Photobiomodulation, Photomedicine, and Laser Surgery Volume XX, Number XX, 2020 © Mary Ann Liebert, Inc.

Pp. 1-9 DOI: 10.1089/photob.2019.4785 Photobiomodulation for Exercise and Muscle Recovery

Effect of Photobiomodulation Therapy in the 1500 m Run: An Analysis of Performance and Individual Responsiveness

Rodolfo André Dellagrana, PhD,^{1,2} Mateus Rossato, PhD,^{1,3} Lucas B.R. Orssatto, MSc,⁴ Raphael Luiz Sakugawa, MSc,¹ Bruno Manfredini Baroni, PhD,⁵ and Fernando Diefenthaeler, PhD¹

Abstract

Objective: The aims of this study were to verify the effects of photobiomodulation therapy (PBMT) on time trial run performance over 1500 m, as well as on individual responsiveness of recreative runners.

Materials and methods: Nineteen recreationally trained runners participated in a randomized, crossover, double-blind placebo-controlled trial. The study was divided in four sessions: (1) incremental maximal running test; (2) 1500 m run control (without placebo or PBMT); and (3, 4) PBMT or placebo before 1500 m run. PBMT or placebo was applied over 14 sites per lower limb immediately before time trial run using a mixed wavelength device (33 diodes: 5 LASERs of 850 nm, 12 LEDs of 670 nm, 8 LEDs of 880 nm, and 8 LEDs with 950 nm). PBMT delivered 30 J per site, with a total energy dose of 840 J. Physiological variables [maximal oxygen uptake (VO_{2MAX}), velocity associated to VO_{2MAX} (vVO_{2MAX}), peak of velocity, and respiratory compensation point (RCP)] were assessed during incremental maximal test. During 1500 m races we accessed the following: time, heart rate, and lower limb rate perception exertion per lap, total time, and blood lactate concentration

Results: PBMT had no significant difference and likely trivial effect for performance in the total time trial run over 1500 m compared to placebo. In the responsiveness analyses, 10 participants positively responded to PBMT, whereas total time reduced for responders (-10.6 sec; -3.18%) and increased for nonresponders (+6.0 sec; +1.73%). Responders presented higher aerobic parameters (VO_{2MAX} and RCP) than nonresponders. Moreover, responders had lower time per lap and [Lac] (1 and 3 min) when PBMT was applied.

Conclusions: PBMT applied immediately before running in noncontrolled environment was not able to improve the 1500 m performance of recreationally trained runners. However, responders to PBMT presented higher aerobic capacity than nonresponders.

Keywords: running performance, ergogenic aid, low-level laser therapy, light-emitting diode therapy, athletics

Introduction

PHOTOBIOMODULATION THERAPY (PBMT) involves the employment of red or near-infrared photons to induce chemical changes in a target tissue. 1,2 Currently, the PBMT has been applied before exercise to provoke an ergogenic effect.³ The mechanism behind PBMT ergogenic effects involves the absorption of light particles (photons) by tissue, which may induce biochemical changes of cells, mainly on mitochondrial level.^{2,4} In summary, the immediate effect of PBMT seems to be related to membrane-bound chromophores that act as photosensitizers inducing changes in membrane permeability and transport mechanism. 1,5 Since the photons reach the mitochondria, they are absorbed by cytochrome enzymes (e.g., cytochrome c oxidase) and provoke a series of physiological effects triggered by changes on the production of reactive oxygen species and synthesis rates of adenosine triphosphate^{1,4}

Keeping the PBMT effects on mitochondrial level in mind, practitioners of exercises highly reliant on oxidative

Laboratório de Biomecânica (BIOMEC), Centro de Desportos, Universidade Federal de Santa Catarina, Florianópolis, Brazil.

²Programa de Pós-Graduação em Ciências do Movimento, Universidade Federal de Mato Grosso do Sul, Campo Grande, Brazil.

³Laboratório de Desempenho Humano, Faculdade de Educação Física, Universidade Federal do Amazonas, Manaus, Brazil.

⁴School of Exercise and Nutrition Sciences, Queensland University of Technology, Brisbane, Australia.

⁵Programa de Pós-Graduação em Ciências de Reabilitação, Departamento de Fisioterapia, Universidade Federal de Ciências da Saúde de Porto Alegre, Porto Alegre, Brazil.

metabolism could benefit with PBMT application before exercise. Recent studies have explored the ergogenic effects of PBMT applied immediately before exercise protocols in delaying the onset of skeletal muscle fatigue, and consequently performance improvement.³ Thus, positive results have been found for isometric,⁶ isokinetic,⁷ cycling,^{8–10} and running exercises.^{11–14} Previous studies involving running tests have observed positive effects of PBMT on a range of physiological and performance parameters, such as maximal oxygen uptake (VO_{2MAX}), biochemical markers (e.g., creatine kinase and lactate dehydrogenase), running economy, neuromuscular economy, peak of velocity (PV), and total time to exhaustion, both in untrained individuals^{11,14} and recreationally trained runners.^{12,13}

Despite the promising findings of previous studies, ^{11–14} PBMT was only applied before running tests performed on treadmills, always into a laboratory-controlled environment. This limitation reduces the external validity of positive results and, consequently, the practical relevance for the athletic population. Just a few studies aimed to investigate the PBMT effect in a noncontrolled environment. ^{15,16} Pinto et al. ¹⁵ demonstrated that preconditioning PBMT can enhance performance of high-level rugby players during an anaerobic field test (Bangsbo Sprint test). De Marchi et al. ¹⁶ observed that PBMT applied in futsal players before an official match was effective in preventing fatigue and muscle damage. However, the effects of PBMT on exercise performance during aerobic field tests or races remain unexplored.

