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Impact of Photobiomodulation Therapy Dosing Strategies on Strength, Clinical Outcomes, and Metabolic Responses: A Blinded Randomized Clinical Trial

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Abstract

Introduction: Recent evidence suggests that the combination of exercise and photobiomodulation therapy (PBMT) enhances muscle performance, including improvements in strength, hypertrophy, and fatigue resistance. As muscle tissue changes after training, a dose progression over time may show additional effects. However, there needs to be more clarity regarding the optimal physical parameters for enhancing muscle performance. Thus, the aim was to evaluate the impact of strength training combined with PBMT at fixed or progressive doses on strength performance, metabolic activity, and clinical outcomes in healthy individuals.

Methods: This was a double-blind, randomized clinical trial. Fifty-six male participants were randomly allocated into four groups: Sham, minimal dose (60 J), maximal dose (300 J), and incremental dose (60–300 J). Baseline assessments included body composition analysis and isokinetic dynamometry (peak torque and total work of the quadriceps femoris and hamstring muscles), followed by ten sessions of strength training combined with PBMT applied before each exercise session, which consisted of three sets of stiff and squats. PBMT irradiation was applied to the quadriceps and hamstrings. Training loads and psychophysiological responses were monitored throughout the intervention. Participants were reassessed at the end of the training period and followed up for a total duration of seven days.

Results: No significant differences were observed between the groups in isokinetic strength parameters ($P>0.05$), although small to moderate effect sizes favored the Incremental and Maximal Dose groups. Similar patterns were found for psychophysiological responses and training loads across the groups.

Conclusion: In the context of this research model, PBMT combined with strength training did not yield superior outcomes in muscle strength, psychophysiological, or metabolic parameters compared to the different dosing strategies evaluated.

Keywords: Low-level light therapy; Muscle strength; Exercise training; Work load; Physical therapy.

Introduction

Photobiomodulation therapy (PBMT) refers to the application of electromagnetic radiation to biological tissues using LASER (light amplification by stimulated emission of radiation) or LED (light-emitting diodes)[1] and has improved muscle performance in experimental studies[2–4] and also in humans.[1,5,6] The most explored theory at the moment indicates the cellular alterations caused by light absorption near cytochrome c-oxidase, besides the interaction in the mitochondrial electrical transport chain, referring to the repercussions as an increase in oxidative enzymatic activity and an increase in energy synthesis, being a biological source of vital energy for muscular activity, thus supporting the hypothesis of an increase in sports performance in response to adenosine triphosphate (ATP) levels.[6–9] Therefore, it is possible to discuss the possibilities of managing the spectrum of oxidative stress, in which PBMT influences outcomes such as reactive oxygen species (ROS) and lactate and blood glucose levels.[10,11] However, an adequate selection of parameters is fundamental to achieving these outcomes since an inadequate appointment may result in adverse or ineffective effects.[12]

Enwemeka[13] and Bjordal[12] underlined the control of physical variables, highlighting that, for a complete and satisfactory production of favorable outcomes, the domain of physical parameters must be present in the therapist's capabilities. Nevertheless, in addition to the interaction of optics and the physical domain, one should know that musculoskeletal tissue is dynamic and adaptive.[14]

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Although the optimal dose points for stimulation have been discussed,[1] the interference of the alterations promoted by the training itself and the proposed therapy is rarely considered. Thus, in the same way as the changes present in irradiated tissues, the specificity of the intervention can be better explored with constant evolutions. Several studies have consistently reported average improvements in maximum voluntary contraction and cross-sectional area, supporting the robustness of these findings.[15,16]These results suggest that tissue alterations—such as changes in cross-sectional area, volume, and optical properties—may influence photobiomodulation outcomes, potentially requiring dose adjustments to optimize its effects.

Recently, some studies have indicated that traditional high-resistance load exercise can stimulate mitochondrial biogenesis and improve mitochondrial respiratory function in skeletal muscle.[17,18] Thus, considering the aforementioned mechanism—closely linked to mitochondrial energy outcomes and their direct stimulation—it is reasonable to propose a progressively adjusted photobiomodulation stimulus, aligned with the physiological adaptations promoted by load training. However, the available literature on photobiomodulation presents significant gaps regarding the optimal physical parameters for improving muscle performance,[19] particularly in determining whether energy delivery should remain constant or be progressively adjusted throughout the training period. Current methods described in the literature do not address this perspective, limiting a more detailed analysis of biological responses in populations that could benefit from the technique.

Thus, the objective of this study was to analyze the effects of strength training associated with PBMT, in fixed or increasing doses, on strength capabilities, metabolic activity, and clinical scales in healthy individuals. In this sense, once the parameterization available to the individual can be optimized, increasing muscle performance during activities can promote benefits not only in a sports environment but also for individuals exposed to a rehabilitation program. This offer may provide a new perspective for the therapist and the assisted individual.

Materials and Methods

Ethics

The Ethics Committee of the Clinical Hospital of the Ribeirão Preto Medical School, under protocol 4.721.982, approved this study. The research was carried out at the Laboratory of Physiotherapeutic Resources (LARF) of the Ribeirão Preto Medical School of the University of São Paulo (FMRP-USP). This study was registered as a clinical trial on ClinicalTrials.gov (NCT03860766). The volunteers were adequately informed about the research project, its objectives, and its characteristics, and all signed the informed consent form.

Design

This is a double-blind, randomized clinical trial. The research team conducted recruitment. The researcher responsible for the analyses and the participants did not know which group they would be allocated to. Two other researchers conducted the assessments and intervention protocols, and another one was responsible for data processing and analysis.

The eligible participants were randomized and allocated to one of the four groups: (1) PBMT 60 J (minimal dose); (2) PBMT 300 J (maximal dose); (3) PBMT 60-300 J (incremental dose); and (4) Sham group (placebo photobiomodulation). Randomization was performed by an investigator who was not involved in data collection and outcome assessment, using digital software (Excel, Microsoft Corporation by Impressa Systems, Santa Rosa, California, USA), and the secrecy of allocation was maintained by opaque envelopes that were sealed and only opened by the responsible researchers who applied the intervention, after the evaluation and before the intervention. The randomization process was conducted in blocks using simple random sampling, ensuring that each participant in the study had an equal chance of being selected. The investigator responsible for evaluations and the patients were blinded to the patient's group allocation throughout the study period.

