± 8.7</td>
<td>51.9 ± 36.3</td>
</tr>
<tr>
<td>Longest run (km)</td>
<td>39.8 ± 36.7</td>
<td>20.1 ± 3.7</td>
<td>42.9 ± 42.9</td>
</tr>
<tr>
<td>Finishing time (minutes)</td>
<td>204.1 ± 58.4</td>
<td>255.8 ± 15.7</td>
<td>235.1 ± 44.6</td>
</tr>
</tbody>
</table>

Testing and Procedures

Subjects visited the Human Performance Laboratory at the University of Wisconsin-La Crosse four different days as part of this study. Each visit was at a similar time of day, and each subject abstained from exercise for the day prior to the session. The purpose of session one (PRE) was to record the baseline measurements of CK, DOMS, and PRS. Subjects reported to the laboratory 24-48 hours prior to their respective marathon. After completion of a questionnaire asking about the subject’s training and nutritional habits, 50 microliters of capillary blood was drawn via finger stick to be used for the blood analysis. After the blood sample was collected, subjects were then asked to walk down a flight of ten stairs, 19.05 cm tall by 27 cm wide, as normally as possible without assistance. The subjects then rated their soreness using a Likert scale of 0-10 with 0 being “no soreness at all” and 10 being “was unable to walk down the stairs”. Finally, subjects ran 1.6 km at 80% of their marathon goal pace on a treadmill (Fitnex Fitness Equipment, Inc., Dallas, TX). After completion of the run, subjects were asked, “If you were to race again today, based on the run, how recovered do you feel you are?” using the PRS scale (Figure 1) developed by Laurent et al. (2010). The same order was followed in the days following the marathon on D1, D3, and D6, with a questionnaire that
included questions about their recovery protocol and dietary intake since the last visit to the laboratory.

**Perceived Recovery Status Scale**

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
<th>Expected Performance</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Very well recovered / Highly energetic</td>
<td>Expect Improved Performance</td>
</tr>
<tr>
<td>9</td>
<td>Well recovered / Somewhat energetic</td>
<td>Expect Improved Performance</td>
</tr>
<tr>
<td>8</td>
<td>Moderately recovered</td>
<td>Expect Similar Performance</td>
</tr>
<tr>
<td>7</td>
<td>Adequately recovered</td>
<td>Expect Similar Performance</td>
</tr>
<tr>
<td>6</td>
<td>Somewhat recovered</td>
<td>Expect Declined Performance</td>
</tr>
<tr>
<td>5</td>
<td>Not well recovered / Somewhat tired</td>
<td>Expect Declined Performance</td>
</tr>
<tr>
<td>4</td>
<td>Very poorly recovered / Extremely tired</td>
<td>Expect Declined Performance</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. The Perceived Recovery Status Scale (Laurent et al., 2011).

**Blood Analysis**

Blood samples were centrifuged at 13,000 revolutions per minute for 3 minutes (MSE Micro-Centaur, Sanyo, Beckenham, UK), stored in a refrigerator at 2-8°C Celsius, and analyzed within seven days of collection. During the blood analysis, 2.0 milliliters of Creatine Kinase Reagent (Catalog #C7512; Pointe Scientific Inc., Canton, MI) was pipetted into a cuvette warmed to 37°C Celsius in a water bath. Upon reaching 37°C Celsius, 50 microliters of high value control solution was pipetted into the reagent and remained in the water bath for two minutes. After 2 minutes, the cuvette was then transferred to the spectrophotometer (Spectronic 20 D+, Thermo Fisher Scientific, Madison, WI) which was zeroed out by distilled water, at a wavelength of 340 nm. Absorbance was measured immediately and every minute for the next three minutes. The change in absorbance per minute was averaged and multiplied by a factor of 6,592 in order to find the general CK value. If the control was within the acceptable range, this process was repeated again using a low value control solution. If the low value control produced a CK value within the acceptable range, samples were then able to be read. The same process was repeated
using 50 microliters of serum collected from the subject to find their serum CK value in terms of international unit (IU) per liter.

Statistical Analysis

Three separate analysis of variance (ANOVA) with repeated measures and Bonferroni post hoc analysis were used to determine significant differences in the dependent variables (DOMS, PRS, and CK) from PRE to post-marathon trials. Outliers were found via the boxplot method and removed (Warner, 2013). Effect size (ES) was calculated using Cohen’s d to determine the magnitude of the effects using the criteria: <0.2, minimal; 0.2-0.5, small; 0.5-0.8, medium; >0.8, large (Cohen, 1988). Pearson correlations were used to find relationships among the independent variables (volume and long run) and dependent variables (DOMS, PRS, and CK) on peak and D6. To determine the magnitude of the dependent variables, peak values were used since not all subjects peaked on the same day. Values on D6 were also used to determine the relationship with return to baseline. Statistical significance was accepted at an alpha value of <0.05. Data were evaluated using SPSS version 22.0 software (SPSS Inc., Chicago, IL).
RESULTS

Results of CK, DOMS, and PRS are reported in Table 1. Comparisons of CK, DOMS, and PRS were made to PRE in order to determine return to baseline. Complications during the CK assay caused the data for three subjects to be discarded. Another subject’s CK data was removed due to being an outlier via the boxplot method described by (Warner, 2013). Therefore, CK data represent six subjects. No statistical difference was identified for CK among PRE and the different time points; however, large effect sizes were identified indicating practical differences existed. Creatine kinase values increased from PRE to D1 (p=0.23, ES=1.55), remained elevated on D3 (p=0.91, ES=0.99) and on D6 (p=1.0, ES=0.97).

Table 2. CK, DOMS, and PRS at measured time points (mean ± SD).

<table>
<thead>
<tr>
<th></th>
<th>PRE</th>
<th>D1</th>
<th>D3</th>
<th>D6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatine Kinase (IU)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=6</td>
<td>71.6 ± 23.8</td>
<td>560.1 ± 443.9</td>
<td>262.2 ± 270.5</td>
<td>240.7 ± 244.2</td>
</tr>
<tr>
<td>DOMS (AU)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=10</td>
<td>0.20 ± 0.08</td>
<td>5.45 ± 0.99*</td>
<td>1.70 ± 0.63</td>
<td>0.85 ± 0.51</td>
</tr>
<tr>
<td>PRS (AU)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=10</td>
<td>9.50 ± 0.22</td>
<td>2.60 ± 0.65*</td>
<td>5.80 ± 0.63*</td>
<td>7.15 ± 0.53*</td>
</tr>
</tbody>
</table>

IU, International Units; AU, arbitrary units; CK, Creatine Kinase; DOMS, delayed onset muscle soreness; PRS, Perceived Recovery Status; PRE, Pre-marathon; D1, 1 day post-marathon; D3, 3 days post-marathon; D6, 6 days post marathon.

*Significant difference (p<0.05) from PRE

Delayed onset muscle soreness increased from PRE to D1 (p= 0.002, ES=7.5). By D3, DOMS was not significantly different from PRE (p=0.22); however a very large effect size was still present (ES=3.3). On D6, DOMS was not significantly different from PRE (p= 0.96) although a very large effect size was observed (ES=1.8).
Perceived recovery status decreased significantly compared to PRE on D1 and had a very large effect size \((p<0.001, \text{ES}=14.8)\). On D3, perceived recovery status remained lower than PRE \((p<0.001, \text{ES}=7.84)\) and remained below PRE on D6 \((p=0.008, \text{ES}=5.79)\).

