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Kathleen Nichole Thiriot
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The Effect of Photobiomodulation Therapy on
Exercise-Induced Muscle Damage

Kathleen Nichole Thiriot

A thesis submitted to the faculty of
Brigham Young University
in partial fulfillment of the requirements for the degree of
Master of Science

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ABSTRACT

The Effect of Photobiomodulation Therapy on Exercise-Induced Muscle Damage

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Master of Science

Purpose: To explore the difference between continuous and pulsed photobiomodulation (PBMT) versus a placebo treatment when using a red-blue light combination over multiple treatment sessions to decrease the symptoms of muscle damage in the quadriceps muscle after a bout of muscle damaging exercise.

Methods: Thirty-six healthy, nonactive male and female participants were randomly assigned to one of three groups: continuous PBMT, pulsed PBMT, and placebo treatment. Participants were assessed for muscle damage with knee extension maximal isometric and isokinetic contractions, as well as Visual Analog Scale (VAS) and Lower Extremity Functional Scale (LEFS) scores. Blood creatine kinase (CK) was also analyzed. Participants were given treatment immediately prior to undergoing a bout of damaging eccentric exercise. Participants were treated with PBMT for the next 4 consecutive days for a total of 5 treatments.

Results: The continuous treatment group lost significantly less isokinetic average peak torque than the placebo treatment when averaged across all time points postexercise. However, for isometric testing, the continuous group had more reduction in force compared to the placebo group. Between the treatment groups, the continuous treatment group had significantly more muscle soreness measured by the VAS and had significantly less function in daily tasks reported on the LEFS patient-oriented outcome scale. There was no significant difference in level of creatine kinase between the treatment groups.

Conclusion: Pulsed photobiomodulation treatments had no significant effect when compared to the placebo group. Continuous photobiomodulation helped to reduce isokinetic force loss, yet exacerbated all other muscle damage markers following exercise relative to the placebo condition.

Keywords: photobiomodulation, phototherapy, LLLT, cold laser therapy, pulsed, continuous and a combination of these

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INTRODUCTION

Individuals commonly experience exercise-induced muscle damage (EIMD) following an unaccustomed physical activity.¹ Muscle damage has been described as morphological changes within the muscle including disruption of the sarcomeric Z-disc, in which structural damage causes leakage of proteins into the blood.² Evidence of EIMD includes disruption of intracellular muscular structure, prolonged impairment of muscular function, stiffness and swelling,³ delayed onset muscle soreness (DOMS), weakness and increases in circulating muscle proteins such as creatine kinase (CK).⁴ Exercise-induced muscle damage most commonly occurs following an eccentrically loaded exercise,^{3,5} potentially leading to pain and decreased muscle performance. Many strategies have been used to decrease signs and symptoms associated with EIMD, including ice massage, manual massage, ultrasound, and anti-inflammatory drugs.⁶⁻⁹

Recently there has been an increase in research focusing on the application of photobiomodulation (PBMT) to reduce muscle damage and to increase recovery rate after exercise.¹⁰ Photobiomodulation has been found to be effective in decreasing markers of muscle damage when used prior to a muscle damaging bout of exercise.^{11,12} Several studies¹¹⁻¹³ have found that when subjects were irradiated before exercise, they had decreased circulating CK activity,¹⁰ reduced impairment to maximum voluntary contraction¹² and a decrease in perceived pain and soreness in the days after exercise.¹¹

Different PBMT parameters have been studied and suggested to have different responses in the body. Most commonly, red and near infrared wavelengths of 600-1100 nm are used in studies to decrease muscle damage. Some studies have used multi-wavelength-emitting devices to produce a red wavelength, 640 nm, and two infrared wavelengths, 875 nm and 905nm, simultaneously.¹¹ Multi-wavelength-emitting PBMT devices have been found to be superior to

placebo groups in reducing markers of muscle damage.^{11,14} Other studies have also found a decrease in muscle damage from using only red wavelengths^{13,15} or only infrared wavelengths.^{12,16,17} Blue light has been previously used to kill bacteria and decrease acne.¹⁸ However, until now, no studies have been performed to determine the effectiveness of blue light on muscle damage following exercise.