To maintain participant blinding, they wore opaque glasses that prevented them from seeing the equipment. Additionally, the device did not emit any sound during handling or therapy application. To ensure blinding within the research team, neither the evaluators nor those responsible for the statistical analysis were involved in the irradiation or training process.

Participants

Sample size was calculated using Ene software (v3.0, Universitat Autònoma de Barcelona, Spain), based on Vanin et al.[20] Considering peak torque means of 233.16 ± 27.99 N·m and 280.90 ± 38.68 N·m, the highest SD, a power of 80%, and $\alpha = 0.05$, the estimated sample was 12 participants per group. Accounting for a 15% dropout rate, 14 participants per group were recruited (total n = 56).

Inclusion criteria were: males aged 18–40 years, no musculoskeletal injury in the previous 3 months, no cardiovascular disease, and no use of anabolic agents, anti-inflammatories, or analgesics 72 hours before testing. Volunteers were excluded if they missed more than two consecutive training sessions, could not complete the protocol, or engaged in lower-limb strength/hypertrophy training outside the study.

Due to the SARS-CoV-2 pandemic, participants with symptoms or confirmed infection were removed, and all wore masks during training—a relevant consideration for data interpretation.

The methodology of the study applied all the guidelines established by the CONSORT - Consolidated Standards of Reporting Trials[21] and adhered to photobiomodulation reporting standards proposed by Hamblin.[22]

Assessment Procedures

The evaluations occurred three times: before the first training session, between 24 and 48 hours after the last session, and seven days after the second evaluation. For the first and second evaluations, the volunteers were submitted to anamnesis, physical examination, and isokinetic dynamometry. Only the isokinetic dynamometry was performed for the third evaluation (follow-up). The sequence of events is presented in Figure 1. The primary outcome of this study is peak torque during maximum voluntary contraction. Secondary outcome measures involved external load volume, blood lactate, heart rate analysis, and clinical scales such as pain and perceived exertion.

Anamnesis and Physical Examination

The following data were collected: personal data (name, phone number, gender, age, lower limb dominance), mass, height, body mass index (BMI), previous diseases, drug use, and current history of surgery, physical therapy, or physical training. During the physical examination, the thigh perimetry was measured, defining a midpoint between the anterosuperior iliac spine and the base of the patella,[23] bilaterally, with the individual in dorsal decubitus and without contraction of the area evaluated.

Isokinetic Dynamometry

Muscle performance was assessed using a Biodex System 4 Pro isokinetic dynamometer (Biodex Medical Systems®, NY, USA) to measure peak torque and total work of the quadriceps and hamstrings bilaterally. Volunteers first completed 8–12 submaximal repetitions at 60°/s for warm-up and familiarization. They were then positioned and secured according to equipment specifications. The test protocol included five maximal concentric knee flexion/extension contractions at 60°/s, followed by a 120-second rest. Next, participants performed 20 maximal concentric contractions at 270°/s, over a 90° range of motion. Extension was limited to avoid passive hamstring insufficiency. Verbal encouragement was provided throughout to ensure maximal effort. Testing began with the dominant limb, followed by the non-dominant.

Training Protocol

The participants attended 10 training sessions, with a frequency of two sessions per week for five weeks. The individual sessions were conducted in a sports gym with artificial lighting and uncontrolled room temperature. The training protocol was applied by researchers adequately trained before the study to familiarize themselves with and standardize the execution and gesture requirements during the proposed exercises. The training sessions were conducted according to participants' time availability

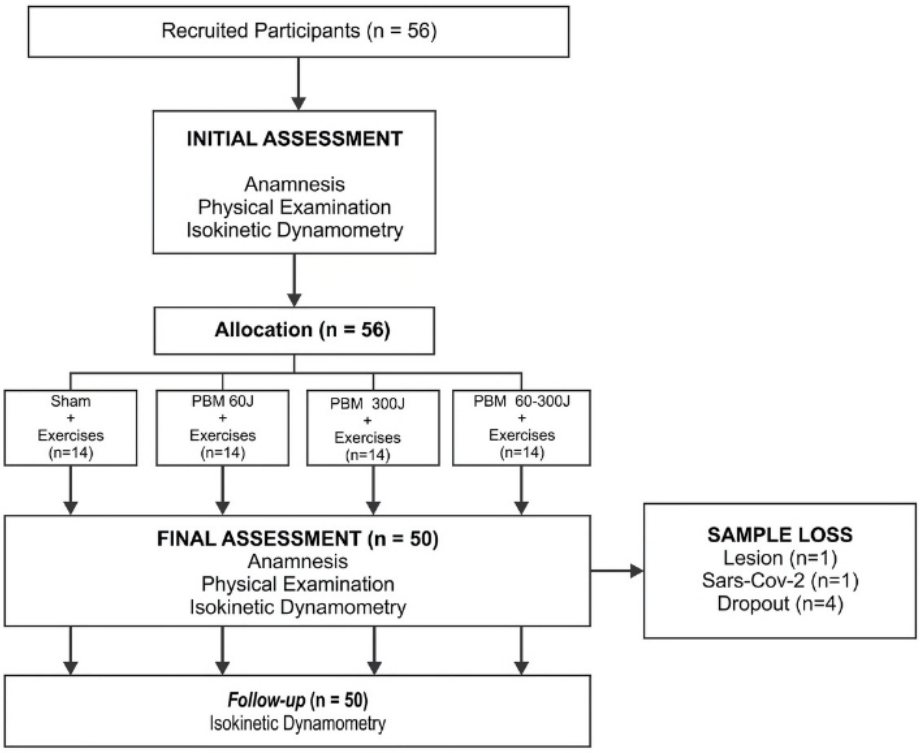


Figure 1. Flowchart of the Study

and preferences, which were maintained throughout the training. The complete protocol can be seen in Figure 2.

One-Repetition Maximum (1RM)

Before the first training session, the volunteers performed the 1RM test to quantify the squat and the stiff training load. For the warm-up, the volunteers did the exercise to be evaluated with the barbell weight only, then performed eight to 12 repetitions at 50% of body mass, followed by three repetitions at 70% of perceived 1RM. After a three-minute break, the 1RM test was performed, changing the load, when necessary, with the number of attempts limited to five. A two-minute rest was adopted between each attempt, and the maximum load was lifted in a single movement. The participant should not be able to perform a second repetition.