The individual responsiveness to PBMT is also poorly explored in the literature. ^{10,14} In a preliminary study with six male futsal players, Leal Junior et al. ¹⁰ reported that all volunteers presented reduced creatine kinase (CK) and lactate levels after performing Wingate anaerobic test when previously treated with PBMT. Miranda et al. ¹⁴ found that 17 out of 20 healthy male participants positively responded to PBMT, improving performance in an incremental treadmill test. Considering that main PBMT effect is related to mitochondrial activity, we hypothesized that the effect could be maximized in aerobically trained individuals, given that, at least in theory, these individuals would present higher predominance of Type I muscle fibers (oxidative fibers) and higher mitochondrial content. However, to the best of our knowledge, there is no study that addressed this aspect.

In summary, investigating the effect of PBMT applied immediately before events that simulate real sport competitions is imperative to demonstrate real-world application and translation to clinical practice. Concurrently, it seems necessary to understand PBMT individual responsiveness and identify factors that discriminate responders and non-responders, providing information of who can be benefited of PBMT. Therefore, the purpose of this study was to verify the effects of PBMT on performance during a time trial run over 1500 m, as well as on individual responsiveness of recreative runners.

Materials and Methods

Participants

Twenty recreationally trained runners voluntarily participated in this study. The following inclusion criteria were adopted: (1) male runners 18–35 years of age; (2) training routine with three to five running sessions per week in the

last 6 months; and (3) 6 months of previous experience in 1500 m races. One participant who presented lower limb injury during data collection period was excluded. Therefore, 19 runners (27.3±3.3 years, 74.5±9.3 kg, and 178.9±6.5 cm) were eligible to participate in this study. The number of subjects was determined following a statistical power of 0.80, significance level of 0.05, and the effect size based on the relative risk of increased time to exhaustion (4.12 sec) in favor of PBMT. Tonsequently, a minimum of 10 subjects was determined to detect the effects of PBMT versus the placebo. The G*Power version 3.1.9.2 software was used to determine the sample size. All subjects provided written informed consent. Ethical approval was obtained from the local Human Research Ethics Committee (Protocol No. 61599116.1.0000.0121).

Study design

This study was designed as a crossover, randomized, double-blind, and placebo-controlled trial. The research was divided into four phases, with a 7-day interval between trials. The study protocols were performed on four different days at about the same hour. On the day before each test, subjects were solicited to avoid vigorous exercises of the lower limbs, and alcohol and caffeine intake. In the first phase, subjects underwent incremental maximal running test, to assess maximum oxygen uptake (VO_{2MAX}), velocity associated with VO_{2MAX} (vVO_{2MAX}), PV, maximal heart rate (HR_{MAX}), and respiratory compensation point (RCP). In the second phase, participants performed a time trial run over 1500 m, which was characterized as control condition. In the two remaining days (third and fourth phases), participants underwent (1) placebo or PBMT treatments and (2) time trial run over 1500 m (Fig. 1). In addition, for field tests (1500 m), the environment factors were monitored minute-by-minute using data of Laboratory of Energy Conversion Engineering and Energy Technology allocated at local University (-27.6040 S and -48.5184 W), for which the coefficient of variation among days of tests was <15% for temperature $(21.0^{\circ}C \pm 1.7^{\circ}C)$ and relative humidity $(86.7\% \pm 10.4\%)$. The researchers responsible for testing were blinded to the participants' allocation to the treatment. A single researcher was responsible for the randomization of the PBMT and placebo applications. This researcher was instructed not to inform the participants or the other researchers regarding the treatment used in each testing phase (i.e., third and fourth). Moreover, participants used opaque goggles that blocked the view during treatment application. Since PBMT does not cause any sensitive stimulus (i.e., warm, cold, itching, skin irritation, and pain), volunteers were also blinded to treatment order.

Incremental maximal running test

 ${
m VO}_{2{
m MAX}}$ was measured using an incremental maximal running protocol performed on a motorized treadmill (Imbramed Millenium Super ATL, Model 10200, Porto Alegre, Brazil) with the gradient set at 1%. The initial speed was set at 6 km/h for 30 sec and was then incremented by 0.5 km/h every 30 sec, until voluntary exhaustion. During the test, levels of oxygen uptake (VO₂) and carbon dioxide (CO₂) produced were measured breath-by-breath using an opencircuit indirect gas exchange system (Quark PFTergo;

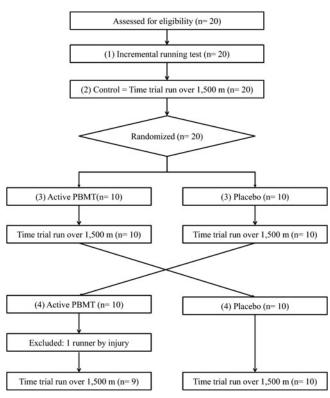


FIG. 1. Study design.

COSMED SRL, Rome, Italy). The equipment was calibrated with known gas samples for oxygen and carbon dioxide, whereas the ventilation flow was calibrated using a syringe with a volume of 3 L (model 5530; Hans Rudolph).