Pulse duration is another parameter of PBMT that may be altered to achieve the desired outcomes. Treatments can be continuous, when the stimulation is constant throughout the whole treatment, or pulsed, when the stimulation goes on and off during the treatment. Pulsed PBMT treatments, in combination with continuous treatments, have been shown to reduce markers of muscle damage.^{13,19} Few studies have used only pulsed treatment parameters. De Marchi et al²⁰ performed a study in which they compared continuous treatments to pulsed treatments for decreasing muscle damage. It was found that the pulsed treatment groups had significantly less CK activity and lower modified VAS scores for DOMS when compared to the continuous treatment. Similar to other studies performed, De Marchi only had one treatment prior to the muscle damaging bout of exercise. With this in mind, our goal was to explore the difference between pulsed and continuous PBMT versus a placebo treatment when using a red-blue light combination over multiple treatment sessions to decrease muscle damage markers after a bout of exercise.

METHODS

Research Design

We used a placebo-controlled, randomized laboratory study in which participants were divided into one of three treatment groups. These groups consisted of a continuous PBMT group, pulsed PBMT group and a placebo group. Each participant came in for baseline measurements,

then 2 to 3 days later participants were given a PBMT treatment and completed a muscle-damaging protocol immediately following. After, participants went through strength testing and muscle soreness tests. Each day following, participants came in for PBMT treatment, strength and soreness testing. The schedule was as follows for the different measurements: Isometric strength, isokinetic strength and muscle soreness were all tested at baseline, immediately postexercise and 24 hours, 48 hours, 72 hours and 96 hours postexercise. Serum CK levels were measured at baseline and again at 48 hours and 96 hours postexercise. Our dependent variables for this study were isometric strength, isokinetic strength, muscle soreness, and serum CK. Our independent variables were treatment group and time.

Procedures

All data collection occurred in the Human Performance Research Laboratory in the Department of Exercise Sciences at a large western university. Each participant made 6 visits to the Human Performance Research Laboratory. Baseline measurements were taken at the first visit after eligibility was confirmed. During this visit, the participant's age, weight, height, sex and leg dominance information were recorded. The participant completed a visual analogue scale (VAS) and lower extremity functional scale (LEFS) to determine level of soreness before exercise. We then took a blood sample from an antecubital vein at the elbow to evaluate baseline levels of serum CK. Baseline strength measurements were measured by isometric and isokinetic dynamometry. Peak torque and average peak torque were recorded for the isometric test. Peak torque, average peak torque and average power were recorded for the isokinetic test.

The second visit occurred 2 to 3 days following baseline measurements. During this visit, the first dose of PBMT treatment was given for 30 minutes directly followed by the eccentric exercise protocol. After this, participants went through isometric and isokinetic

strength testing and recorded VAS and LEFS for soreness and function. Over the next 4 consecutive days, PBMT treatments were given, VAS and LEFS measurements were taken and isometric and isokinetic strength tests were performed. Blood samples were taken again 48 hours and 96 hours postexercise to determine levels of CK in the blood.

Participants

Participants for this study included 36 healthy males and females (males = 20, females = 16; age = 21–35, avg = 23; average height = 174.3 cm; average mass = 78.2 kg), with no musculoskeletal injury to the lower limb within 3 months prior to the study. Participants were classified as moderately active to not active meaning they participated in 30 minutes of physical exercise 1 to 3 times per week or less for the past 6 months. Participants were excluded if they were pregnant, had cardiovascular disease or cancer, suffered from epilepsy, or were classified as more than moderately active. Participants were recruited from the local university community and self-reported verbal responses to the study eligibility requirements. This study was reviewed and approved by the Institutional Review Board for the Use of Human Subjects at our University prior to the recruitment of subjects and collection of any data.

Photobiomodulation

Participants were randomly assigned into 1 of 3 treatment groups: continuous dosage, pulsed dosage or a placebo group. All three groups were given treatment for 30 minutes before a muscle-damaging bout of exercise, and before muscle testing in the next 4 consecutive days. The researcher used the light treatment patches to deliver the PBMT treatment. Patches were 50 cm² and the device produced a wavelength of 640 nm +/- 20 nm and 450 nm +/- 20 nm simultaneously. The patches were attached to the body surface of the quadriceps muscles with a hydrogel that also aided in transfer of the light. The PBMT device has a maximum pulsating

laser power of 5.4 mW with an average combined power of 1.8 mW over the entire surface of the patch. All PBMT treatments were administered in direct contact with the skin at 4 irradiation sites shown in Figure 1. During a continuous power PBMT treatment, the power was produced during the entire treatment. Pulsed treatments had intermittent periods alternating between the device producing power and the device not producing power. The pulsed treatment had a 33% duty cycle. The placebo treatment was given with the same device as the others, however it was set in a mode in which no power was produced when the device was turned on. Treatments occurred immediately prior to the muscle damaging protocol and before strength and soreness testing over the next 4 consecutive days for a total of 5 treatments.