Pearson correlations were determined for Peak values and D6 values for each dependent variable compared to the subject’s longest run and weekly volume (Table 2). Peak values are the values for each dependent variable with the greatest change from PRE, regardless of which test day it was observed on. The values given as D6 provide information of the state of each variable six days following the marathon. No significant correlations were found between longest run \((p=0.27 \text{ to } 0.64, r=-0.16 \text{ to } 0.39)\) or weekly volume \((p=0.19 \text{ to } 0.87, r=-0.55 \text{ to } 0.31)\) and any the dependent variables.

Table 3. Correlation data of CK, DOMS and PRS at Peak and D6 compared to Long Run and Volume of marathon training

<table>
<thead>
<tr>
<th></th>
<th>CK Peak (n=6)</th>
<th>CK D6 (n=6)</th>
<th>DOMS Peak (n=10)</th>
<th>DOMS D6 (n=10)</th>
<th>Lowest PRS (n=10)</th>
<th>PRS D6 (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long Run</td>
<td>(r=-0.136)</td>
<td>(r=-0.386)</td>
<td>(r=-0.387)</td>
<td>(r=-0.159)</td>
<td>(r=0.235)</td>
<td>(r=0.305)</td>
</tr>
<tr>
<td></td>
<td>(p=0.644)</td>
<td>(p=0.450)</td>
<td>(p=0.269)</td>
<td>(p=0.660)</td>
<td>(p=0.514)</td>
<td>(p=0.392)</td>
</tr>
<tr>
<td>Volume</td>
<td>(r=-0.306)</td>
<td>(r=-0.550)</td>
<td>(r=-0.452)</td>
<td>(r=-0.253)</td>
<td>(r=0.305)</td>
<td>(r=-0.061)</td>
</tr>
<tr>
<td></td>
<td>(p=0.288)</td>
<td>(p=0.258)</td>
<td>(p=0.190)</td>
<td>(p=0.481)</td>
<td>(p=0.392)</td>
<td>(p=0.868)</td>
</tr>
</tbody>
</table>

CK, Creatine Kinase; DOMS, Delayed Onset of Muscle Soreness; PRS, Perceived Recovery Status; D6, 6 days post-marathon
DISCUSSION

The primary purpose of this study was to investigate the relationship between volume of marathon training and longest run on muscle damage, as indicated by DOMS and CK, and PRS. The hypothesis was that volume of marathon training and longest run would have a significant relationship in the attenuation of peak muscle damage, improve PRS, and faster return to baseline of the tested variables. To test this hypothesis, correlational data compared peak values of each dependent variable rather than using the data from different days following the marathon since not all subjects or dependent variables peaked on the same day. Peak values showed the extremes of muscle damage and a decrease in perceived recovery status. Values on D6 were also used in correlation data to determine if there was a relationship between weekly mileage or longest run and the return to baseline status of each dependent variable. However, the results of this study indicated muscle damage and PRS were not related to the longest run or the volume of marathon training in the last 10 weeks prior to running a marathon.

A significant amount of muscle damage occurred from the marathon as indicated by DOMS and CK. Both CK and DOMS peaked at D1, suggesting the greatest amount of muscle damage was evident 1 to 2 days post-marathon. Although no difference was found in DOMS between PRE and D3 or D6, a practical difference was found by a large effect size (ES=0.97 to 1.55). Nosaka (2008) reported that following repeated maximal eccentric muscle actions of the forearm flexors, DOMS peaks one day post unaccustomed exercise, and returns to baseline gradually over 5 to 6 days. On the contrary, Quinn and Manley (2012) found no change in DOMS in males who were training for a marathon.
immediately post and 6 days post a 26 km long run, despite significant increases in CK. The conflicting results in studies suggest that there is no general pattern of DOMS after unaccustomed exercise and may be different based upon training status, and type of unaccustomed exercise.

Serum CK peaked 7.8-fold greater than baseline at D1 and remained elevated throughout the testing period. Kobayashi et al. (2005) found a 15-fold increase in serum CK, 24 hours post-marathon and returned to near baseline 1 week following the race. Peak CK one day post-marathon was also found by Kratz et al. (2002) who reported a 22-fold increase in CK-MB (a muscle specific subunit of CK), 24 hours post-marathon. The lower relative peak of CK in the current study may be due to our subject pool consisting of five women and one man, compared to men only in the study by Kobayashi et al. (2005), and mostly men in Kratz et al. (2002). Women have been shown to have a lower peak in CK likely due to higher levels of estrogen, which may protect cell membranes from muscle damage (Tidus, 2005). In addition, our study was an observational study where the subjects’ recovery activities were not controlled. Subjects in the study by Kobayashi et al. (2005) were restricted to daily activities and did not return to training until 2 weeks after the marathon. Due to the subjects not being restricted from training in the current study, three of the six subjects with CK data returned to exercise after D3, potentially preventing them from returning to baseline CK. The differences between DOMS and CK return to baseline in our study may be due to the subjectivity of the DOMS scale (Nosaka, Newton, & Sacco, 2002; Quinn & Manley, 2002), and/or the variability in CK measures.
The repeated bout effect is a phenomenon that, following a single bout of unaccustomed exercise, protects the muscle from further muscle damage from subsequent similar exercise sessions as a result of adaptations within the muscle (Highman & Altland, 1963). The results of the current study found no significant correlations between DOMS or CK and volume of marathon training or longest run. This would suggest that neither the volume of a single run, nor total volume of training, provides a protective adaptation causing an attenuation of DOMS and CK via the repeated bout effect.

In the current study, PRS was significantly lower on D1 compared to PRE, signifying the subjects would expect a decrease in performance if they raced again that day. Recovery status at PRE was recorded to determine if the subjects felt recovered going into the marathon. In the study validating the Perceived Recovery Status scale used, Laurent et al. (2011) suggested a rating of “5” was an adequate recovery status where the subject could expect a similar performance. If the subject’s PRS was greater than “7”, the subject suggested they felt they could exceed their performance. If the subject perceives to expect similar or improved performance, they will likely return to productive training, which was the case in the current study as three subjects felt adequately recovered to return to exercise on D3 after reporting 7 to 8 on the Perceived Recovery Status scale. Many subjects remained below PRE recovery status on D3 and D6 indicating that even six days after the marathon they did not feel as energized as before the marathon. Interestingly, return to baseline took longer for PRS during the testing period compared to DOMS and CK. Since recovery is a function of physiological, psychological, and emotional factors (Jeffreys, 2005), the psychological or emotional factors may take longer to return to baseline (Bishop, Jones, & Woods, 2008). During a
marathon, there is a large amount of psychological stress as runners need to push through mental barriers of fatigue, thus causing psychological and emotional fatigue, which may prolong the recovery period. Recent research has demonstrated that perceived stress and perceived recovery were reported to take up to 2 weeks following an ultra-marathon race (Nicolas, Banizette, & Millet, 2011). The recovery period in the Nicolas et al. (2011) study is likely longer than the current study due to the greater race distance. No significant relationship was found between PRS and the volume of marathon training and the longest run. This may suggest that the marathon stimulated a greater amount of psychological and emotional stress than the subject’s training.