Training Session

Volunteers performed squat and stiff-leg exercises in randomized order at each session. Each exercise comprised three sets at a slow-to-moderate pace, with repetitions to concentric failure. Sessions occurred twice weekly, using 75% of 1RM load.[24,25] Set intervals were 2 minutes, and 3–5 minutes between exercises. Load adjustments were made: + 10 kg if average reps exceeded 12, and −10 kg if below 8. Feedback and verbal encouragement were provided as needed. Internal load monitoring included heart rate (Polar OH1, Polar Electro Oy, Finland), blood lactate, pain scale, and perceived exertion.

Blood lactate was measured before and 5 minutes after warm-up, in the 1st and 3rd sets of both exercises, post-training, and after 3, 5, and 7 minutes of rest. Samples (25 µL) of arterialized blood from the earlobe were collected in heparinized capillaries and stored in 1.5 mL Eppendorf tubes with 50 µL of 1% NaF[26]. Analysis was performed with a lactometer (Model 2300 Sport, Yellow Springs Instruments, USA), with results expressed in mmol/L.[27] The Rating of Perceived Exertion (RPE) and the Numerical Pain Scale (NPS) were assessed before and after each session. Participants rated both on a 0–10 scale, where 0 indicated "none" and 10 "maximum," following Foster et al[28] for RPE and Ferreira-Valente[29] for NPS.

Photobiomodulation

Two LED blankets[30] were used, with equidistant distribution between the emission points (1.5 cm). The limb to be irradiated first was randomized in all training sessions. One LED blanket was positioned over the quadriceps femoris muscles and the other over the hamstring muscles simultaneously. For the group with a progressive dose, the initial energy of 60 J was applied. Still, at each session, there was an increase of 26.5 J, thus finishing with 300 J. In the Sham group, the total application time matched that of the minimal dose group, but without actual light emission. The positioning of the blankets and the use of opaque glasses for blinding were

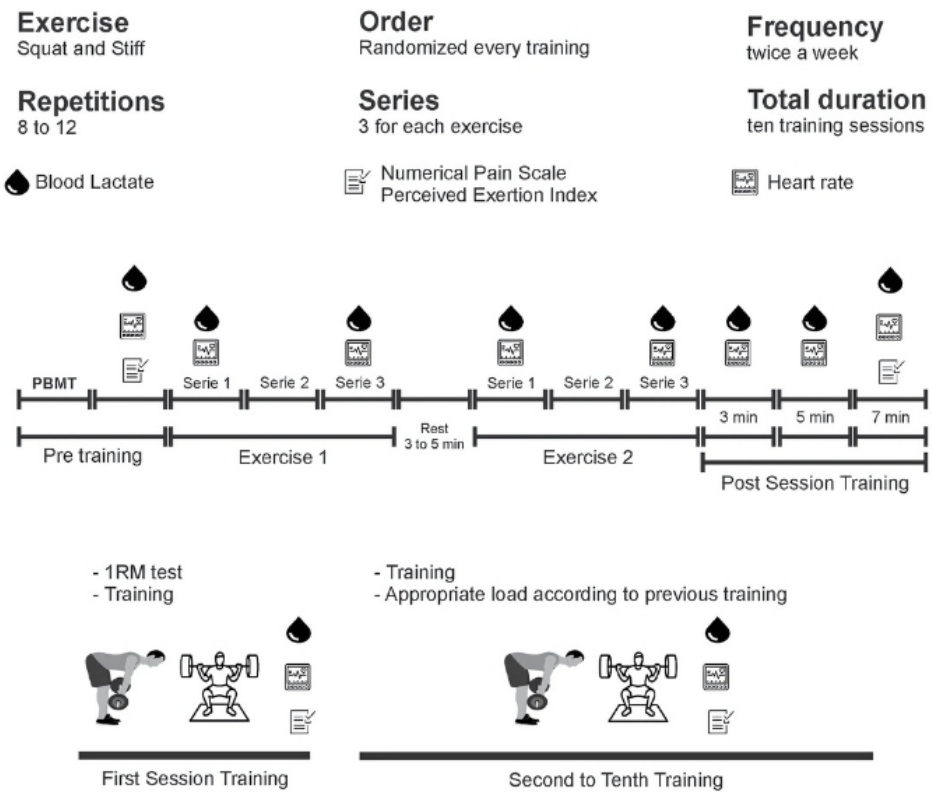


Figure 2. Training Protocol of the STUDY

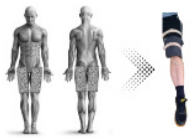
maintained consistently across all groups.

All LEDs were previously checked for wavelengths, angle of radiation, power, and power density. It is emphasized that in the presence of melanodermic volunteers, the final energy applied at each training session was increased by 10% of the predicted. The information on the physical parameters of the LED blankets is shown in Table 1.

Statistical Analysis

Statistical analysis was performed using GraphPad Prism v7.0 (GraphPad Software, San Diego, CA, USA). Descriptive statistics summarized participant characteristics as means and standard deviations (SD). Data normality was assessed with the Shapiro-Wilk test. One-way ANOVA evaluated group-time interactions, with outcomes expressed as mean differences and 95% confidence intervals, followed by Tukey's post hoc test. The significance level was set at $P<0.05$. Effect sizes (Cohen's d) were interpreted as small (<0.2), moderate (~0.5), or large (>0.8)[31]. Missing isokinetic data were addressed using the Expectation-Maximization method after confirming randomness via Little's test,[32] both performed in SPSS v2.0 (SPSS, Inc., Chicago, IL). Only participants who completed all training sessions were included in the analysis.