Muscle Damage Protocol

Participants participated in an eccentric exercise protocol as described by Deyhle et al.²¹ Participants were seated in the dynamometer chair adjusted in tilt, height, depth and recline. Rotation of the shaft arm was adjusted so the fulcrum of the machine was lined up with the participant's knee for maximum comfort and movement ability. Participants began the protocol by extending their knee and pushing against the lever arm with maximum force until they reached 40 degrees of extension at a fixed rate of 180 degrees per second. Once participants reached 40 degrees of extension, they continued to extend their knee and push against the lever arm as it pushed them back into flexion at a rate of 120 degrees per second. Verbal encouragement was given throughout the exercise as participants performed 10 sets of 10 reps with a 1-minute rest between each set. Participants rested for 5 minutes and this protocol was repeated 2 more times for a total of 30 sets or 300 reps.

Evaluation of Strength Loss

Evaluation exercises to determine maximal isometric and isokinetic force production at baseline and each day throughout the 5 days of treatment were performed on the dynamometer. Participants were seated in the dynamometer chair and tilt, height, depth, recline and rotation of the shaft arm were adjusted to fit the participant's specific height and limb length. The dynamometer straps were used to stabilize the participant to ensure use of only the quadriceps muscles to accomplish the exercise. Straps were placed over both shoulders crossing the body at the chest. Two more straps were placed around the waist and around the thigh of the involved leg. Participants were allowed to perform 3 to 5 practice knee flexion/extension repetitions to familiarize themselves with the test before testing occurred.

The isometric test was performed by contracting maximally against the stationary lever arm at 70 degrees of flexion for 5 seconds, repeated 3 times with a 5-second rest between each maximal effort. Verbal encouragement was given while they performed this action. Peak torque and average peak torque were recorded and participants were allowed to rest for 2–3 minutes before performing the isokinetic strength test. The isokinetic test was performed by the participants giving maximum effort while performing 3 concentric knee flexion and extension contractions against a lever arm moving at a fixed rate of 60°/sec. Verbal encouragement was also given during this test. Peak torque, average peak torque and average power were recorded.

Evaluation of DOMS

Participants completed a modified 100 mm visual analogue scale (VAS) to measure their perception of muscle soreness. A visual of a modified VAS pain scale is shown in Figure 2. The modified VAS is a 100 mm horizontal line with anchor points at each end. The left anchor point reads “not sore” and the right anchor point reads “extremely sore.” In the middle of the

horizontal line reads “mildly sore.” Participants rated their pain by drawing a single vertical line at the point that most closely described their pain. Researchers then measured their pain in mm. Participants were asked to do a body weight squat before rating their overall pain at the time they were filling out the form. Participants’ modified VAS scale was recorded at baseline, directly before the treatment to see immediate effects of the treatment, after the muscle damaging protocol, and each consecutive day of treatment directly following the PBMT treatment. At these same time points, participants also completed the Lower Extremity Functional Scale (LEFS) via Qualtrics which has a broader base of functional questions.

Blood Samples and Creatine Kinase Analysis

Blood samples for CK analysis were collected at baseline, 48 hours postexercise and 96 hours postexercise. Standardized phlebotomy procedures were followed and blood was taken from the antecubital region of the participant’s arm to obtain 5 to 6 ml of blood. Blood was immediately centrifuged, and serum was stored at -80°C for later use. Creatine kinase levels were then analyzed at Utah Valley Hospital, per their laboratory procedures.

Statistical Analysis

Data was analyzed with a repeated measures ANCOVA for each dependent variable. Baseline values were tested as a covariate to account for potential individual variations. All statistics were analyzed in JMP Pro (version 12, SAS Inc., Cary, NC) and the alpha level was set at $P \leq 0.05$. Data was normalized for analysis so isokinetic and isometric data was reported as percent change in participant’s baseline values. VAS and LEFS were also normalized for individual participants as the change in their score from their baseline score. A log transformation was used to normalize CK analysis data.

RESULTS

Isokinetic Force Production

There was no difference at baseline for isokinetic peak torque ($F_{2,32} = 0.517$, $P = 0.602$), average peak torque ($F_{2,32} = 0.924$, $P = 0.408$), and average power between the 3 treatment groups. Across all treatment groups, the eccentric muscle damaging protocol significantly decreased peak torque ($F_5 = 5.16$, $P = 0.0002$), average peak torque ($F_5 = 3.18$, $P = 0.009$), and average power ($F_5 = 3.019$, $P = 0.012$) after exercise. Isokinetic peak torque ($F_5 = 2.629$, $P = 0.075$), and average power ($F_2 = 1.861$, $P = 0.159$) were not significantly different between the treatment groups (treatment main effect) (Figure 3). On average, the continuous treatment group significantly lost 18.25% less force for average peak torque and had a higher rate of recovery when compared to the placebo treatment group ($F_5 = 3.709$, $P = 0.026$) averaging across all time points. There was no significant treatment x time interaction for any of the 3 isokinetic measurements. Means and standard error isokinetic peak torque, average peak torque, and average power are displayed in Figure 4.