Limitations of the current study include the observational study design. The subjects were not limited to what they could do for the six days following the marathon. More control of the subject’s recovery strategies, including exercise and nutrition may help decrease the variability of Peak and D6 values for CK, DOMS, and PRS during the week following the marathon. Another limitation was the small sample size (n=10) in our study causing a lack of significant power. The small sample size may be a reason why a large effect size was found while no statistical differences were found. There also was a lack of homogeneity of independent and dependent variables as there was a wide range of performances. A greater number and homogeneity of subjects may help improve significance. Lastly, a more specific assay should be used for muscle damage. A general CK assay, such as the one used, may not be specific enough to measure purely muscle damage and produced a large standard deviation, likely preventing reaching significance.
Practical Applications

Volume of marathon training, as well as longest run, showed little if any benefit in attenuating muscle damage and soreness, or improving recovery status. In order to return to productive training after a marathon, muscle damage and soreness should return to pre-marathon levels in order to train most optimal conditions. Based on the results of the current study, coaches should not expect the marathoner to return to productive training based on their long run or volume of miles run 10 weeks prior to the marathon. Coaches should also not increase volume of training in order to improve recovery after a marathon.
REFERENCES


APPENDIX A

INFORMED CONSENT
Title of Study: Volume of Marathon Training on Muscle Damage, Soreness and Recovery: an Observational Study

Primary Researcher: Kevin Gries
407 23rd Street
La Crosse, WI 54601

Emergency Contact: Kevin Gries
(920) 980-5562
Gries.Kevi@uwlax.edu

Purpose and Procedure
- The primary purpose of this study is to determine the relationship of volume of marathon training on muscle damage, muscle soreness, and speed of recovery.
- The secondary purpose of this study is to develop an understanding of the volume of miles ran needed to enhance recovery after a marathon in order to continue training.
- My participation will involve four total sessions which will be conducted one to two days prior to the marathon, one day post marathon, three days post marathon, and six days post marathon.
- Each session will last approximately 20 minutes.
- During all tests, I will complete a questionnaire. A small amount of blood will be then be collected from my fingertip to measure for amount of muscle damage.
- I will then walk down a flight of stairs and be asked to rate how sore I am. The session will then be concluded after I run a mile at a speed slower than my average marathon pace and will be asked how ready I am to race again.

Potential Risks
- I may experience finger soreness from the blood sample and muscle soreness and fatigue from running the marathon.
- Individuals trained in CPR and First Aid will be in the testing location and testing will be terminated if complications occur.
- The risk of serious or life-threatening complications, for health individuals, like myself, is near zero.

Rights & Confidentiality
- My participation is voluntary. I can withdraw or refuse to answer any questions without consequences at any time.
- I can withdraw from the study at any time for any reason without penalty.
- The results of this study may be published in scientific literature or presented at professional meetings using grouped data only.
- All information will be kept confidential through the use of number codes. My data will not be linked with personally identifiable information.
Possible benefits

- I and other athletes may benefit by understanding how the volume of miles before a marathon can impact the rate of recovery.

Questions regarding study procedures may be directed to Kevin Gries (920-980-5562), the principal investigator, or the study advisor Dr. Glenn Wright, Department of Exercise and Sport Science, UW-L (608-785-8689). Questions regarding the protection of human subjects may be addressed to the UW-La Crosse Institutional Review Board for the Protection of Human Subjects, (608-785-8124 or irb@uw lax.edu).

(Date) (Signature of Participant)

(Date) (Signature of Individual Obtaining Consent)
APPENDIX B
SESSION QUESTIONNAIRES
## Training Log

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Pre-Race Questionnaire

What is your goal time to complete the marathon?

Have you done speed work or high intensity intervals? If yes please describe.

Have you strength trained during these last 10 weeks? If yes, please describe.

What is your longest run during these last 10 weeks? What pace did you run your long runs?

Do you have a stretching routine? If yes, please describe.

Do you currently ingest supplements and/or anti-inflammatory medications? If yes, what kind and how much per day?
Post Race Questionnaire

Marathon Time ____________________________

Have you taken medications and/or supplements since the competition of the marathon? If so what kind and how much per day?

Have you used ice or heat therapy for your sore muscles (including Icy-Hot or any similar topical cream)? If yes, how often per day?

Did you get a massage within 24 hours of the marathon? If so, how long? What body parts?

Have you done any modes of exercise since the marathon? If yes, what type and duration?

What did you eat and drink immediately after the marathon until 4 hours after the completion of the marathon?

How often did you ingest energy gels, Gu’s, sports drink (i.e. Gatorade) or other carbohydrate throughout the marathon?

Any cool down activity or stretching within 30 minutes of completion of marathon
Session 3 and 4 Questionnaire

Have you taken medications and/or supplements since the previous session? If so, what kind and how much per day?

Have you used ice or heat therapy for your sore muscles (including Icy-Hot or any similar topical cream) since last session? If yes, how often per day?

Have you done any modes of exercise since last session? If yes, what type and duration?
APPENDIX C

SORENESS SCALE
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APPENDIX D

REVIEW OF THE LITERATURE
Review of the Literature

The purpose of this paper is to review the literature to understand the mechanisms attributed to exercise-induced muscle damage, including the efficacy of using creatine kinase as a marker to determine the degree of muscle damage. This paper is also intended to summarize the different aspects that affect muscle damage, delayed onset of muscle soreness, and recovery as they relate to running a marathon.

Muscle Damage

Muscle damage most notably occurs after unaccustomed eccentric exercises, which causes soreness within the muscle groups being utilized. Muscle damage occurs at the cellular level, most notably, the sarcolemma (Fridén, Sjöström, & Ekblom, 1983). During muscle contraction, adenosine triphosphate (ATP) is required to detach the actin and myosin cross bridges following shortening. However, lengthening of the sarcomere during eccentric muscle actions leads to forcible cross bridge detachment. The forcible cross bridge detachment can lead to a lack of myofilament overlap, the result of overstretched sarcomeres. These overstretched sarcomeres are repeatedly strained or “popped” and cause damage to the muscle protein titin, which will cause the sarcolemma to be disrupted and broken down (Morgan, 1990). The damage of the sarcolemma will then cause an imbalance of calcium ions within the sarcoplasmic reticulum and the sarcoplasm which will activate proteases that break down the Z-lines and possibly components of the thin filaments (Hikida, 1978) within the myofibrils. The damage of the muscle membrane releases mitochondria and the damaged components of the myofibrils into the extracellular space. The increase in cellular debris in the extracellular space will
then allow erythrocytes and macrophages to enter the muscle fiber as part of the inflammatory response (Hikida, Staron, Hagerman, Sherman, & Costill, 1983).

A review of the literature by Sayers and Dannecker (2004), suggested that the ultrastructural damage initiates the inflammatory response which causes edema of the damaged area within the muscle. The increase in fluid may put pressure on nerve endings causing pain—pain is associated with muscle damage and may be due to the proliferation of monocytes into the tissues. Monocytes synthesize prostaglandins which make the type III and type IV afferent nerve endings more sensitive, causing an increased perception of pain (Sayers & Dannecker, 2004).