Table 1. Representation of the Physical Parameters Used During Photobiomodulation Therapy

Parameters	LED Blanket
Wavelength	940 ± 10 nm
Frequency	Continuous
Number of diodes per blanket	180
Diode diameter	0,178 cm²
Emitter source area per blanket	480 cm²
Power density per blanket	2,25 mW/cm²
Diode power output	6 mW
Total power per blanket	1,08 W
Total time of application per limb	PBM 60 J: 56 seconds PBM 300 J: 278 seconds PBM 60-300 J: 56 to 278 seconds Sham: 56 seconds
Total energy per site	PBM 60 J: 60 J PBM 300 J: 300 J PBM 60-300 J: 60 to 300 J Sham: No emission
Total energy applied per training session	PBM 60 J: 240 J PBM 300 J: 1200 J PBM 60-300 J: 240 to 1200 J Sham: No emission
The application was performed in direct contact with the skin bilaterally. The order of application was randomized (right or left). The quadriceps and hamstrings muscles were stimulated simultaneously.	

Results

Although 56 individuals were recruited for the present study, six were excluded from the sample, as presented in Figure 1. A total of 50 individuals were included in the study and randomized into four groups. An 11% drop was observed, consistent with the parameters considered during the analysis for sample size. All the included volunteers completed ten training sessions. Recruitment and insertion of participants happened between October 2020 and July 2021. The clinical and demographic characteristics of the individuals in this study are described in Table 2.

No significant differences were observed between the groups in the present study for the peak torque evaluated. After the training sessions, the exception was the non-dominant limb at the follow-up when comparing the 60 J group with the 300 J and Incremental groups. The outcome of all relationships can be seen in Table 3. For the Total Work variable, at 60º/sec, no differences were observed between the groups analyzed. The results can be seen in Table 4. Likewise, at 270º/sec, no significant differences were observed (Table 5).

The external load offered during the training protocol was increasing, as expected. However, it is highlighted that there were no statistically significant differences between the groups. In effect size analysis, a moderate effect can be observed in the total load of the tenth training session between the groups sham vs. maximal (d = -0.672) and maximal vs. incremental (d = 0.553). For the squat, it was observed in the first session between sham vs. minimum (-0.633), sham vs. incremental (-0.628), maximum vs. incremental (0.692), and in the tenth session between sham vs. minimum (-0.51), sham vs. maximum (-0.832), maximum vs. incremental (0.747). For stiff, a large effect was obtained in the first session for sham vs. incremental (1.002) and moderate for minimum vs. incremental (0.733) and maximum vs. incremental (0.56), and moderate effects in the fifth session between sham vs. incremental (0.63), minimum vs. incremental (0.76), maximum vs. incremental (0.657). The graph of load evolution can be seen in Figure 3. Similarly, variables assessing the psychophysiological demand for exercise showed no statistically significant differences, such as the NPS, RPE, or training heart rate (Figure 4). A single point between the Sham and 300 J RPE groups showed a difference. It should be noted that for heart rate and lactate, the maximum value and the delta of the session (Δ = maximum-minimum) were considered.

The observed delta lactate (Δ Lactate) showed no statistically significant differences between the groups during the training protocol. The average blood lactate concentration was stable (between 8.3 and 10.9 mmol/L) among the groups, and there were no significant changes within the same group between training sessions.

Table 2. Characteristics of the participants in the PBM 60 J, PBM 300 J, PBM 60-300 J, and Sham groups.

Outcomes	PBM 60 J		PBM 300 J		PBM 60-300 J		Sham	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
n	13		12		12		13	
Age, years	24.31 (3.45)	-	24.67 (4.12)	-	24.83 (2.95)	-	23.31 (4.03)	
Height, m	1.77 (0.09)	-	1.77 (0.05)	-	1.78 (0.08)	-	1.74 (0.06)	
Weight, kg	85.01 (17.89)	84.73 (16.1)	89 (20.95)	89.12 (20)	85.17 (12.84)	84.6 (12.7)	76.91 (15.09)	75.97 (13.11)
Body Mass Index, kg/m²	27.03 (3.76)	26.98 (3.24)	28.37 (6.63)	28.4 (6.28)	26.95 (4.18)	26.8 (4.37)	25.38 (3.69)	25.1 (3.27)
Dominant Thickness, cm	56.36 (6.80)	57.83 (5.05)	57.71 (4.79)	59.04 (5.88)	57.21 (5.31)	58.42 (5.53)	54.15 (5.19)	54.71 (5.09)
Non-Dominant Thickness, cm	56 (6.62)	57.33 (4.94)	57.67 (5.38)	59.08 (6.46)	56.65 (5.82)	57.88 (4.91)	54.31 (5.96)	54.58 (5.12)
One-repetition maximum - Stiff	93.97 (24.72)	-	95.69 (18.86)	-	102.9 (22.24)	-	91.91 (21.27)	-
One-repetition maximum - Squat	97.08 (19.11)	-	109.6 (12.24)	-	110.4 (23.73)	-	107.1 (21.67)	-

Table 3. Evaluation of Muscle Performance by Dynamometer Isokinetic (Peak Torque - 60º/s) Between the Groups After an Exercise Protocol Associated With Photobiomodulation