Isometric

There was also no difference at baseline between the 3 treatment groups for isometric peak torque ($F = 1.035$, $P = .367$) and average peak torque ($F = .956$, $P = .395$). Across all treatment groups, the eccentric muscle damaging protocol significantly decreased peak torque ($F = 3.147$, $P = 0.001$) and average peak torque ($F = 3.98$, $P = 0.002$) after exercise. The continuous group lost 9.6% more force for peak torque when compared to the placebo group ($P = 0.0428$) (Figure 5). There was no difference between the treatment groups across all time points for average isometric torque ($F = 2.609$, $P = 0.076$). There was not a significant treatment x time

interaction for either of the 2 isometric measurements. Means and standard error for isometric peak torque and average peak torque are displayed in Figure 6.

Muscle Soreness

Baseline measurements were not significantly different between groups for VAS ($F = 3.048, P = 0.061$) and LEFS ($F = 0.623, P = 0.543$). Muscle soreness measured by VAS ($F = 24.145, P = < .0001$) increased due to the eccentric exercise across all time points and functionality measured by LEFS ($F = 18.34, P = < .0001$) decreased across all time points (time main effect). Between the treatment groups, the continuous treatment group had significantly more muscle soreness measured by the VAS ($F = 15.072, P = < .0001$) and had significantly less function reported on the LEFS patient oriented outcome scale ($F = 14.042, P = < .0001$) (Figure 7). There was not a significant treatment group x time interaction for either the LEFS or VAS scales. Means and standard errors for the LEFS and VAS scales are displayed in Figure 8.

Creatine Kinase

There was no CK difference between the treatment groups at baseline ($F = 1.444, P = 0.25$). The eccentric exercise protocol significantly increased the concentration of CK ($F = 12.057, P = < .0001$) in the bloodstream across all time points (time main effect). However, there was no significant difference between the treatment groups ($F = 2.837, P = 0.064$) (treatment main effect). Means and standard errors for CK concentration are displayed in Figure 9.

DISCUSSION

This study was conducted to determine the effect of pulsed and continuous PBMT versus a placebo treatment, when used prior to an eccentric exercise protocol and over multiple treatment sessions, on muscle damage markers. For this particular study, we decided to perform the irradiation treatment prior to the muscle damaging exercise based on previous research

reporting superior results to studies in which treatment is given after exercise.^{11,12,19,22} The eccentric muscle-damaging protocol immediately altered isometric and isokinetic muscle performance, increased circulating CK activity and increased muscle soreness for all treatment groups. Our results indicated no difference of CK activity throughout the treatment period between the continuous, pulsed or placebo PBMT. We also found no difference between a pulsed treatment and a placebo treatment in their affect toward the participants' pain or in self-reported lower extremity functionality. However, we found that those given a continuous PBMT treatment reported greater pain levels, as reported by a modified VAS, and reduced self-reported functionality, as reported by the LEFS test.

Previous research has found that continuous red/infrared and infrared PBMT treatments prior to muscle-damaging exercise increases the ability of subjects to produce maximum voluntary contraction (MVC).^{11,12} Regarding isokinetic contractions for our research, the continuous treatment group lost significantly less average peak torque than the placebo treatment group when averaged across all time points. In contrast, regarding isometric contractions, the continuous group produced significantly less force than the placebo group. No previous studies have used isometric contractions as a form of assessing muscle damage after exercise, and although strength can differ based on age, height and sex,²³ there were no significant differences between the groups at baseline for either isokinetic or isometric strength tests. There is conflicting research from previous studies about the relationship between isokinetic and isometric exercise. Osternig et al²⁷ found no evidence linking isokinetic strength values with isometric strength values. However, Otis²⁴ found a strong relationship between isokinetic and isometric strength. Otis found position of the joint and velocity of the isokinetic measurement to have a significant effect on strength. For our study, because we used only one joint angle and one

velocity for isokinetic measurement, we may not have a broad enough understanding of what was really happening. Therefore, further research should be performed to understand the physiologic changes across different contractions after a PBMT treatment.