Other studies have observed ultrastructure damage after subjects participated in running a marathon. For example, Hikida et al. (1983) observed significant damage of ultrastructural proteins after a marathon via muscle biopsies from the runners. Immediately post-marathon, muscle fibers were found to contain free erythrocytes and mitochondria in the extracellular spaces. Erythrocytes and leukocytes were also found within the gaps of the myofibrils, while Z-line streaming and empty basal lamina tubes were also observed. Interestingly, these examples of muscle damage were only found in few muscle fibers immediately post marathon and were extremely variable. Warhol, Siegel, Evans, and Silverman (1985) also surveyed muscle biopsies immediately post marathon and found the mitochondria damage to be independent of the myofibrillar damages, along with the previously mentioned indicators of muscle damage. The mitochondrial damage was indicated by the destruction of mitochondrial matrix and the dissolution of the cristae, the inner membrane of the mitochondria.
The greatest amount of muscle damage has been found to occur 1 to 3 days after the marathon. Muscle damage after exercise has been attributed to the slow rise and fall of proteolytic enzyme activity, which has been found to breakdown muscle up to 3-5 days after exhaustive exercise (Vihko, Salminen, & Rantamaki, 1978). Vihko, et al (1978) showed the sarcolemma often disrupted and the sarcomeres heavily shortened into contracture knots, the mitochondria in this region were sometimes swollen as well. Due to the sarcolemma being severely damaged, extensive gaps were observed within the muscle fiber. Mitochondria were often free in the extracellular space in both damaged and undamaged muscle fibers, and in some instances myofibrils were also found in the extracellular space. From 3 to 7 days post marathon, a high amount of disrupted sarcolemma and disorganized myofibrils were still apparent (Vihko, et al. 1978).

After 7 days, evidence shows that most of the damaged fibers begin to resynthesize intracellular glycogen (Warhol et al., 1985). Existing myofibrils may also contain satellite cells as well as interstitial cells resembling fibroblasts. This indicates that myofibrils are still in the process of rebuilding, which was initiated at 3 days post marathon. The rebuilding process has been found to be fully complete 10 weeks after the marathon (Warhol et al., 1985).

Structural damage occurs most notably during eccentric exercise (Armstrong, 1984) likely because during eccentric contractions the type II, fast twitch motor units are selectively recruited (McHugh, Connolly, Eston, & Gleim, 1999) requiring a large amount of force from the recruited fibers. Therefore, most of the damage within the muscle fibers during unaccustomed exercise occurs in the type II fibers (McHugh et al., 1999). However, during endurance exercise, such as the marathon, any muscle damage,
which may include a loss of mitochondria from the muscle cells, may diminish performance due to loss of the high amount of energy that mitochondria produce. Thus, muscle damage during a marathon and marathon training needs to be minimized for optimal performance.

**Markers for Muscle Damage**

Muscle damage after an exercise bout can be difficult to ascertain through direct measurement such as magnetic resonance imaging (MRI) or a muscle biopsy, as these processes take specific training and equipment. Instead, an indirect measurement of muscle damage can be found by testing for muscle proteins within the blood stream. These muscle proteins include: lactate dehydrogenase, 3-methylhistidine, myoglobin, and creatine kinase (CK) (Sorichter, Puschendorf, & Mair, 1999). Creatine kinase measurement will be examined in the following paragraphs.

When the structural integrity of the muscle cell is degraded by the unaccustomed exercise and excessive eccentric contraction forces, muscle cell proteins and the enzymes involved within those muscle proteins will then be found in the blood stream at different times post-exercise. For example, with muscle damage at the sarcolemma, CK that escapes from muscle cells will be taken up by the lymphatic system where it is transported to the thoracic duct and enters the blood stream at the subclavian vein. Blood concentrations of CK peak approximately 24 hours post-exercise when exercise causing muscle damage has occurred (Havas, Komulainen, & Vihko, 1997). Myoglobin, another popular marker for muscle damage, will peak at 24-72 hours post-exercise, but has a half-life of 2-3 days compared to a half-life of 1.5 days for CK. Creatine kinase also has a higher sensitivity compared to myoglobin (Eberman & Kahanov, 2011). Measurement of
these enzymes in the blood following exercise allows the estimation of the level of muscle damage.

Studies testing the extent of muscle damage in healthy individuals during exercise most commonly use CK and/or myoglobin. Creatine kinase is tested most commonly due to the low cost of the assays, and the magnitude of increase after muscle damage is much higher than the aforementioned proteins (Clarkson, 2007). Creatine kinase is the key enzyme for maintaining a constant ATP/ADP ratio during rapid energy turnover and catalyzes phosphate exchange between the high free energy phosphates ATP and phosphocreatine (PCr) via the reaction: \( \text{PCr} + \text{ADP} + \text{H}^+ \rightleftharpoons \text{Creatine (Cr)} + \text{ATP} \) (Wallimann, Wyss, Brdiczka, Nicolay, & Eppenberger, 1992).

Creatine Kinase is a dimer which consists of two subunits, M and B. These subunits can be combined together to form CK-MM, CK-MB, and CK-BB (Burger, Richterich, & Aebi, 1964). In skeletal muscle, the CK-MM dimer makes up 96-100% of the total CK within the muscle. Trace amount of CK-MB and CK-BB also exists in skeletal muscle (Kanemitsu, 1988). Elevated total CK, as well as CK-MB, in the serum of healthy individuals have been found to be sensitive markers of muscle damage (Apple et al., 1985).

Base levels of serum CK in the general population are variable: 35-175 U/L. Due to the relatively large variability between individuals, studies should only compare CK levels as a percent change from different data collection sessions. After intense exercise, CK levels can rise to 10,000-200,000 U/L. This is, however, in extreme circumstances, and the individual may be experiencing rhabdomyolysis—clinically diagnosed muscle damage—which can ultimately lead to kidney failure. There is no universal standard for
how much CK can increase before it is considered serious muscle damage, but CK levels
greater than 5,000 U/L are generally considered indicative of severe muscle damage
(Baird, Graham, Baker, & Bickerstaff, 2012).

Delayed Onset of Muscle Soreness

After unaccustomed exercises, muscle damage can induce delayed onset of
muscle soreness (DOMS) (Clarkson & Hubal, 2002). In order to prevent soreness, the
magnitude of muscle damage needs to be attenuated. A variety of studies have found that
exercise induced muscle damage has resulted in decreased strength and rate of force
development, signifying DOMS is linked to a decrease in neuromuscular ability (Eston,
Finney, Baker and Baltzopoulos, 1996). Along with the decrease in neuromuscular
ability, DOMS causes a decrease in force, range of motion, and performance due to the
damage of the ultrastructural proteins (Edwards, Hill, Jones, & Merton, 1977).

The chief complaint with individuals who have muscle damage is the delayed
onset of muscle soreness (DOMS); however, DOMS cannot always be a reliable estimate
of muscle damage, due to the subjective pain the subject is feeling. Quinn and Manley
(2012) observed that CK increased over the 72 hours following a submaximal 26 km run,
but subjects did not report soreness. Quinn and Manley (2002) hypothesized that this
weak correlation between DOMS and CK may have been due to the subjectivity of the
DOMS scale. The subjects were not given a familiarization period to be able to determine
how the various levels of the scale felt like. Furthermore, Nosaka, Newton and Sacco
(2002) also reported a weak correlation between DOMS and indirect muscle damage
markers, such as CK, during various eccentric exercise protocols. The authors suggested
that this weak correlation may again be due to the subjectivity of the DOMS scale.
Repeated bout effect

Following an initial bout of damaging exercise, a successive bout of similar exercise typically results in less muscle damage (Slade, Bickel, & Dudley, 2004). This is known as the repeated bout effect. First observed by Highman and Altland (1963), the repeated bout effect refers to adaptations within the muscle following a single bout of unaccustomed, usually eccentric, exercise that protects the muscle from further muscle damage with subsequent eccentric exercise and therefore a decrease in the indirect markers of muscle damage. A number of theories have been proposed to explain the repeated bout effect, but no specific theory seems to be overwhelmingly accepted. Here, the neural theory variations, the connective tissue theory, and the cellular theory will briefly be overviewed.