Outcomes			Sham *vs.* 60 J Mean Diff. (95% CI)	Sham *vs.* 300 J Mean Diff. (95% CI)	Sham *vs.* 60-300 J Mean Diff. (95% CI)	60 J *vs.* 300 J Mean Diff. (95% CI)	60 J *vs.* 60-300 J Mean Diff. (95% CI)	300 J *vs.* 60-300 J Mean Diff. (95% CI)
Dominant	Extension	Pre	14.9 (-30; 59.8)	-17.7 (-63.6; 28.1)	-19.7 (-65.5; 26.2)	-32.7 (-78.5; 13.2)	-34.6 (-80.4; 11.2)	-1.9 (-48.7; 44.8)
		Post	4.8 (-40.6; 50.2)[a]	-22.3 (-68.6; 24.1)	-21.9 (-68.2; 24.5)	-27 (-73.4; 19.3)	-26.6 (-73; 19.7)	0.39 (-46.9; 47.6)
		Follow-up	24.6 (-26.8; 76.1)[a]	-19 (-69.1; 31.1)	-21 (-70; 27.9)	-43.6 (-95.1; 7.8)[a]	-45.7 (-96; 4.7)[a]	-2.1 (-51; 46.9)
	Flexion	Pre	-3.1 (-27.7; 21.5)	-0.86 (-26; 24.3)	-12.3 (-37.4; 12.8)	2.3 (-22.9; 27.3)	-9.2 (-34.3; 15.9)	-11.4 (-37; 14.2)
		Post	-14.3 (-43.5; 14.8)[a]	-10.9 (-40.7; 18.8)[a]	-22.6 (-52.4; 7.1)[b]	3.4 (-26.4; 33.1)	-8.3 (-38.1; 21.4)	-11.7 (-42.1; 18.6)
		Follow-up	-0.5 (-26.2; 25.1)	-9.8 (-34.8; 15.2)[a]	-17.5 (-41.8; 6.9)[a]	-9.2 (-34.9; 16.4)[a]	-16.9 (-42; 8.2)[a]	-7.7 (-32.1; 16.7)
Non-Dominant	Extension	Pre	24.8 (-22.1; 71.8)	-30.9 (-78.8; 17.1)	-13 (-61; 34.9)	-55.7 (-103.7; 7.7)*	-37.9 (-85.9; 10.1)	17.8 (-31.1; 66.7)
		Post	7.8 (-36.7; 52.3)[a]	-21.9 (-67.4; 23.5)[a]	-20.1 (-65.5; 25.3)	-29.7 (-75.2; 15.7)[b]	-27.9 (-73.3; 17.5)[a]	1.8 (-44.5; 48.2)[a]
		Follow-up	24.7 (-27.3; 76.7)	-29.7 (-80.4; 20.9)	-28.2 (-77.6; 21.3)[a]	-54.5 (-106.5; -2.4)*	-52.9 (-103.7; -2)*[a]	1.6 (-47.9; 51.1)[a]
	Flexion	Pre	2.5 (-22.1; 27.2)	-7.8 (-32.9; 17.4)	-8.8 (-34.0; 16.3)	-10.3 (-35.5; 14.9)	-11.4 (-36.5; 13.8)	-1.1 (-26.7; 24.6)
		Post	-6.3 (-33.3; 20.7)[a]	-8.0 (-35.6; 19.5)	-24.7 (-52.3; 2.8)[b]	-1.7 (-29.3; 25.8)[b]	-18.4 (-46; 9.1)[a]	-16.7 (-44.8; 11.4)[b]
		Follow-up	-0.8 (-26.3; 24.8)	-4.9 (-29.8; 20)[a]	-17.4 (-41.7; 6.9)[a]	-4.1 (-29.7; 21.4)[a]	-16.6 (-41.6; 8.4)[a]	-12.5 (-36.8; 11.8)[b]

Diff., Difference; CI, confidence interval. *$P<0.05$; [a] Small effect size; [b] Moderate effect size.

Discussion

The scientific production in PBMT rises annually, especially regarding clinical outcomes.[1] It is important to notice that the knowledge of the clinical effects has considerably overcome the understanding of the basic science related to photobiomodulation, even interfering with the ideal physical parameterization.[7] It is known that regardless of the light-generating source and when physical parameters are in similar conditions, the outcome should be equivalent.[13,33] On the other hand, Leal-Júnior et al[1] pointed out that the most current therapeutic window regarding muscle performance is still inconclusive. Thus, although there is such an emphasis on the volume of material produced, contradictory results are constant, and the evidence is conflicting or has significant gaps to be filled in.[5]

To our knowledge, this was the first study that applied increasing doses of energy delivered per session, given that the tissue will present variations over time due to exposure to the proposed protocol. The PBMT Incremental 60-300 J is justified because of the characteristics of constant changes present in muscle tissue.[14] However, no statistically significant differences were found between the study groups for the variables of

Table 4. Muscle Performance Evaluation by Dynamometer Isokinetic (Total Work - 60º/s) Between the Groups After an Exercise Protocol Associated With Photobiomodulation

Outcomes			Sham vs. 60 J Mean Diff. (95% CI)	Sham vs. 300 J Mean Diff. (95% CI)	Sham vs. 60-300 J Mean Diff. (95% CI)	60 J vs. 300 J Mean Diff. (95% CI)	60 J vs. 60-300 J Mean Diff. (95% CI)	300 J vs. 60-300 J Mean Diff. (95% CI)
Dominant	Extension	Pre	41.3 (-141.5; 224)	-28.1 (-214.6; 158.4)	-1.2 (-187.8; 185.3)	-69.4 (-255.9; 117.1)	-42.5 (-229; 144)	26.9 (-163.3; 217)
		Post	-100.1 (-311.5; 111.4)[b]	-139.4 (-355.2; 76.4)[b]	-157.5 (-373.3; 58.3)[b]	-39.4 (-255.1; 176.4)	-57.4 (-273.2; 158.4)	-18.1 (-238.1; 202)[a]
		Follow-up	71.3 (-189.9; 332.5)	-5 (-259.2; 249.2)	-27.1 (-275.5; 221.2)	-76.3 (-337.5; 184.9)	-98.4 (-353.9; 157.1)[a]	-22.1 (-270.5; 226.2)[a]
	Flexion	Pre	42.9 (-94.5; 180.2)	14.2 (-126; 154.3)	-42.9 (-183.1; 97.3)	-28.7 (-168.9; 111.5)	-85.8 (-226; 54.4)	-57.1 (-200; 85.9)
		Post	-127 (-288; 34.1)[a]	-59.6 (-223.9; 104.8)	-152.8 (-317.2; 11.6)	67.4 (-97; 231.8)[a]	-25.9 (-190.2; 138.5)	-93.3 (-260.9; 74.4)[a]
		Follow-up	13.9 (-148.5; 176.2)[a]	3.7 (-154.4; 161.8)[a]	-48.8 (-203.3; 105.6)[a]	-10.2 (-172.5; 152.2)	-62.7 (-221.5; 96.2)	-52.5 (-207; 101.9)
Non-Dominant	Extension	Pre	40.5 (-151.1; 232.1)	-99 (-294.5; 96.6)	-72.5 (-268; 123.1)	-139.5 (-335; 56.1)	-112.9 (-308.5; 82.6)	26.5 (-172.9; 225.9)
		Post	0.4 (-209.5; 210.3)[c]	-74 (-288.3; 140.3)[b]	-88 (-302.2; 126.3)[c]	-74.4 (-288.7; 139.9)[b]	-88.4 (-302.6; 125.9)[a]	-14 (-232.5; 204.5)[a]
		Follow-up	101.3 (-157.4; 360)[a]	-35.1 (-286.9; 216.7)	-18.1 (-264.1; 227.9)	-136.4 (-395.1; 122.3)[a]	-119.4 (-372.5; 133.7)	17 (-229; 263)
	Flexion	Pre	22.4 (-118.4; 163.2)	-35.5 (-179.2; 108.2)	-48.9 (-192.6; 94.8)	-57.9 (-201.6; 85.8)	-71.3 (-215; 72.4)	-13.4 (-160; 133.2)
		Post	-61.1 (-190.5; 68.3)[b]	-20.3 (-152.3; 111.8)	-63.4 (-195.5; 68.7)	40.9 (-91.2; 173)[b]	-2.3 (-134.4; 129.8)[b]	-43.2 (-177.9; 91.6)[a]
		Follow-up	10.4 (-117.6; 138.5)	29.3 (-95.3; 153.9)[a]	-34.1 (-155.9; 87.6)	18.9 (-109.2; 146.9)[b]	-44.6 (-169.8; 80.7)	-63.4 (-185.2; 58.4)[b]