The attainment of VO_{2MAX} was defined using the criteria proposed by Bassett and Howley. 18 The VO_{2MAX} was considered the highest at 15 sec average obtained during the test or, in the presence of plateau in the VO₂ response, it was considered the average of the final 30 sec of exercise. HR was monitored throughout the test, in which HR_{MAX} was defined as the highest value recorded during the test. The vVO_{2MAX} was defined as the minimal velocity at which VO_{2MAX} occurred. PV was defined as the last velocity that was maintained for 30 sec. The RCP was determined based on ventilatory equivalent for O₂ and CO₂ (V_E/VO₂ and V_E/ VCO₂). ¹⁹ A visual inspection to determine the RCP was carried out independently by two experienced researchers. The RCP values detected by the two researchers were then compared. If the two RCP values were within 3% [mL/(kg·min)], then those values were averaged and accepted. If the two RCP values were more than 3% different, a third researcher would have to independently analyze the exercise test data to detect RCP. Thus, the velocity at RCP (vRCP) and VO₂ concerning RCP (VO₂RCP) were determined.

PBMT/placebo treatment

PBMT or placebo treatments were applied using a Chattanooga Intelect Mobile Laser 2779 system (Chattanooga Group, Guildford Surrey, United Kingdom) on the right and left lower limbs immediately ($\sim 20 \, \text{min}$) before time trial run over 1500 m (Table 1). Treatments were ap-

TABLE 1. TABLE TO REPORT PARAMETERS IN EXPERIMENTAL AND CLINICAL PHOTOBIOMODULATION THERAPY ARTICLES

Manufacturer	Chatanooga group
Model identifier	Laser 2779 system (T5338) 2013
Year produced Number and type of emitters (laser or LED)	5 lasers and 28 LEDs
Wavelength and bandwidth, nm	5 lasers (850) 12 LEDs (670)
,	8 LEDs (880) 8 LEDs (950)
Pulse mode, CW or Hz, duty cycle	Continuous
Beam spot size at target, cm ²	5 lasers (0.06) 12 LEDs (1.92) 16 LEDs (1.28)
Irradiance at target, mW/cm ²	5 lasers (1666.6) 12 LEDs (5.20) 8 LEDs (19.53)
If pulsed peak irradiance, mW/cm ²	8 LEDs (11.71) 1703.1
Exposure duration, sec Radiant exposure, J/cm ² Radiant energy, J	32 0.9933 30
Number of points irradiated Area irradiated, cm ² Application technique	28 30.2 Cluster
Number and frequency of treatment sessions Total radiant energy over entire treatment course, J	2 840

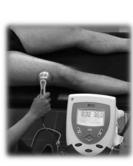
plied on 14 sites on each lower limb: 8 sites on the quadriceps, 4 sites on the hamstrings, and 2 sites on the gastrocnemius (Fig. 2). The placebo was applied exactly the same way, however, with the equipment turned off. The probe was held stationary on skin contact at 90° angle with light skin pressure. 12,13

Blood lactate concentration

For third and fourth phases (placebo or PBMT), capillary blood samples ($25 \,\mu\text{L}$) were obtained from the ear lobe of each volunteer, and blood lactate concentration ([Lac]) was measured using an electrochemical analyzer (YSI 1500 Sport; Yellow Springs Instruments, Ohio). The analyzer was calibrated in accordance with the manufacturer's recommended procedures. Blood samples were taken at rest and at first, third, and fifth minute after time trial run over 1500 m.

Time trial run (1500 m)

The time trial run over 1500 m were held at an outdoor 400 m track. Before the race, participants performed a standard warm-up with specific running exercises monitored by researcher responsible for the time trial test. The variables analyzed were first (0–300 m), second (301–700 m), third (701–1100 m), and fourth (1101–1500 m) lap times and the total time (0–1500 m). In addition, the HR was monitored throughout the time trial run (Polar H6 Bluetooth,





Power density (mW/cm²) Frequency Dose (J) Cluster size (cm²) Number of sites	11.71 Continuous 0.50 30.2 28
Number of diodes Power output (mW) Spot size (cm ²)	8 15 1.28
Prequency Dose (J) LEDs (950nm)	Continuous 0.80
Spot size (cm²) Power density (mW/cm²)	1.28 19.53
Number of diodes Power output (mW)	8 25
LEDs (880nm)	
requency Oose (J)	Continuous 0.30
Power density (mW/cm ²)	5.20
Power output (mW) Spot size (cm ²)	10 1.92
LEDs (670nm) Number of diodes	12
Frequency Dose (J)	Continuous 3.2
Power density (mW/cm ²)	1666.6
Spot size (cm ²)	0.06
Number of diodes Power output (mW)	5 100

FIG. 2. PBMT parameters and application sites (black dots on the muscles). PBMT, photobiomodulation therapy.

Finland), and rating of perceived exertion for fatigue in the lower limbs (lower limbs RPE) was annotated at 300-, 700-, 1100-, and 1500-m distances using the Borg scale, which consists of 11 statements scored from 0 to 10.²⁰ The total and partial time of the time trial run over 1500 m were determined by two researchers who set the time with a stopwatch, and the average of the time was considered.