Antoniali et al¹¹ found infrared PBMT treatments beneficial in decreasing DOMS measured through VAS scores and increasing LEFS scores using a single continuous treatment prior to exercise. However, we found that those given a continuous treatment to have significantly more pain and decreased LEFS scores. We also found no difference between pulsed and placebo groups for these subjective measures. Although our studies were very similar, Antoniali et al¹¹ only performed one PBMT treatment, whereas we gave multiple treatments over an extended period of time. The multiple treatments would increase the total energy delivered to the quadriceps muscle to 3456 J (4 treatments x 864 J per treatment) compared to 60, 180, or 300 J based on the randomly assigned group in the study performed by Antoniali et al.¹¹ Our data may be explained with the Arndt-Schulz principle which states that a weak stimulus will accelerate activity and a stronger stimulus will increase activity further. However, there comes a point when the stimuli reaches a peak and any stimuli over that threshold will cause a negative response.²⁵ Giving one continuous treatment prior to exercise may have been enough to create a response, multiple treatments given over the healing period of time may have caused an inhibitory effect on the tissue.

Conversely, our lack of results for our pulsed treatment group may be explained by a shorter wavelength from our blue light as well as a lower power given. Our device had an average power of 2.4 mW/cm² whereas Antoniali et al¹¹ used a device that produced an average power of 32.5 mW/cm². Our PBMT treatment may have had a hard time penetrating the treatment surface or not going very deep into the muscle and therefore giving us no results.

Hashimi et al²⁶ conducted a review of 33 studies determining the best parameters for phototherapy. Nine of these studies directly compared a continuous phototherapy treatment to a pulsed phototherapy treatment for conditions such as wound healing, pain, and nerve regeneration. Although 7 of the 9 studies found the pulsed wavelength to be superior to continuous and placebo treatments, our study found pulsed PBMT treatments to be very similar to placebo treatments in decreasing the amount of muscle damage markers in the body after muscle damaging exercise. We did not have a true control of participants who underwent the muscle damaging exercise but did not receive any treatment. Therefore, we don't know the full extent of how the placebo effect may have affected the participants. We took our exercise protocol from a study performed by Deyhle et al²¹ in which they performed no treatment for participants after undergoing the exercise protocol. Participants from Deyhle et al had an increase of muscle damage markers and returned to pre-exercise levels in a similar time frame as participants in the placebo group in our study. We observed in our study that the body reacted similarly to a sham treatment as it did with a pulsed treatment. Because our placebo group had similar results to a group given no treatment, it is unlikely that our findings were affected by a placebo effect.

We had several limitations for this study. Participants in this study were blinded, but the researcher was not. Of the participants, most were university students in similar geographic locations. Because participants were nonactive and nonathletes, they may have reacted differently to exercise or to the treatment than an athlete and the data can therefore only be applied to a general population. Further research would need to be performed on athletes to understand how PBMT treatments may affect their sport. We also did not have a true control group of participants who received no treatment. Therefore, we do not fully understand the

extent to which the placebo effect may have contributed to having no significance in reducing markers of muscle damage in the pulsed treatment group. However, studies similar to ours have seen significant differences between treatment and placebo groups without true control groups.^{11,12}

CONCLUSION

We found participants in the continuous PBMT group had increased pain and decreased function as a result of muscle-damaging exercise. Those treated with continuous PBMT also had decreased isometric contraction strength when compared to other groups. Participants irradiated with pulsed PBMT had no significant difference in markers of muscle damage when compared to the placebo treatment. It appears that pulsed PBMT has no effect on muscle damage after exercise. Although continuous PBMT was detrimental for most markers of muscle damage, it aided in recovery and decreased isokinetic force loss. This study increases our knowledge of proper parameters when using red/blue light PBMT. However, further research should explore the effects of a single treatment of red/blue PBMT to determine whether they are similar to previous studies performing a single treatment with red/infrared PBMT.

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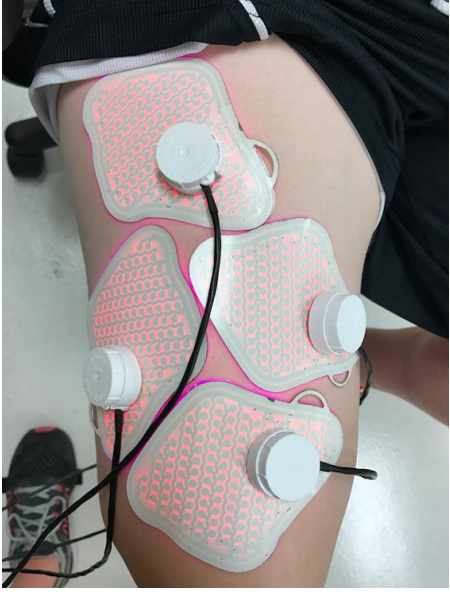


Figure 1. PBMT electrode patch placement

How sore are you feeling today?