Diff., Difference; CI, confidence interval. *$P<0.05$; [a] Small effect size; [b] Moderate effect size; [c] Large effect size.

Table 5. Muscle Performance Evaluation by Dynamometer Isokinetic (Total Work - 270º/s) Between the Groups After an Exercise Protocol Associated With Photobiomodulation

Outcomes			Sham vs. 60 J Mean Diff. (95% CI)	Sham vs. 300 J Mean Diff. (95% CI)	Sham vs. 60-300 J Mean Diff. (95% CI)	60 J vs. 300 J Mean Diff. (95% CI)	60 J vs. 60-300 J Mean Diff. (95% CI)	300 J vs. 60-300 J Mean Diff. (95% CI)
Dominant	Extension	Pre	174.3 (-355.5; 704.2)	-100 (-640.7; 440.8)	-201.8 (-742.5; 338.9)	-274.3 (-815; 266.5)	-376.1 (-916.9; 164.6)	-101.8 (-653.3; 449.6)
		Post	-138.7 (-600; 322.6)[b]	-258.4 (-729.2; 212.3)[a]	-258.1 (-728.9; 212.7)	-119.8 (-590.5; 351)[a]	-119.4 (-590.2; 351.4)[a]	0.4 (-479.7; 480.5)[a]
		Follow-up	112.8 (-450.8; 676.3)	-225.2 (-773.7; 323.4)[a]	-273.6 (-809.5; 262.4)	-337.9 (-901.5; 225.7)	-386.3 (-937.6; 165)	-48.4 (-584.3; 487.5)
	Flexion	Pre	-107.4 (-508.9; 294)	55.7 (-354.1; 465.4)	-158.3 (-568; 251.5)	163.1 (-246.6; 572.9)	-50.8 (-460.6; 358.9)	-214 (-631.8; 203.9)
		Post	-52.9 (-421.1; 315.3)[a]	-91.8 (-467.6; 283.9)	-248.8 (-624.5; 127)[a]	-38.9 (-414.7; 336.8)[a]	-195.9 (-571.6; 179.9)	-156.9 (-540.1; 226.3)[a]
		Follow-up	79.8 (-321.2; 480.8)	-84.6 (-474.9; 305.7)	-238.3 (-619.7; 143)[a]	-164.4 (-565.4; 236.6)[a]	-318.1 (-710.4; 74.2)	-153.7 (-535; 227.6)[a]
Non-Dominant	Extension	Pre	225.8 (-266.9; 718.5)	-225 (-727.9; 277.9)	-199.8 (-702.7; 303.1)	-450.8 (-953.7; 52.1)	-425.6 (-928.5; 77.3)	25.3 (-487.6; 538.1)
		Post	19.2 (-412.8; 451.1)	-205.6 (-646.4; 235.3)[a]	-334 (-774.9; 106.8)[a]	-224.8 (-665.6; 216.1)[a]	-353.2 (-794; 87.7)[a]	-128.4 (-578; 321.2)
		Follow-up	127.5 (-387.7; 642.6)[a]	-174.6 (-676.1; 326.8)[a]	-285.4 (-775.3; 204.5)[a]	-302.1 (-817.3; 213)[b]	-412.9 (-916.8; 91.1)[b]	-110.7 (-600.6; 379.2)
	Flexion	Pre	-115.1 (-434.4; 204.2)	-107.4 (-433.2; 218.5)	-158.1 (-484; 167.7)	7.7 (-318.1; 333.6)	-43 (-368.9; 282.8)	-50.7 (-383; 281.6)
		Post	-78.1 (-395.8; 239.7)	-120.2 (-444.6; 204.1)	-192.2 (-516.6; 132.1)	-42.2 (-366.5; 282.2)	-114.2 (-438.5; 210.1)[a]	-72 (-402.8; 258.7)
		Follow-up	23.9 (-317.1; 365)[a]	-39.8 (-371.8; 292.2)[a]	-143.5 (-467.8; 180.9)	-63.7 (-404.8; 277.4)[a]	-167.4 (-501.1; 166.2)[a]	-103.7 (-428; 220.7)

Diff., Difference; CI, confidence interval. *$P<0.05$; [a] Small effect size; [b] Moderate effect size; [c] Large effect size.