In the three simulated events, some factors during the test were controlled,²¹ as follows: (1) no feedback of performance (e.g., pace, time, and HR frequency) either during or after the trial until all trials are completed; (2) no distractions during performance trials (e.g., music and conversations); (3) participants ran alone on track to avoid influence of another runner's pace; (4) do not give performance clues by taking measures or giving drinks at set time points; (5) temperature and humidity kept constant; and (6) equipment such as shoes kept the same in each trial. In addition, before starting the data collection, five participants of this study performed two time trial run over 1500 m, in which it was possible to verify the variation between two races without placebo or PBMT effects. Thus, the mean and standard deviation of first and second time trials run were 316.8 ± 15.2 and 315.0 ± 10.7 sec, respectively (mean difference = 1.8 sec, coefficient of variation = 4\%, effect size = 0.15, and trivial effect).

Statistical analyses

Data normality was verified using the Shapiro-Wilk test. Values are presented as mean and standard deviation. The paired Student's t-test was used to compare treatments (PBMT vs. placebo) for total time trial run over 1500 m. Two-way ANOVA (analysis of variance) with repeated measures [treatment factor (PBMT and Placebo) and lap factor (first, second, third, and fourth laps)] was used to compare the time, HR, and rating of perceived exertion. A similar statistical approach was performed to blood lactate concentration variable [treatment factor (PBMT and Placebo) and time factor (pretest, and first, third, and fifth minute after test)]. All statistical analyses were performed using IBM SPSS Statistics for Windows, version 21.0 (IBM Corp, Armonk, NY) software. For all statistics, the significance level was set at p < 0.05.

Before data collection, five subjects performed two 1500 m time trial run in different days, without PBMT or placebo application, to identify the smallest worthwhile effect.²² Therefore, reductions or increases of running time to PBMT compared to placebo, superior or lower to the smallest effect from observed standard deviation, were considered positively or negatively affected by PBMT. Thus, runners who improved their performance during time trial run with PBMT application (time reduction larger than 2.62 sec) were considered responders (beneficial effects with PBMT application). However, runners who did not improve their performance by 2.62 sec were considered nonresponders.

The magnitude-based inference analysis was also used to examine practical significances. The magnitude of differences between groups (placebo vs. PBMT and responders vs. nonresponders) was calculated. We adopted the criteria of Cohen for the analysis (>0.2: small; >0.50: moderate; >0.80: large). The changes that the true (unknown) mean

changes were positive or negative [i.e., greater than the smallest worthwhile change (0.2 multiplied by the betweenparticipant standard deviation)], and trivial were determined. Quantitative changes of a positive or negative effect were assessed qualitatively, as follows: <1% = most unlikely; 1-5% = very unlikely; 5-25% = unlikely; 25-75% = possibly; 75-95% = likely; 95-99% = very likely; and >99% = mostlikely. If the chances of positive and negative effects were both >5%, then the true difference was assessed as unclear.²³ This study assessed the time trial run over 1500 m in three different conditions (i.e., control, placebo. and PBMT treatments). However, considering the control condition was always performed at first session, and no differences were found between control and placebo treatments (trivial effects, p > 0.05) for all variables, we used just comparisons between placebo and PBMT treatments.

Results

The runners presented VO_{2MAX} , HR_{MAX} , and VO_2RCP of $52.0\pm4.3\,\text{mL/(g\cdot min)}$, $190\pm7\,\text{bpm}$, and $43.6\pm4.2\,\text{mL/(kg\cdot min)}$, respectively. The velocity of time trial run over $1500\,\text{m}$ in control, placebo, and PBMT treatments was 16.0 ± 1.3 , 16.0 ± 1.2 , and $16.2\pm1.4\,\text{km/h}$, respectively. In addition, runners performed the time trials at $99.7\%\pm4.0\%$, $99.7\%\pm3.2\%$, and $100.6\%\pm4.8\%$ of vVO_{2MAX} in the control, placebo, and PBMT treatments, respectively. According to the study design, the control condition was always performed at the second phase (after first phase—incremental maximal running test). Considering similar results between control and placebo conditions, the results section was focused on comparisons between PBMT and placebo treatments.

For comparison between placebo and PBMT treatments, for all participants, no significant difference was observed for total time trial run over $1500\,\mathrm{m}$ ($p\!>\!0.05$), and the magnitude-based inference indicated *trivial* (mean difference=2.7 sec) (Fig. 3). Time, HR, and lower limb RPE are presented in Fig. 4, in which no treatment-lap interaction ($F\!=\!0.300,\ p\!=\!0.825;\ F\!=\!0.732,\ p\!=\!0.537;\ \mathrm{and}\ F\!=\!1.333,\ p\!=\!0.273,\ \mathrm{respectively})$ or treatment effect ($F\!=\!1.363,\ p\!=\!0.258;\ F\!=\!0.002,\ p\!=\!0.961;\ \mathrm{and}\ F\!=\!0.004,\ p\!=\!0.948,\ \mathrm{respectively})$ was observed. However, a significant lap effect

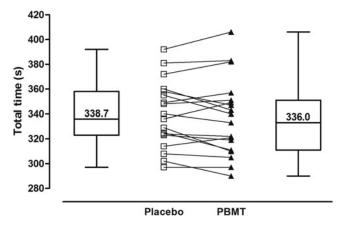


FIG. 3. Total time at 1500 m race for placebo and PBMT treatments.

was shown for time, HR, and lower limb RPE (F=313.228, p<0.001; F=104.482, p<0.001; and F=154.829, p<0.001, respectively). Similarly, no treatment-time interaction (F=0.726, p=0.541) or treatment effect (F=0.026, p=0.874) was observed on [Lac], but a significant effect was observed for time (F=363.374, p<0.001) (Fig. 4).