The neural theory suggests that neural adaptations may play a role in the repeated bout effect. This theory proposes that the repeated bout effect changes motor unit activation which limits the extent of damage to the muscle fibers. As stated previously, eccentric movements require selective activation of a fewer number of type II, high threshold motor units (Enoka, 1996; Moritani, Muramatsu, & Muro, 1988). Golden and Dudley (1992) proposed that this highly selective motor unit activation during eccentric contractions provides an opportunity to “learn” more efficient recruitment for a repeated bout. However, there are other variations of neural adaptation theory. One such variation proposes an increased type I motor unit activation to contribute to the eccentric contraction, thus decreasing the amount of force needed per muscle fiber involved (McHugh et al., 1999). Others have proposed an increased synchronization of motor unit firing following eccentric activity (Pierrynowski, Tiidus, and Plyley, 1987). These
suggested neural adaptations would lead to a greater sharing of the eccentric load on
greater number of muscle fibers, decreasing the force imposed on each fiber, thus
lessening damage.

Eccentric exercise seems to improve force production and neural adaptations
greater than concentric exercise. Hortobagyi et al. (1996) found eccentric training
increased eccentric strength 3.5 times more than concentric training increased concentric
strength in maximal voluntary contractions during a single leg knee flexion after a 12
week training protocol. These authors also observed that eccentric training increased
EMG activity seven times greater during concentric tests compared to concentric training
on an eccentric test. Due to this significant increase in EMG activity, as well as strength
from eccentric training, the authors suggested that neural adaptations are greater
following eccentric training than following concentric training. The neural adaptations
from eccentric training support the neural theory by increasing recruitment of muscle
fibers during eccentric contractions, causing a decrease of muscle damage after an initial
bout of training.

However, a study by Nosaka, Newton, and Sacco (2002) provides evidence that
the neural theory of the repeated bout effect may be accompanied by other mechanisms
as well. Nosaka, et al. (2002) compared muscle damage following high intensity
eccentric elbow flexion exercises within 4 days of each other on untrained individuals.
The subjects completed one set of 24 repetitions in which the elbow flexors were
electrically stimulated at the highest intensity they could tolerate and then were forcibly
extended the elbow from 90 degrees to full extension at a constant joint velocity. The
subjects had significant muscle damage after the first session, followed by significantly
less muscle damage after the second bout of exercise 2 weeks later, demonstrating the
effects of the repeated bout effect did occur. Since motor unit recruitment was stimulated
via an electrical stimulation rather than through neural activation, this study suggests that
the attenuated muscle damage after an initial bout of exercise may be due to factors other
than neural adaptations.

The connective tissue theory to explain the nature of the repeated bout effect has
been proposed by Armstrong, Warren, and Warren (1991). The authors suggest that
muscle damage occurs when the noncontractile connective tissue elements, such as the Z-
line proteins desmin and synemin, are disrupted and myofibrillar integrity is lost. During
an eccentric contraction, the sarcomeres' elongation is highly non-uniform as some
sarcomeres maintain length while others are stretched beyond the point of filament
overlap (Morgan, 1990). The excessive stretch of sarcomeres past the point of filament
overlap causes excess stress on the passive structures and connective tissue to maintain
the serial tension (Morgan, 1990). This may lead to damage to the sarcomere, including
connective tissue damage, Z-line streaming and damage to the thin filaments also seen in
marathon running (Hikida, 1978).

Support of the connective tissue theory comes from Lapier, Burton, Almon and
Cerny (1995). The authors found a significant increase in ratio of intramuscular
connective tissue to muscle mass after a bout of unaccustomed exercise in rats. This was
also accompanied by an increase in passive stiffness, defined as change in muscle force
over change in muscle length. As the sarcomeres become forcibly over-stretched during
eccentric exercise, muscle damage occurs. McHugh et al. (1999), suggested that an
increase of intramuscular connective tissue, and thus passive muscle stiffness, there may be a greater resistance to over-stretch and cause muscle damage.

Lastly, another proposed theory contributing to the repeated bout effect is the cellular theory. The cellular theory of the repeat bout effect suggests that muscle damage is the result of irreversible sarcomere strain during eccentric contractions (McHugh et al., 1999). Aspects of the cellular theory include removal of weak sarcomeres that have been damaged with the initial unaccustomed eccentric exercise (Byrnes et al., 1985) and longitudinal addition of sarcomeres (Fridén, Seger, Sjöström, & Ekblom, 1983).

Newham, Jones, Ghosh, and Aurora (1988) found a significant relationship between muscle fiber length and the magnitude of muscle damage. As muscle fiber length increased, there was significantly lower magnitude of muscle damage. Newham et al. (1988) suggested based off of this relationship, to attenuate muscle damage on the next exercise bout, there may be a longitudinal addition of sarcomeres to increase the length of the fiber. The cellular theory is also indirectly supported by the elevated rates of protein synthesis after dorsiflexion eccentric exercise in mice (Ingalls, Wenke, Nofal, & Armstrong, 2004). The increase in protein synthesis may suggest that sarcomeres are being added longitudinally. Due to contradicting and inconsistent findings, more research is needed to find the mechanism of action for the repeated bout effect. In reality, it is most likely a mixture of all of the above theories.

The repeated bout effect has been shown to vary in its protective function based upon the volume of stress during the initial activity that produced muscle damage (Howatson, Van Someren, & Hortobagyi, 2007). For example, 2 weeks after performing three sets of 15 maximal voluntary repetitions of eccentric elbow flexion, Howatson et al.
(2007) observed a significant reduction in muscle damage when repeating the same protocol. However, a group of subjects that performed only one set of ten maximal voluntary repetitions of the elbow eccentric extensions on the first exercise session experienced significantly greater muscle damage when performing three sets of 15 reps in the final exercise session 2 weeks later. There was no difference in work done between the first and second sessions.

On the contrary, Chen, Nosaka, and Sacco (2007) found intensity of the first exercise bout is a larger factor to receive the biggest muscle damage protection offered by the repeated bout effect. Subjects were placed in to groups performing 30 eccentric elbow flexion at 100%, 80%, 60%, and 40% of their MVC. Two to three weeks later, the subjects then completed 30 eccentric elbow flexion repetitions at 100% of their MVC. Those who completed the higher intensity in the first exercise bout had the least amount of muscle damage after the second exercise bout. Based off of these contradictory results, more research is needed to determine the best strategy to gain the most benefit from the repeated bout effect.

If the time period between the unaccustomed exercise bout and the next exercise bout is too long, the repeated bout effect has shown not to occur. Nosaka, Clarkson, McGuiggin, and Byrne (1991) found indirect markers of muscle damage, such as CK, maximal voluntary contraction, range of motion, and soreness following exercise were lower at 6 weeks following the initial bout of unaccustomed exercise compared to 10 weeks following the initial bout. The indirect measurements of muscle damage utilized by Nosaka et al. (1991) have been shown to attenuate after a secondary bout of the unaccustomed exercise on the elbow flexors linearly from 2 weeks after the initial bout
until 36 weeks after the initial bout. The repeated bout effect has been found to lose its preventative effect 36 weeks after the initial training bout (Nosaka, Sakamoto, Newton, & Sacco, 2001; Nosaka, 2008).