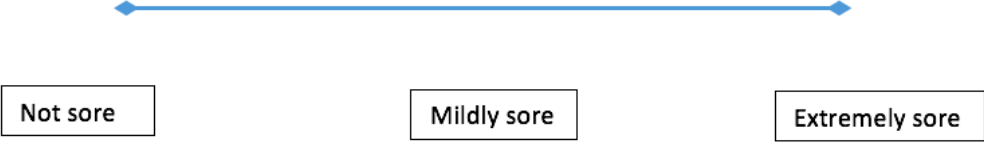


Figure 2. Modified VAS form participants used to present their level of soreness

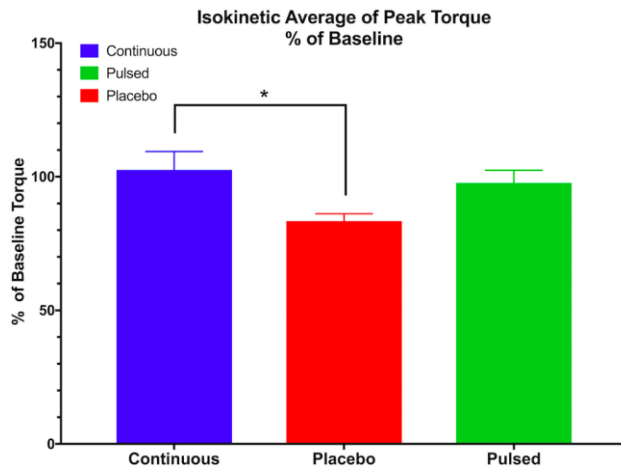


Figure 3. Isokinetic Average of Peak Torque. Data are means \pm SE and are normalized to the participants' baseline value. * indicates significant difference between average isokinetic values ($P < 0.05$).

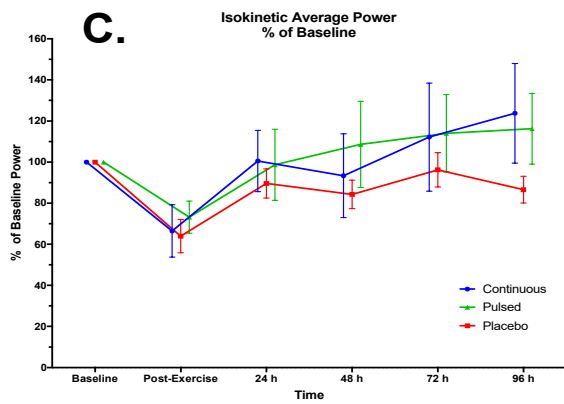
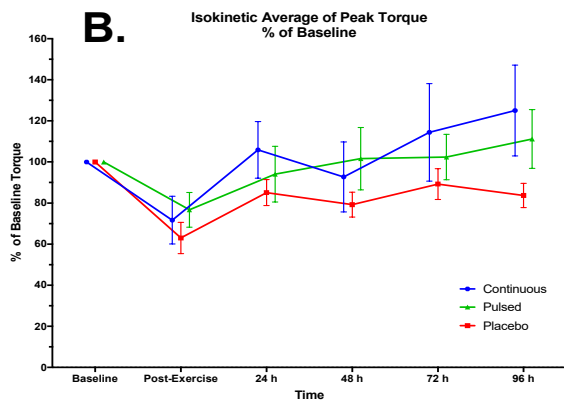
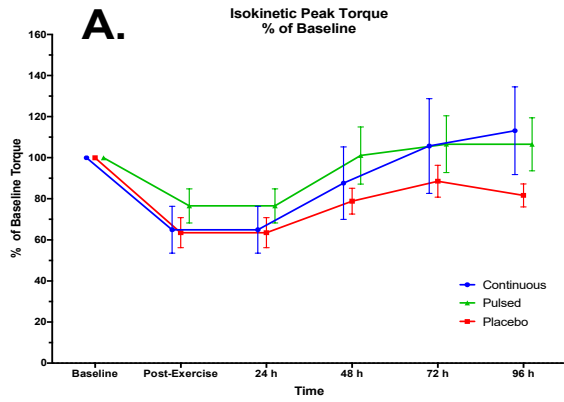


Figure 4. Isokinetic peak torque (A), average peak torque (B), and average power (C). Data are means \pm SE and are normalized to the participants' baseline value.