In Table 1, the responsiveness analysis showed that 52.6% (*n* = 10) of runners improved their performance in the time trial run over 1500 m with PBMT applied immediately before exercise, while 47.4% (*n* = 9) of runners worsened or did not change the performance. Comparing responders and nonresponders, *likely* and *very likely negative* effects (high values for nonresponders) were observed over time at first, second, third, and fourth lap in the PBMT condition. Further, in the PBMT condition, responders presented lower [Lac] at 1 and 3 min after the 1500 m test (*likely* and *very likely* effects, respectively). Also, higher HR was observed at second, third, and fourth lap for nonresponders in the placebo condition (*very likely* effects). In addition, Table 2 showed that responders had better total time at 1500 m (*very likely* effects), VO_{2MAX}, and vRCP (*likely* effects).

Discussion

To the best of our knowledge, this study is the first to verify the effects of PBMT applied immediately before a simulate middle distance running (i.e., 1500 m). Independent of training conditioning, practical strategies to improve performance should be provided for runners. ²⁴ Thus, PBMT as a nonpharmacological and noninvasive tool could be inserted to maximize performance in training sessions and real competitions. The main findings of this study support that PBMT was not able to improve runners' performance at 1500 m. On the other hand, the results showed that most conditioned runners positively responded to PBMT, reducing the 1500 m run total time and [Lac] near to peak (Table 2).

Considering that previous studies have shown beneficial effects on total time to exhaustion during progressive maximal treadmill tests, 11,13,14 in this study, we verified whether this positive effect of PBMT applied immediately before tests in a laboratory-controlled environment could be reproduced in a time trial run over 1500 m at an outdoor 400 m track. Contrary to laboratory-controlled studies, results including the whole sample suggested that PBMT was not effective to improve 1500 m run performance in recreationally trained runners. However, the responsiveness analysis showed that PBMT ergogenic effects can be dependent of individual conditioning level, since runners with higher aerobic capacity improved their time trial run performance with PBMT compared to placebo application. When we look only to the responder runners, PBMT improved running performance around $10.6 \sec (-3.18\%)$. This improvement may seem quite discreet, but 8.7 sec was the difference between the 1st and the 12th placed in the final of 1500 m men on IAAF (International Association of Athletics Federations) World Championships Doha Qatar 2019.

In this study, PBMT applied immediately before time trial run over 1500 m did not change the lower limb perceived fatigue. Previous studies involving PBMT as preconditioning to running exercise assessed RPE during maximal^{8,14} and submaximal¹³ tests in a laboratory-controlled environment,

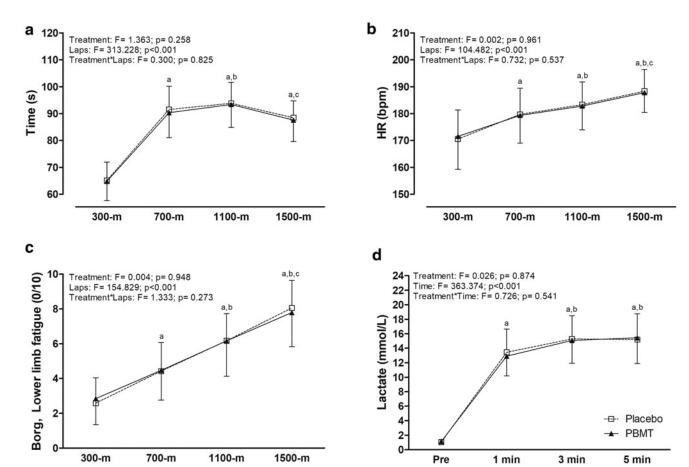


FIG. 4. Effect of PBMT on time per lap, HR, ratio of perceived effort (Borg scale-RPE), and blood lactate concentration during 1500 m race. Analysis with all runners (n = 19). a = different from 300 m (a - c) and pre-running (d); b = different from 700 m (a - c) and 1 min (d); c = different from 1100 m (a - c). HR, heart rate.

which preclude comparisons with our results. Noteworthy, contradictory results have been observed in these studies, Miranda et al. 14 showed that RPE dyspnea was lower during test after PBMT than after placebo, whereas Da Silva Alves et al. 8 observed no significant difference for RPE dyspnea and lower limb fatigue. Further, Dellagrana et al. 13 observed that PBMT had beneficial effects for RPE (overall fatigue) during a submaximal running test in laboratory. In the responsiveness analysis, the lower limb perceived showed unclear results. Regarding exercises in a noncontrolled environment, future studies are necessary to understand the impact of PBMT on perceptual responses.