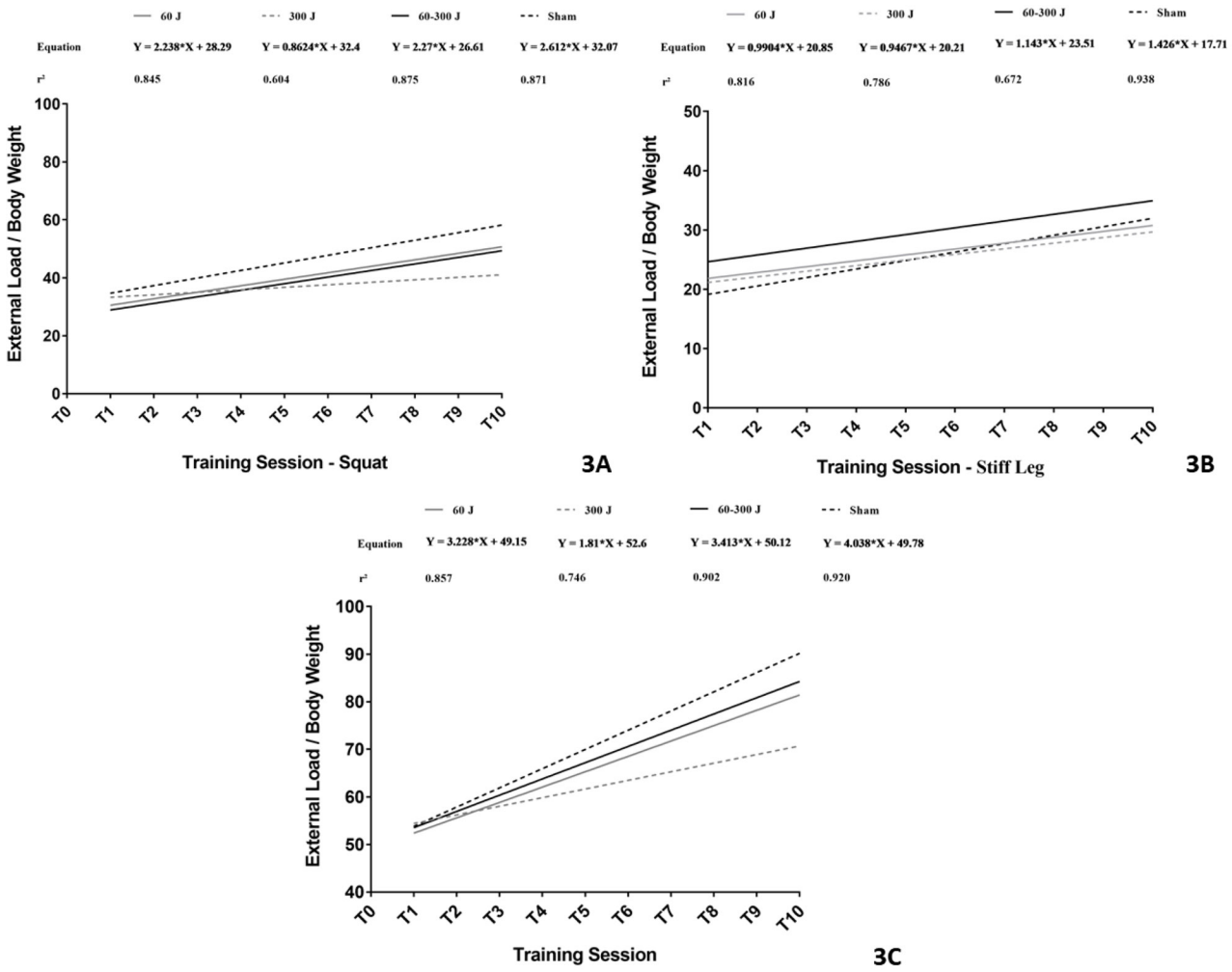


Figure 3. Linear Regression Analysis of External Load During Resistance Exercises: (A) Squat Exercise, (B) Stiff-Leg Deadlift Exercise, and (C) Combined Total Volume Load From Both Exercises

interest in the protocol, although small to moderate effect sizes favored the Incremental and Maximal Dose groups for strength parameters. Similar patterns were observed for psychophysiological responses and training loads across the groups. Here the importance of distinguishing statistical significance from clinical relevance is recognized, with effect sizes providing a measure of magnitude and offering a more practical interpretation of the results. In our study, while some comparisons did not reach statistical significance, the small to moderate effect sizes suggest potential clinical relevance, warranting further investigation.

The first point of emphasis, therefore, is the physical parameters imposed. The energy was chosen based on the lowest and highest values found in the literature for increasing the performance of the quadriceps femoris[1,34] considering that the minimum exposure time per muscle area was also respected, as well as the form of a contact application. However, the power parameter can be better explored, such as the due specificity of the wavelength employed.

Zagatto et al[35] showed in their study that the power might directly interfere with protocols like ours. Ferraresi[5] points out that the use of different power equipment is still being investigated since there has yet to be an achieved consensus on such parameters, but higher powers are more indicated. It should be noted that the other specifications follow the premises predicted in the literature, such as wavelength and distance between the emitters, as can be seen in Guirro et al.[30] Among the specifications, it is also worth mentioning the care with the individuality of the volunteer, such as skin tone; for example, if the volunteer presented Fitzpatrick skin type greater than or equal to 4, there was a 10% increase in the energy applied.

Although not showing favorable outcomes for using photobiomodulation as an exercise adjunct therapy in this protocol, the results are not isolated from the literature. As Ferraresi[5] indicated, the current literature still presents controversies and particularities, often due to different therapeutic objectives or physical parameterization. De Carvalho et al[36] conducted a clinical trial to evaluate the