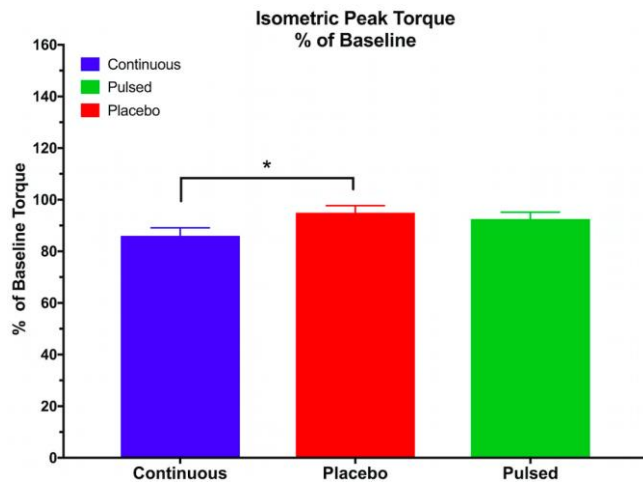


Figure 5. Isometric Peak Torque. Data are means \pm SE and are normalized to the participants' baseline value. * indicates significant difference between average isometric values ($P < 0.05$).

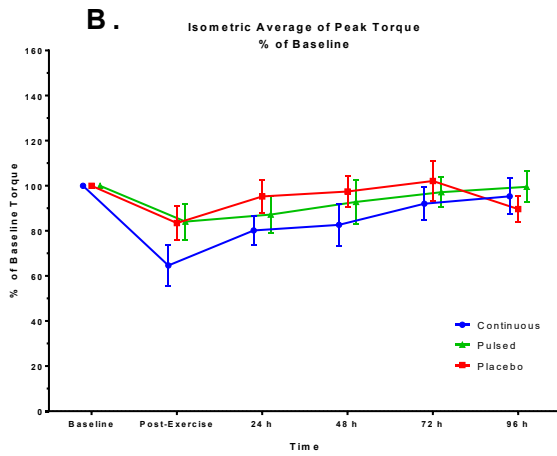
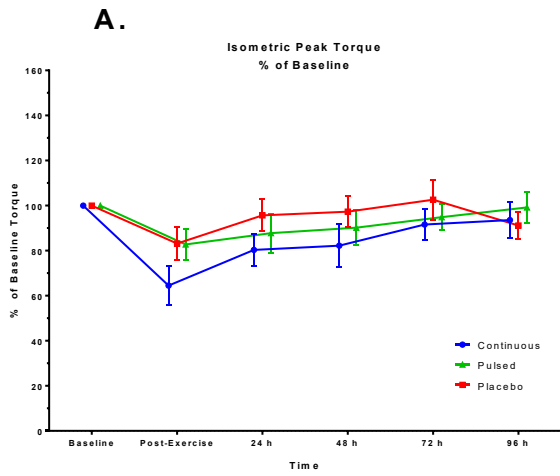


Figure 6. Isometric peak torque (A), average peak torque (B). Data are means \pm SE and are normalized to the participants' baseline value.