Training status is an important factor when studying mechanisms of adaptability within the muscle. While comparing indicators of muscle damage between trained male distance runners and untrained males, Evans et al. (1986) found the trained men had higher resting CK levels and attenuated peak CK levels 24 hours post exercise compared to the untrained individuals who peaked at 5 days following exercise on a cycle ergometer at 250 watts for 45 minutes. The untrained subjects also had a 10-fold greater increase in CK compared to the peak CK for the trained subjects. Higher resting CK levels have been seen previously in trained male athletes following 9 weeks of training; however, trained female athletes in the same study did not see a significant increase in resting CK following training (Apple et al., 1987).

In addition, Hoffman, Kang, Ratamess, and Faigenbaum, (2005) observed an attenuation of muscle damage over the course of a football season. An attenuation of muscle damage has also been observed as training status changed through the course of a football season. Hoffman, Kang, Ratamess, and Faigenbaum, (2005) observed significant elevations of CK during preseason football practices; however CK levels returned to baseline after 3 weeks of practice and were maintained through the rest of the season. The authors proposed a potential “contact adaptation” of skeletal muscles from the repeating trauma of collisions during repeated football practices during the football season.
In marathon running, there is also repeated trauma from foot contacts to the surface of the road and may produce a similar “contact adaptation” during distance running. Hamill, Bates, Knutzen, and Sawhill (1983) found a positive relationship between running velocity and ground reaction force. It is also likely that the “contact adaptation” is very similar to the mechanisms described about the repeated bout effect mentioned previously. Therefore, as running velocity increases over the course of a marathon, more trauma of the skeletal muscles may occur, suggesting that running at velocities at or above marathon pace during training may be more beneficial to minimize muscle damage via the repeated bout effect. However to our knowledge, no study has been completed investigating the relationship between different endurance training loads and muscle damage following the marathon.

Endurance Running and Muscle Damage

Studies have shown a significant increase in muscle soreness and muscle damage up to 7 days after long distance running (Hikida et al., 1983; Kobayashi, Takcuchi, Hosoi, Yoshizaki, & Loepky, 2005; Siegel, Silverman, & Holman, 1981). The specific nature of why submaximal, long duration exercise causes this significant amount of muscle damage is still unknown. However, it has been found that during endurance exercise, a high percentage of type I, highly oxidative, motor units are activated. It was originally proposed that motor units were selectively degenerated during endurance training (Vihko et al., 1978); thus, type IIa fibers may be selectively degenerated, type IIx fibers would convert to IIa with training, and total percentage of type II fibers would decrease. This relative decrease would then cause a relative increase in type I, highly oxidative fibers, which tends to be found in endurance athletes (Hikida et al., 1983).
Muscle damage during endurance exercise, consisting of high volume and low intensity contractions has been found to be significant. Muscle damage has been shown to occur during a high volume of concentric and eccentric contractions, such as downhill running (Baumann et al., 2014). After a 30 minute bout of downhill running at 55% \( V_{O2\text{peak}} \), CK doubled and there was a decrease in muscle force two days following the bout of exercise.

Another study by Millet et al. (2011) found significant changes in muscle function and damage after the completion of a 166-km race down a mountainous terrain, where the start line had an altitude of 9,500 m greater than the finish line. Compared to baseline CK, experienced runners showed a 127-fold increase in CK immediate post-race, then decreased to 26-fold from baseline 2 days later and decreased further to only two-fold greater than baseline 5 days following the race. CK returned to baseline on the 6\(^{th}\) day following the race.

During endurance running performance, there is significant muscle damage (Hikida et al., 1983). Following a relatively flat terrain marathon, post-race CK values tripled from baseline, peaked 15-fold compared to baseline measures 24 hours following the race and then returned to near baseline 1 week following the race (Kobayashi, et al., 2005). This pattern was confirmed by a study from Kratz et al. (2002), where CK was six-fold higher than baseline immediately following a marathon and peaked 24 hours later where CK was 18-fold higher compared to baseline. The lesser rise in CK during the marathon studied by Kratz et al. (2002) compared to the previous running studies by Millet et al. (2011) and Baumann et al. (2014) is most likely due to the large amount of
eccentric contractions that occur in downhill running that occurred during the latter studies.

Gender and Age Differences as a Factor of Muscle Damage

Gender differences may also cause a difference in muscle damage and CK levels. Studies on female animals have demonstrated lower baseline levels of CK and blunted CK responses to exercise (Amelink, Koot, Erich, Van Gijn, & Bar 1990; Komulainen, Koskinen, Kalliokoski, Takala, & Vihko, 1999). In humans, women have been found to have a faster responding inflammatory response causing an earlier peak in CK. Men demonstrated a greater prolonged inflammatory response to exercise causing a later peak in CK compared to women (Heavens et al., 2014). Upon comparing men and women’s CK response from high intensity exercise, men had approximately four-fold greater peak compared to women (Heavens et al., 2014).

A possibility of why women have an attenuated peak in CK following exercise may be due to their greater levels of estrogen. In amenorrheic women, as well as postmenopausal women who are not taking hormone replacement treatments, peak CK levels were greater compared to premenopausal eumenorrheic women (Thompson, Scordilis, & De Souza, 2006). Premenopausal women likely have a lesser response due to higher estrogen levels in seen in postmenopausal and amenorrheic women. Estrogen was found to possibly be important for protecting cell membranes from muscle damage. Therefore, if estrogen levels are low, cell membranes may be more susceptible to damage (Tiidus, 2005).

Women who completed 9 weeks of endurance training have been found to have no change in resting CK following training (Apple et al., 1987). In contrast, men subjects
in the same study saw an increase in resting CK after 9 weeks of endurance training (Apple et al., 1987). This demonstrates that the endurance training in women may not realize the same amount of muscle damage or women may have a greater muscle adaptability via the repeated bout effect from endurance training. Differences in estrogen and muscle mass between men and women may account for these differences in CK response. However, more research is needed to determine the exact mechanism.

Age may also play a role in the extent of muscle damage during exercise. Fell and Williams (2008) found that skeletal muscle in aging athletes can lead to greater exercise-induced damage and a slower repair and adaptation response. However, this was refuted when Lavender and Nosaka (2006) found no significant changes in muscle damage after unaccustomed eccentric elbow flexion by males 19-25 years old compared to 41-57 years old individuals. More research is needed on muscle damage and age to determine if there is a relationship.

**Marathon Performance**

The amount of muscle damage and marathon completion time has been found to have an inverse relationship; CK levels in the blood in the 24 hours following a marathon are higher in those with the lower (faster) marathon completion times (Siegel, Silverman, & Lopez, 1980). Runners who completed the marathon in 3 hours and 30 minutes or less had a 25-fold increase in CK compared to an 11-fold increase in CK in those who completed the marathon above 3 hours and 30 minutes. A hypothesis of this conclusion may be due to the positive correlation between ground reaction force and total impulse versus running velocity (Hamill et al., 1983). Since a faster marathon pace relates to a greater amount of force per foot contact, there will be a greater amount of trauma per
each foot contact that the body will have to absorb. As suggested by Hoffman et al. (2005), a high amount of trauma from collisions can lead to a large amount of muscle damage. Therefore, the greater velocity an athlete runs during a marathon, the greater amount of trauma per foot contact, leading to a greater amount of muscle damage.