It is known that during intense exercises, high levels of [Lac] may be associated to impairment of whole body exercise performance. Although no change was observed for [Lac] with all runners analysis, *very likely* and *likely* effects were observed for [Lac] after 1- and 3-min time trial run over 1500 m, respectively, in favor of the responders compared to nonresponder runners in the PBMT condition. In addition, [Lac] pre-running was higher for responders in comparison with nonresponders. This means that when a runner is responsive to PBMT effects, [Lac] will be reduced during middle-distance running. Similar results have been addressed during strength exercise, submaximal treadmill running, and sport team field test. Although mechanistic studies are necessary to elucidate the positive effects of

PBMT on [Lac], evidences have shown that PBMT immediate action is related to increased mitochondrial membrane potential²⁷ and higher enzyme activity in respiratory chain.^{28,29} Thus, this effect could be beneficial to improve the lactate oxidation in mitochondria.³⁰

Some studies that compared responders and nonresponders to PBMT pre-exercise only analyzed time and distance during treadmill test, 14 and biochemical markers during Wingate test. 10 However, this seems to be the first study to report a relationship between PBMT ergogenic effect and conditioning level of volunteers. Responder runners had better physiological (aerobic power and capacity) and performance (time at 1500 m) parameters than nonresponder runners. It makes sense, since main action of PBMT involves absorption of photons by endogenous chromophores in the mitochondria (i.e., cytochrome c oxi-² and endurance-trained individuals present higher predominance of Type I muscle fibers (oxidative fibers), and high mitochondrial content.³¹ This hypothesis highlights the need for further studies including well-trained runners. At the same time, our findings open an interesting perspective of use for PBMT by competitive runners, precisely those athletes who are desperately searching for resources capable of improving their performance even in a few seconds.

Since PBMT has a dose-dependent effect, including a single treatment dosage may be cited as a limitation of this

Table 2. Responsiveness Analysis for Time Trial Run Over 1500 m, and Comparisons Between Responders and Nonresponders for Best Time at 1500 m and Physiological Variables

		a	lando				DDMT	
		I.	Flacebo			I	r DIM I	
	$Responders \\ (n = 10)$	Nonresponders $(n=9)$	$Diff \pm 90\%$	NAT/P (qualitative inference)	Responders $(n=10)$	Nonresponders $(n=9)$	$Diff \pm 90\%$ CL	N/T/P (qualitative inference)
Time first lap (sec)	64.8 ± 6.5	65.3±7.8	-0.5 ± 5.8		61.9 ± 5.7	68.0±7.6	-6.1 ± 5.5	96/1/3 (very likely –)
Time second lap (sec)	90.9 ± 6.5	92.1 ± 11.0	-1.2 ± 7.5	1	86.0 ± 5.2	95.1 ± 10.7	-9.1 ± 7.1	98/0/2 (very likely –)
Time third lap (sec)	91.3 ± 5.4	96.5 ± 9.4	-5.3 ± 6.4		89.3 ± 4.3	97.9 ± 10.0	-8.6 ± 6.5	98/0/2 (very likely –)
Time fourth lap (sec)	85.3 ± 3.9	91.8 ± 6.9	-6.6 ± 4.6	98/0/1 (very likely –)	84.5 ± 5.4	90.9 ± 9.4	-6.4 ± 6.4	95/1/5 (likely –)
HR first lap (bpm)	166.7 ± 9.8	174.7 ± 10.8	-8.0 ± 8.3	•	171.7 ± 11.6	171.2 ± 13.5	0.5 ± 10	.
HR second lap (bpm)	175.9 ± 7.7	183.9 ± 10.4	-8.0 ± 7.5	95/1/4 (very likely –)	178.6 ± 9.7	180.1 ± 11.6	-1.5 ± 8.6	
HR third lap (bpm)	180.0 ± 7.2	186.9 ± 8.8	-6.9 ± 6.5	95/1/4 (very likely –)	181.6 ± 8.2	184.2 ± 9.9	-2.6 ± 7.4	
HR fourth lap (bpm)	185.1 ± 7.4	191.8 ± 7.7	-6.7 ± 6.1	96/1/3 (very likely –)	185.3 ± 7.4	190.7 ± 6.8	-5.4 ± 5.7	
Borg first lap	2.2 ± 0.6	3.0 ± 2.0	-0.8 ± 1.3	•	2.5 ± 1.2	3.2 ± 1.8	-0.7 ± 1.2	
Borg second lap	4.0 ± 1.2	4.9 ± 1.9	-0.9 ± 1.4		4.3 ± 1.5	4.7 ± 2.0	-0.4 ± 1.4	
Borg third lap	6.2 ± 1.5	6.1 ± 1.7	0.1 ± 1.3	1	6.3 ± 2.0	6.0 ± 2.2	0.3 ± 1.7	
Borg fourth lap	8.2 ± 1.7	7.8 ± 1.5	0.3 ± 1.3		8.2 ± 1.9	7.3 ± 2.0	0.9 ± 1.6	
[Lac] pre-running (mmol/L)	1.08 ± 0.39	0.96 ± 0.36	-0.1 ± 0.3		1.20 ± 0.32	1.08 ± 0.33	0.1 ± 0.3	
[Lac] I min (mmol/L)	12.36 ± 3.31	14.61 ± 2.79	-2.3 ± 2.4	92/3/5 (likely –)	11.69 ± 1.34	14.24 ± 3.23	-2.6 ± 2.1	97/2/2 (very likely –)
	14.37 ± 3.52	16.28 ± 2.66	-1.9 ± 2.5		13.85 ± 1.94	16.40 ± 3.75	-2.6 ± 2.5	94/2/4 (likely –)
[Lac] 5 min (mmol/L)	14.37 ± 3.85	16.06 ± 3.21	-1.7 ± 2.8		14.52 ± 2.19	16.46 ± 4.53	-1.9 ± 3.0	
				Performance				
	Respond	Responders $(n=10)$	Nonre	Nonresponders $(n=9)$	$Diff \pm 90\%$ CL	Т.	N/T/P (q	N/T/P (qualitative inference)
Best time at 1500 m (sec) VO _{2MAX} , mL/(kg·min)	321.7 ± 18.6 53.5 ± 3.1		345.6 ± 32.1 50.3 ± 4.9		-23.9 ± 21.7 3.1 ± 3.4		96/2/ 5/2	96/2/1 (very likely –) 5/2/92 (likely +)
$^{\text{VVO}_{2\text{MAX}}}$, km/h	16.4 ± 1.3		15.9 ± 1.7		0.4 ± 1.2			
PV, km/h	18.1 ± 1.1		17.6 ± 0.8		0.5 ± 0.7			
vRCP, km/h	13.8 ± 1.0		13.1 ± 1.2		0.7 ± 0.9		5/1	5/12/84 (likely +)
VO ₂ RCP, mL/(kg·min)	44.0 ± 4.8		43.2 ± 3.8		0.7 ± 3.4			I