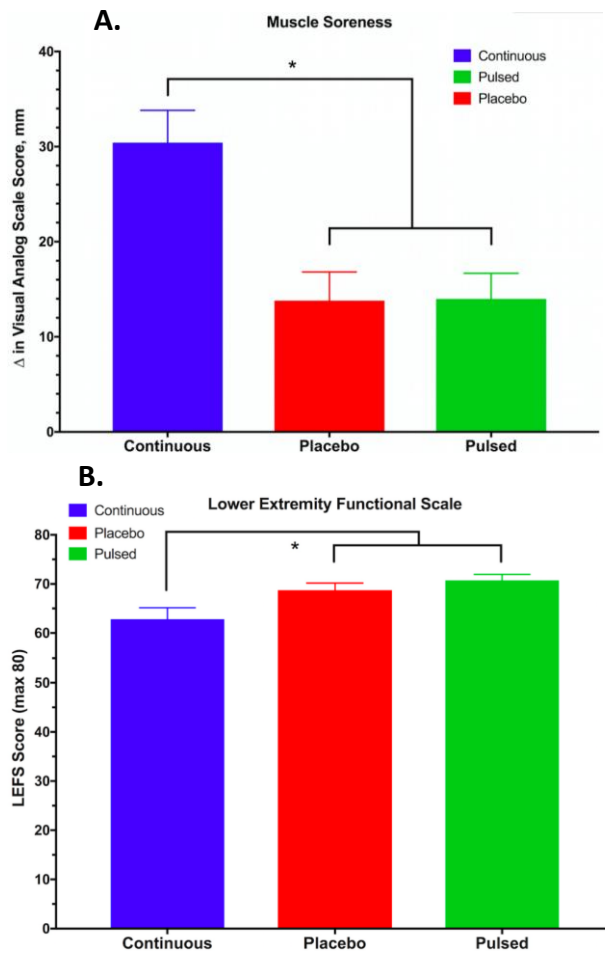


Figure 7. VAS scores (A), LEFS scores (B). Data are means \pm SE and are normalized to the participants' baseline value. * indicates significant difference between average muscle soreness values ($P < 0.05$).

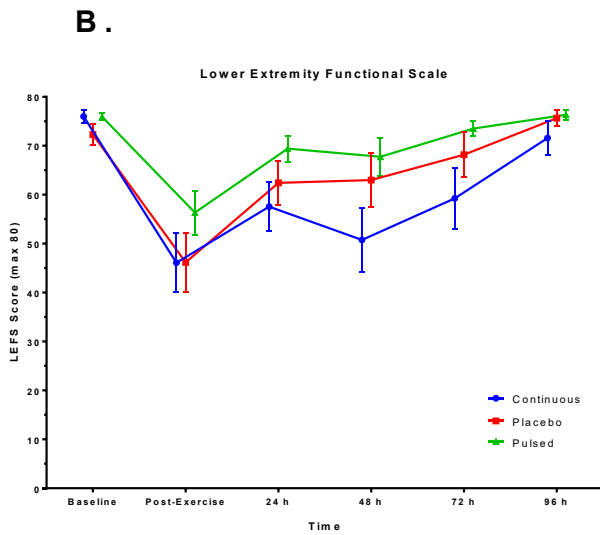
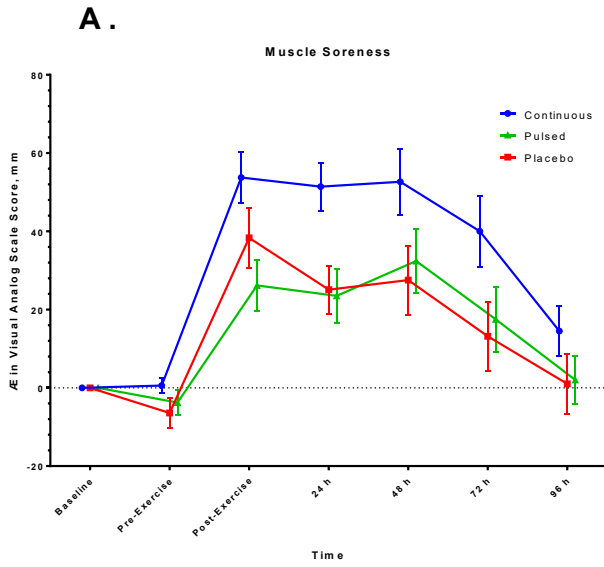


Figure 8. VAS score (A), LEFS score (B). Data are means \pm SE and are normalized to the participants' baseline value.

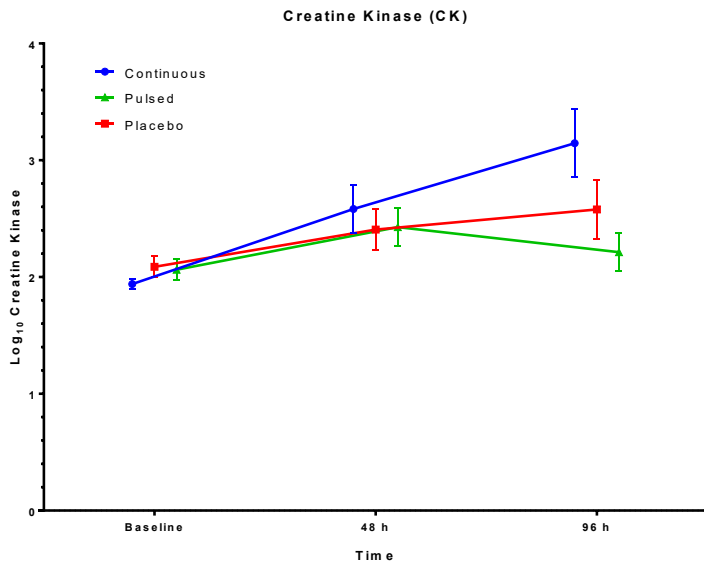


Figure 9. Means and standard deviations for Log of Creatine Kinase levels after exercise.