In a marathon, the athlete has to use their energy wisely as using their stores too early in the race may lead to slowing down. Foster et al. (2012) found that athletes who slowed their pace the most in the last 10-kilometers of a marathon, compared to the first 15-kilometers, ran a slower overall time. On the contrary, marathon runners who completed the marathon faster than 3 hours ran near their average training pace for the entire race. This would indicate that marathon performance may be related to the ability to maintain a fairly constant pace. Foster et al. (2012) also found that as the volume of marathon training increased, as well as the number of runs greater than 30-km, the amount of slowdown decreased, suggesting training causes helpful physiological adaptations. Therefore, marathon pacing is not only important for the optimal performance of the marathon, but it also may play a role in the amount of muscle damage. Del Coso et al. (2013) measured subject's paces every 5-km of the marathon and found those who slowed their pace each 5-km, while still giving a maximal effort throughout the marathon had significantly higher blood markers for muscle damage. A potential reason for the decrease in pace and increase of muscle damage is due to improper substrate utilization during the marathon. Baracos, Greenberg, and Goldberg (1984) indicated that during high metabolic demanding activities, such as marathon running, muscle damage may occur. In order for the intracellular calcium to return to the sarcoplasmic reticulum after a muscle contraction, ATP is needed. If the cell cannot
metabolize substrates and match the ATP demands of the cell, intracellular glycogen will remain in the cytosol. The buildup of calcium in the cytosol activated the calcium dependent proteolytic pathways, causing muscle damage.

Therefore, it is evident that marathon training plays an important role in marathon performance as well as marathon pacing which may play a role in the magnitude of muscle damage the marathon will cause. Marathon training is comprised of the volume of miles ran and the intensity those miles are ran at. Billat, Demarle, Slawinski, Paiva, and Koralsztein (2001) collected training data to compare top-class marathoners (2 h 6 min 34 s to 2 h 11 min 59 s for males and 2 h 25 min to 2 h 30 min 59 s for females) versus high-level marathon runners (2 h 12 min to 2 h 16 min for males and 2 h 31 min to 2 h 38 min for females). For males, the volume of marathon training was statistically higher for the top-class runners (127.7 ± 16.1 miles vs. 104.1 ± 12.4 miles). On the other hand, volume of marathon training was not significantly different between groups for females (102.9 ± 6.8 miles vs. 93.0 ± 10.5 miles, respectively). However, this high of volume may not be practical for runners who may have jobs or family responsibilities. Therefore, online training plans have become popular. For example, a popular running website “Runner’s World” published an article suggesting runners only need to run 30-50 miles a week in order to successfully complete a marathon (Eyestone, 2014).

The aforementioned suggested training volumes are suggested based off of physiological adaptations during training that will be beneficial for marathon performance. However, research has not studied the effects of the volume of marathon training and its effects on muscle damage caused by the marathon. With an increase in muscle damage, there will also be an increase in muscle soreness, and a decrease muscle
performance. Therefore, if an athlete wants to be able train at a high level after the marathon, knowing how volume of marathon training affects muscle damage and speed of recovery will be useful.

Jeffreys (2005) suggested that recovery is composed of three main categories: physical, psychological, and emotional. Most physical damage that occur from a marathon return to normal within seven days (Hikida et al., 1983; Warhol et al., 1985), including returning to baseline intramuscular glycogen levels (Warhol et al., 1985). Physical damage, as indicated by serum CK, has been reported to have a strong inverse correlation 48 hours post-exercise induced muscle damage (Sikorski et al., 2013). However, an interesting theory of recovery by Bishop, Jones and Woods (2008) is that the psychological factors may take longer to recovery than the physical factors if the source of fatigue is the central governor theory. The central governor theory states the central nervous system signals fatigue during heavy exercise to protect significant damage to the muscles (Bishop et al., 2008). In fact, Noakes, Peltonene, and Rusko (2001) have found that the central governor can even affect cardiac output by preventing producing inhibitory post synaptic potential signals to the working muscles, causing activation of high threshold motor units more difficult. If the athlete ignores the warning signs the central governor provides to stop, a significant amount of psychological stress may be involved. The psychological stress may then lead to a longer recovery time compared to the physiological factors of muscle damage or muscle soreness. Nicolas, Banizette, and Millet (2011) reported that psychological stress may last up to 2 weeks after completion of an ultra-marathon. Therefore, since the cause of fatigue may not be similar to each individual, especially in long events such as a marathon, recovery may not
correlate with muscle soreness due to a high amount of psychological and emotional stress.

**Strategies to Attenuate Muscle Damage**

A series of studies have investigated the effects of various methods of recovery and aiding of muscle damage and DOMS. These strategies ranged from nutrition, anti-inflammatory supplements, and exercise after muscle damage. These strategies have had varied success among subjects with muscle damage.

Nutrition pre, during, and post exercise is suggested to play a significant role in the magnitude of muscle damage. Ingestion of branch chain amino acids (BCAA’s) during a 25-km race has been shown to attenuate muscle damage by 10% compared to those who drank an iso-caloric carbohydrate beverage, as measured by lactate dehydrogenase (Koba et al., 2007). Coombes & McNaughton (2000) supported the supplementation of BCAA’s with carbohydrates (CHO) for 7 days before endurance exercise, as well as immediately pre- and post-exercise, as BCAA’s decrease post exercise CK and lactate dehydrogenase in the blood, indicating less muscle damage. Spencer, Yan, and Katz (1992), suggested that the increase in BCAA’s during exercise may be used as substrates in the Krebs cycle during the aerobic metabolism process. This then prevents damage of the muscle due to the availability of substrate use as a fuel during endurance exercise, thus preventing fatigue and attenuating the blood levels of CK, lactate dehydrogenase, myoglobin and other markers of muscle damage.

Following exercise, ingesting of BCAA’s may be helpful to prevent muscle damage. Nieman (1997) found that ingesting BCAA’s and CHO after prolonged exercise decreases cortisol, a hormone that is released by the adrenal cortex to maintain blood
glucose, if elevated may lead to more muscle damage (Brooks, Fahey, & Baldwin, 2005, pp. 204-205). Therefore, by decreasing cortisol after exercise, ingesting BCAA’s and CHO will prevent further muscle damage.

Ingesting BCAA’s after exercise may also be helpful to help improve the recovery of the muscle from the muscled damage that was done during exercise. The decrease in muscle damage after ingestion of BCAA’s and CHO is thought to be due to a stronger insulin releasing effect after CHO ingestion, compared to amino acid alone. This rise in insulin helps increase transport of glucose as well as the BCAA’s across cell membranes and may help in the inflammatory process to rebuild the muscle, causing an increase in the speed of recovery (Peake, Wilson, Mackinnon, & Coombes, 2005).