Unclear and Possible effects were not considered.

CL, confidence limits; Diff, difference between responders and nonresponders; HR, heart rate; [Lac], blood lactate concentration; N/T/P, Negative/Trivial/Positive (negative = high values for nonresponders); PBMT, photobiomodulation therapy; PV, peak velocity; VO_{2MAX}, maximal oxygen uptake; VO₂RCP, oxygen uptake at respiratory compensation point, vVO_{2MAX}, velocity associated with VO_{2MAX}.

study; however, we chose a PBMT dose successfully used in previous trials. ^{11,13,14} Therefore, the participants' competitive level (i.e., recreational runners) and the method of recording time during the 1500 m run are the main limitations of this study. On the other hand, the strengths of this study were to be the first to investigate PBMT effects on real-life performance conditions and establish a relationship between PBMT effects and the volunteers' conditioning level. Future researches should encompass endurance runners with different competitive levels to confirm or refute the PBMT as an ergogenic agent in high-performance running and determine aerobic capacity cut points for PBMT response. Also, the optimal PBMT dosage, ^{12,13} the best moment to apply PBMT, ³² and the effect of different PBMT devices ³³ should be highlighted for field tests and real competitions.

Conclusions

PBMT applied immediately before time trial run over 1500 m (in noncontrolled environment) was not able to improve the performance; however, it resulted in a wide variability of response among recreational runners. Subjects who positively responded to PBMT (reduced 1500 m run time and lactate concentration compared to placebo) were the most conditioned runners. Our findings are not in complete agreement with the beneficial effects of PBMT applied immediately before running exercise as observed in laboratory-controlled environment. The PBMT resulted in wider intersubject ergogenic response variability, whereas it has been shown effective to improve performance of runners with higher aerobic capacity. Thus, we suggest that coaches and sports professional should consider the competitive level of runners.

Acknowledgments

The authors thank the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior-Brasil (CAPES)—Finance Code 001, Foundation of the State of Amazonas to support research (FAPEAM), and the National Council of Scientific Research (CNPq) Brazil for the provision of scholarships.

Author Disclosure Statement

No competing financial interests exist.

Funding Information

This work was supported by the National Council for Scientific and Technological Development (CNPQ) [Conselho Nacional de Desenvolvimento Científico e Tecnológico] under grant number 481297/2012-0.

References

- Borsa PA, Larkin KA, True JM. Does phototherapy enhance skeletal muscle contractile function and postexercise recovery? A systematic review. J Athl Train 2013;48: 57–67
- Reddy GK. Photobiological basis and clinical role of lowintensity lasers in biology and medicine. J Clin Laser Med Surg 2004;22:141–150.
- 3. Vanin AA, Verhagen E, Barboza SD, Costa LOP, Leal Junior ECP. Photobiomodulation therapy for the improve-

ment of muscular performance and reduction of muscular fatigue associated with exercise in healthy people: a systematic review and meta-analysis. Lasers Med Sci 2018;33: 181–214.