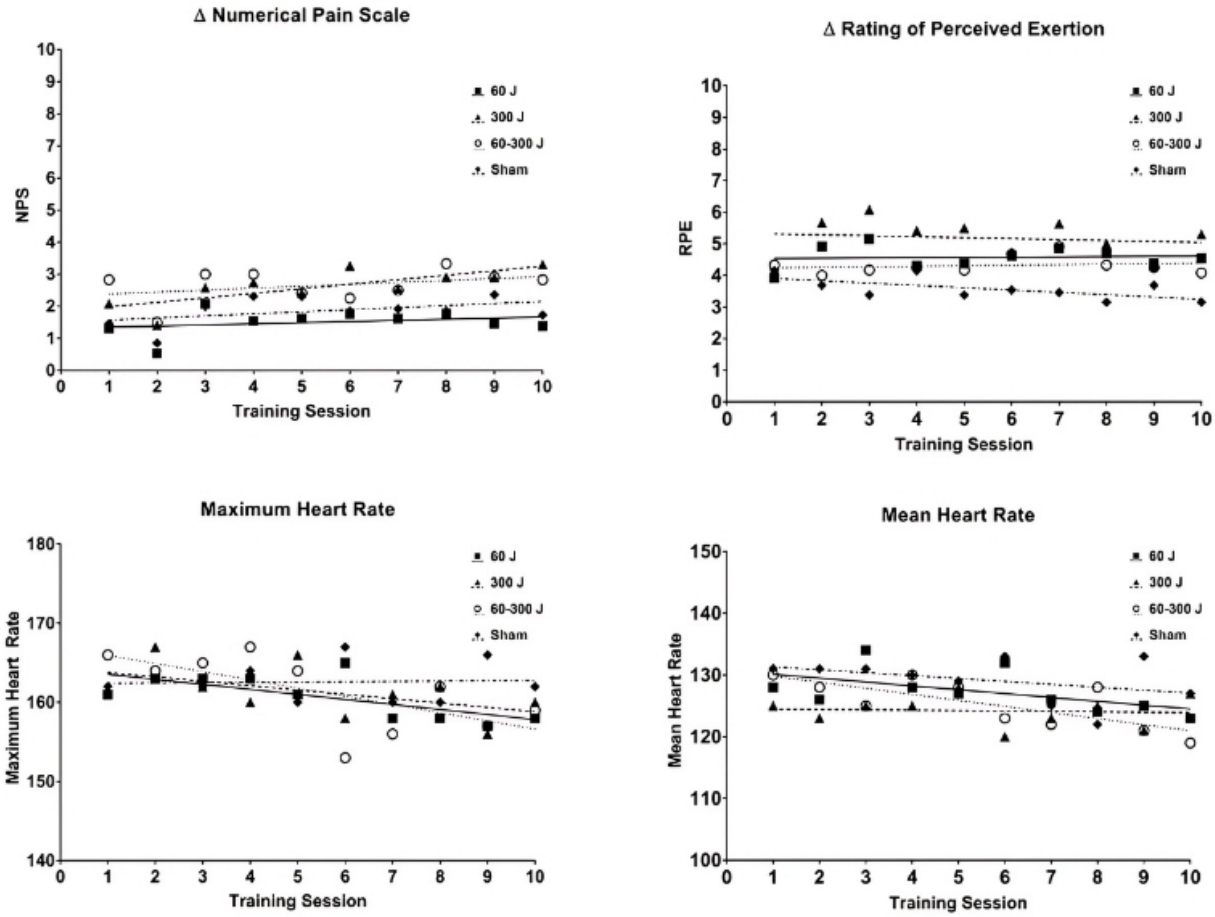


Figure 4. Evolution Per Training Session for the Numerical Pain Scale (NPS), Rating of Perceived Exertion (RPE), and Observed Mean and Maximum Heart Rate. Values are shown by the delta of the session

effects of a three-day sequential application at different wavelengths, not associated with training, in cyclists and observed no difference for incremental tests or peak torque in the isokinetic dynamometer. Similarly, Dutra et al[37] investigated the effects on metabolic and muscle levels of photobiomodulation without observing the positive interaction of its use. In another scenario, now with trained individuals, Machado et al[38] did not observe additional benefits when PBMT was combined with training during a six-week protocol. For training volume analysis, as in the present study, Orssatto et al[39] did not observe positive contributions of PBMT associated with the training protocol.

When young men were evaluated regarding muscle performance, as in the present study, Abreu et al[40] did not observe positive effects of the association of photobiomodulation with exercise. However, studies like Ferraresi et al[23] and Vanin et al[20] present favorable results of muscle performance to its application, considering that the photobiomodulation was applied previously to the proposed training protocol, as well as the present study, and followed the evolution of the participants in an associated way.

Although positive outcomes are faced using photobiomodulation by different systematic reviews,[1,34,41–43] significant variability among the physical parameters and study subjects must be highlighted. One should consider that individual conditions, such as melanin concentration in addition to hemoglobin and subcutaneous lipids, as the main components of light absorption on the surface tissue, may directly interfere with the outcome of interest.[44,45] Therefore, once the light is not absorbed by the target cell, it will not promote biological responses.[44] The present study presented novelties in comparison with the literature. Increasing doses of energy may be an important factor for the adaptation of cellular responses and possible positive modulations once delivered within the therapeutic window already indicated by the literature. Thus, the continuity of studies regarding this physical variable is of interest.

Recent investigations highlight key aspects that help summarize and align the discussion regarding null results in photobiomodulation and performance. Different devices have been used to establish the current state of the art, leading to a high variability in physical outcomes, whether due to intrinsic factors[46] or issues related to the lack

of preventive or corrective maintenance.[47] For instance, De Marchi et al[48] examined how three different devices, with distinct parameters but delivering the same energy, influenced performance and muscle recovery outcomes. In this case, a specific set of parameters proved to be more effective than the others, thus showing the importance of considering factors other than energy in their separate ways. Therefore, we believe that one factor influencing our results may have been the choice of parameters, as some studies have reported positive outcomes with protocols similar to ours. This rationale also guided the selection of energy levels, timing and application format in our study, as presented in the materials and methods section. Additionally, the characteristics of the studied population should be considered, as recent research suggests that training protocols like ours may not be the optimal design for detecting the intended outcomes. At the current state of knowledge, endurance-based activities appear to be more responsive to photobiomodulation.[49]

Although there is evidence for its use, the literature needs to advance in terms of physiological support and parameterization of equipment and protocols. Different populations need to be accessed to observe if, outside the homeostasis conditions of a healthy individual, such benefits can become more evident since this was the population covered here. Finally, different power values should be explored before ignoring the possible benefit of incremental doses.

Some points need to be mentioned, such as a possible neural adaptation during the proposed protocol. However, Machado et al[38] highlighted the non-observation in their protocol and outcomes similar to the one observed here. Additionally, our study presents some limitations, such as the regionality and specificity of the sample, as well as the still unclear interaction of mask use during resistance training. While the power employed remains a topic of discussion, we believe that PBMT was appropriately applied, particularly in a well-defined muscle area. Nonetheless, we acknowledge that the application method may pose a limitation in clinical practice. Therefore, future studies should explore PBMT application in different muscle groups and with varied equipment to determine whether the absence of systemic effects and muscle function improvements persists across different methodologies.

Conclusion

The methodological proposal offered in the present study for PBMT associated with the training protocol did not promote superior results for muscle capacity, psychophysiological and metabolic indices among the different therapy groups or even in comparison with the sham group.

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Writing–original draft: All authors.
Writing–review & editing: All authors.

Competing Interests

Not applicable.

Ethical Approval

The Ethics Committee of the Clinical Hospital of the Ribeirão Preto Medical School, under protocol 4.721.982, approved this study.

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