Anti-oxidant supplements have also been used for strategies to decrease muscle damage. Howatson et al. (2010) found that tart cherry juice with high anti-oxidant compounds, specifically flavonoid, enhanced the anti-inflammatory response after a marathon as indicated by a decrease in muscle damage markers, such as CK and perceived DOMS during a double blind study. The subjects drank 8 ounces of the tart cherry juice every day 6 days before the marathon, day of the marathon, and 2 days after the marathon. The attenuation of muscle damage after the marathon was attributed to the flavonoid compounds ability to enhance the protective effect against muscle damage by reducing the harmful effects of an increase in free radicals after unaccustomed exercise. These free radicals have been found to increase after the completion of a marathon (Kratz et al., 2002). Kuel, Perrier, Elliot and Chestnut (2010) also found an attenuation of markers of muscle damage following ingestion of tart cherry juice immediately after a 26-km run when the subjects drank the tart cherry juice every day for 7 days before the
marathon and day of the marathon. In contrast, Gomez-Cabrera et al. (2006) observed no
decrease in markers of muscle damage when subjects ingested a different anti-oxidant
supplement, allopurinol, only 2 hours before the marathon. Therefore, the allopurinol
may not have been as effective as the tart cherry juice, or anti-oxidant supplementation
needs to occur well before the muscle damage would occur. In fact, Gomez-Cabrera et al.
(2006) suggested that by decreasing the free radicals after exercise it would hinder the
cell adaptations that are beneficial during exercise, thus decreasing the cell’s ability to
prevent muscle damage in the future. Therefore, more research is needed to determine the
effects anti-oxidant supplementations are on muscle damage, recovery, and whether anti-
oxidants should be recommended.

Nonsteroidal anti-inflammatory drugs (NSAIDS) are often prescribed for the
alleviation of DOMS. Cyclo-oxygenase (COX) enzyme is up regulated during exercise
and stimulates a release of prostaglandins which starts the cascade of the inflammatory
response, ultimately causing pain and edema (Burd et al., 2010). Therefore, by blocking
COX, NSAIDS can alleviate the pain that comes with the inflammatory response.
However, Mikkelsen et al. (2011) found that blocking COX enzymes may also inhibit the
release of insulin-like growth factor, a hormone involved with stimulating protein
synthesis in muscle. Based off of current knowledge, NSAIDS are not recommended due
to the blunting of protein synthesis important in repairing muscle after damage as well as
hypertrophy.

Cooling down, low intensity exercise after vigorous exercise, is a common
method to improve recovery. This cooling down strategy has been thought to improve
recovery by improving the process of removing lactate from the blood (Weltman,
Stamford, and Fulco, 1979). However, to date, there have been no studies indicating that lactate build up has been a cause of DOMS (Schwane, Watrous, Johnson, & Armstrong, 1983) as blood lactate levels return to baseline within approximately one hour after exercise (Brooks, Fahey, Baldwin, 2005, pp. 220-222). Law and Herbert (2007) supported that a cool down did not improve muscle soreness 48 hours after the completion of walking backwards on a treadmill with a 13 degree decline for 30 minutes, which caused significant muscle damage. However, Law and Herbert (2007) did find a slight attenuation in muscle soreness when subjects completed a warm up. The decrease in muscle soreness was so small that the authors indicated the attenuation may not justify athletes to warm up before a long distance event, such as a marathon for the purposes of decreasing muscle damage.

When the muscle damage has occurred after the unaccustomed exercise, a popular question is whether or not to exercise on the days following to improve muscle recovery. Chen, Nosaka, and Wu (2008) found no significant difference between maximal voluntary contraction, perceived DOMS and biochemical markers for muscle damage during 30 minutes of level running at 40%, 50%, 60%, and 70% of VO2max each day for 7 days after significant muscle damage produced by downhill running. The active recovery showed no significant improvement in recovery at any of the intensities tested compared to the control group which did passive recovery. These results suggest that recovery from muscle damage is equally benefitted by active and passive recovery strategies. A systematic review by Herbert and Gabriel (2002) found that quality static stretching for 20-30 seconds after exercise on the damaged muscles did not attenuate muscle soreness either.
Lastly, massaging the exercised muscles has been a modality that has been made popular for restorative benefits by the Soviets in the early 1980’s (Burovykh, Samtsova, & Manuilov, 1989). In fact, up to 45% of time spent in therapy on athletes with a sports-related injury consists of massages (Cafarell & Flint, 1992). Although the mechanism of action of massage attenuated muscle damage is not well understood, a systematic review of literature completed by Best, Hunter, Wilcox, and Haq (2008) showed a decrease peak in DOMS and CK when massage of the exercising muscle took place within 3 hours of exercise. For example, Zainuddin, Newton, Sacco, and Nosaka (2005) found DOMS was reduced by 30% in subjects who received a 10 minute massage 3 hours post-exercise compared to those not getting a massage.

An interesting find was that there was little evidence to suggest massages completed immediately after exercise or after 3 hours from post-exercise on the exercised muscle attenuated DOMS and CK (Best et al., 2008). A hypothesis of why a delay is needed for post-exercise is that the muscle tension needs to be minimal in order for the massage to be effective, which may take up to 30 minutes for this relaxation to occur (Wenos, Brilla, & Morrison, 1990). A massage after 3 hours may also not be effective due to the already active catabolic effects of neutrophils, macrophages, and cortisol (Cannon et al., 1990).

Furthermore, Smith et al. (1994), tracked the recovery period from eccentric exercise causing significant soreness in active males. Two hours after exercise, the subjects were given a 30 minute massage on the exercised muscles. Blood analysis was done pre-exercise, 24, 48, 72, 96, and 120 hours post-exercise to find CK and cortisol while more blood was also collected every 30 minutes for 8 hours post-exercise to
determine the neutrophil count. The study showed that neutrophil count was lower over the 8 hours in the massage group compared to the control group. The massage group also had a lower peak in CK and cortisol compared to the control group. This data supports the theory presented by Cannon et al. (1990) whom hypothesized that massages cause an emigration of neutrophils, causing lesser muscle damage due to their catabolic properties.

Due to the variability of massages (time spent on massage, type of massage, and experience of the masseuse) as well as the potential variability that massages have on the attenuation of muscle damage, more research is needed on massages effects on muscle damage.

Because of the popularity of the recommendation for a massage after exercise, many accessories have been created to help produce the same effects of a massage. The most popular is a foam roller. A foam roller is hard shelled cylinder in which the athlete can manually simulate a massage by applying their body weight to exert pressure on soft tissue. A study by Pearcey et al. (2015) found foam rolling to significantly decrease perceived muscle soreness and is an effective tool to simulate the same affects as a massage.

In order to improve muscle recovery from damage, the most important strategy to follow is a nutrition plan that may benefit recovery from muscle damage. This includes having a diet rich in carbohydrates and protein rich in BCAA’s soon after the race. Along with the nutritional strategy, individuals may want to consider getting a massage after exercise. However, more research is needed to determine the effectiveness of these strategies to improve DOMS and recovery.
Conclusion

It has been observed that muscle damage is significant after unaccustomed eccentric exercises. Associated with this muscle damage is delayed onset of muscle soreness, or DOMS—a condition which can significantly alter range of motion and force development, thus decreasing performance. However, it has also been observed that repeating the eccentric exercise after an adequate recovery will attenuate muscle damage. Therefore, in order to better understand how to reduce muscle damage, research is needed to determine the effects of various training volumes on muscle damage.

While training for long endurance events, such as a marathon, the training loads determined by the volume of miles run can vary significantly between different training programs. However, the relationship between volume of running prior to the marathon and muscle damage after a marathon has not been studied. Doing so would help runners determine the adequate amount of volume needed in order to prevent significant muscle damage, as well as DOMS, which causes a decrease in muscle force production and range of motion. This knowledge would also help in improving recovery after a marathon, since if less muscle damage occurs because of sufficient training “mileage”, the marathon runner can return to productive endurance training sooner.
REFERENCES


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