- Karu T. Primary and secondary mechanisms of action of visible to near-IR radiation on cells. J Photochem Photobiol B 1999;49:1–17.
- Klebanov GI, Kreinina MV, Poltanov EA, Khristoforova TV, Vladimirov YA. Mechanism of therapeutic effect of low-intensity infrared laser radiation. Bull Exp Biol Med 2001;131:286–289.
- Rossato M, Dellagrana RA, Lanferdini FJ, et al. Effect of pre-exercise phototherapy applied with different cluster probe sizes on elbow flexor muscle fatigue. Lasers Med Sci 2016;31:1237–1244.
- Baroni BM, Leal Junior ECP, De Marchi T, Lopes AL, Salvador M, Vaz MA. Low level laser therapy before eccentric exercise reduces muscle damage markers in humans. Eur J Appl Physiol 2010;110:789–796.
- Da Silva Alves MA, Pinfildi CE, Nilsen Neto L, Lourenço RP, Azevedo PHSM, Dourado VZ. Acute effects of lowlevel laser therapy on physiologic and electromyographic responses to the cardiopulmonary exercise testing in healthy untrained adults. Lasers Med Sci 2014;29:1945–1951.
- 9. Lanferdini FJ, Bini RR, Baroni BM, Klein KD, Carpes FP, Vaz, MA. Improvement of performance and reduction of fatigue with low-level laser therapy in competitive cyclists. Int J Sports Physiol Perform 2018;13:14–22.
- Leal Junior ECP, Godoi V, Mancalossi JL, et al. Comparison between cold water immersion therapy (CWIT) and light emitting diode therapy (LEDT) in short-term skeletal muscle recovery after high-intensity exercise in athletes—preliminary results. Lasers Med Sci 2011;26:493–501.
- De Marchi T, Leal Junior ECP, Bortoli C, Tomazoni SS, Lopes-Martins RA, Salvador M. Low-level laser therapy (LLLT) in human progressive-intensity running: effects on exercise performance, skeletal muscle status, and oxidative stress. Lasers Med Sci 2012;27:231–236.
- Dellagrana RA, Rossato M, Sakugawa RL, Lazzari CD, Baroni BM, Diefenthaeler F. Dose-response effect of photobiomodulation therapy on neuromuscular economy during submaximal running. Lasers Med Sci 2018;33:329– 336
- Dellagrana RA, Rossato M, Sakugawa RL, Baroni BM, Diefenthaeler F. Photobiomodulation therapy on physiological and performance parameters during running tests: dose-response effects. J Strength Cond Res 2018;32:2807– 2815.
- 14. Miranda EF, Vanin AA, Tomazoni SS, et al. Using pre-exercise photobiomodulation therapy combining super-pulsed lasers and light-emitting diodes to improve performance in progressive cardiopulmonary exercise tests. J Athl Train 2016;51:129–135.
- Pinto HD, Vanin AA, Miranda EF, et al. Photobiomodulation therapy improves performance and accelerates recovery of high-level rugby players in field test: a randomized, crossover, double-blind, placebo-controlled clinical study. J Strength Cond Res 2016;30:3329–3338.
- De Marchi T, Leal Junior ECP, Lando KC, et al. Photobiomodulation therapy before futsal matches improves the staying time of athletes in the court and accelerates postexercise recovery. Lasers Med Sci 2019;34:139–148.
- 17. Leal Junior ECP, Vanin AA, Miranda EF, De Carvalho PTC, Dal Corso S, Bjordal JM. Effect of phototherapy

- (low-level laser therapy and light-emitting diode therapy) on exercise performance and markers of exercise recovery: a systematic review with meta-analysis. Lasers Med Sci 2015;30:925–939.
- 18. Bassett DR, Howley ET. Limiting factors for maximum oxygen uptake and determinants of endurance performance. Med Sci Sports Exerc 2000;32:70–84.
- 19. Boone J, Bourgois J. The oxygen uptake response to incremental ramp exercise. Sports Med 2012;42:511–526.
- Borg G. Psychophysical bases of perceived exertion. Med Sci Sports Exerc 1982;14:377–381.
- Currell K, Jeukendrup AE. Validity, reliability and sensitivity of measures of sporting performance. Sports Med 2008;38:297–316.
- 22. Hopkins WG. Spreadsheets for analysis of validity and reliability (manuscript online). Available at: http://sportscience.sportsci.org (Last acessed October 10, 2018).
- Batterham AM, Hopkins WG. Making meaningful inferences about magnitudes. Int J Sports Physiol Perform 2006; 1:50–57.
- Schubert MM, Astorino TA. A systematic review of the efficacy of ergogenic aids for improving running performance. J Strength Cond Res 2013;27:1699–1707.
- 25. Cairns SP. Lactic acid and exercise performance: culprit or friend? Sports Med 2006;36:279–291.
- Leal Junior ECP, Lopes-Martins RAB, Rossi RP, et al. Effect of cluster multi-diode light emitting diode therapy (LEDT) on exercise-induced skeletal muscle fatigue and skeletal muscle recovery in humans. Lasers Surg Med 2009;41:572–577.
- Bakeeva LE, Manteifel VM, Rodichev EB, Karu, TI. Formation of gigantic mitochondria in human blood lymphocytes under the effect of an He-Ne laser. Mol Biol 1993;27: 608–617.
- 28. Silveira PC, Silva LA, Fraga DB, Freitas TP, Streck El, Pinho R. Evaluation of mitochondrial respiratory chain

- activity in muscle healing by low-level laser. J Photochem Photobiol B 2009:95:89–92.
- Karu T. Multiple roles of cytochrome c oxidase in mammalian cells under action of red and IR-A radiation. IUBMB Life 2010;62:607–610.
- Brooks GA, Dubouchaud H, Brown M, Sicurello JP, Butz CE. Role of mitochondrial lactate oxidation in the intracellular lactate shuttle. Proc Natl Acad Sci U S A 1999;96: 1129–1134.
- 31. Fridén J, Sjöström M, Ekblom B. Muscle fibre type characteristics in endurance trained and untrained individuals. Eur J Appl Physiol 1984;52:266–271.
- 32. Miranda EF, Tomazoni SS, Paiva PRV, et al. When is the best moment to apply photobiomodulation therapy (PBMT) when associated to a treadmill endurance-training program? A randomized, triple-blinded, placebo-controlled clinical trial. Lasers Med Sci 2018;33:719–727.
- 33. De Marchi T, Schmitt VM, Fabro CDS, et al. Phototherapy for improvement of performance and exercise recovery: comparison of 3 commercially available devices. J Athl Train 2017;52:429–438.

Address correspondence to:
Fernando Diefenthaeler, PhD
Laboratório de Biomecânica (BIOMEC)
Centro de Desportos
Universidade Federal de Santa Catarina
Campus Trindade
Florianópolis, SC CEP: 88040-000
Brazil

E-mail: fernando.diefenthaeler@ufsc.br

Received: December 1, 2019. Accepted after revision: April 1, 2020. Published online: November 20, 2020.