European Journal of Applied Physiology (2019) 119:621–632
https://doi.org/10.1007/s00421-018-4052-3

ORIGINAL ARTICLE

Ischemic preconditioning boosts post-exercise but not resting cardiac vagal control in endurance runners

Jeann L. Sabino-Carvalho[1,2] · Tiago Obeid-Freitas[2,3] · Marcelle Paula-Ribeiro[1,3] · Thiago R. Lopes[2,3,4] · Thiago H. N. Ferreira[1,2] · José E. Succi[5] · Antônio C. Silva[2,3] · Bruno Moreira Silva[1,2,3]

Received: 4 July 2018 / Accepted: 7 December 2018 / Published online: 12 December 2018

Abstract

Purpose High cardiac vagal control in endurance athletes has been generally associated with adequate recovery from training and readiness to cope high-intensity training. A method that improves cardiac vagal control in endurance athletes could therefore be advantageous. Accordingly, we sought to test whether ischemic preconditioning (IPC) could enhance cardiac vagal control in endurance runners.

Methods Fifteen subjects underwent IPC, sham ultrasound (SHAM) or control (CT), in random order. Subjects were informed both IPC and SHAM would be beneficial vs. CT (i.e., similar placebo induction), and IPC would be harmless despite ischemia sensations (i.e., nocebo avoidance). Resting cardiac vagal control was assessed via respiratory sinus arrhythmia (RSA) and heart rate variability (HRV) indexes. Post-exercise cardiac vagal control was assessed via heart rate recovery [HR time constant decay (T30) and absolute HR decay (HRR30s)] during 30-s breaks of a discontinuous incremental test. Capillary blood samples were collected for lactate threshold identification.

Results RSA and HRV were similar among interventions at pre- and post-intervention assessments. Lactate threshold occurred at 85 ± 4% of maximal effort. T30 was similar among interventions, but IPC increased HRR30s at 70% and 75% of maximal effort vs. SHAM and CT (70%: IPC = 31 ± 2 vs. SHAM = 26 ± 3 vs. CT = 26 ± 2 bpm, mean ± SEM, $P < 0.01$; 75%: IPC = 29 ± 2 vs. SHAM = 25 ± 2 vs. CT = 24 ± 2 bpm, $P < 0.01$).

Conclusion IPC did not change resting cardiac vagal control, but boosted fast post-exercise cardiac vagal reactivation at exercise intensities below lactate threshold in endurance runners.

Keywords Ischemic preconditioning · Parasympathetic nervous system · Heart rate · Placebo effect · Exercise

Abbreviations

ANOVA	Analysis of variance
CT	Resting control
CV	Coefficient of variation
E/I_{max}	Ratio between the longest R–R interval among all expirations and the shortest R–R interval among all inspirations
E/I_{mean}	Ratio between the mean of the longest R–R interval of each expiration and the mean of the shortest R–R interval of each inspiration
HF	High frequency
HR	Heart rate
HRex	Heart rate at the end of a given stage of the discontinuous incremental
HRR	Heart rate recovery
HRR30s	Heart rate recovery at 30 s post-exercise
HRR60s	Heart rate recovery at 60 s post-exercise
HRV	Heart rate variability

Communicated by Massimo Pagani.

✉ Bruno Moreira Silva
silva.bruno@unifesp.br

[1] Post-graduate Program in Translational Medicine, Federal University of São Paulo, São Paulo, SP, Brazil

[2] Laboratory of Exercise Physiology, Olympic Center of Training and Research, São Paulo, SP, Brazil

[3] Department of Physiology, Federal University of São Paulo, Botucatu street 862, Biomedical Sciences Building, 5th floor, São Paulo 04023-062, SP, Brazil

[4] São Paulo Association for Medicine Development, São Paulo, Brazil

[5] Department of Surgery, Federal University of São Paulo, São Paulo, SP, Brazil

ICC	Intra-class correlation coefficient
IPC	Ischemic preconditioning
LF	Low frequency
LF/HF	Ratio between low- and high-frequency powers of heart rate variability
Ln	Natural logarithm of the RMSSD was divided by the mean R–R interval
RMSSD	Square root of the mean squared differences between consecutive R–R intervals
RRi	R–R intervals
RSA	Respiratory sinus arrhythmia
SEM	Standard error of the mean
SHAM	Sham ultrasound
SWC	Smallest worthwhile change
TP	Total power
T30	Time constant of heart rate decay
VLF	Very low frequency
$\dot{V}O_{2max}$	Maximal oxygen consumption

Introduction

Endurance-trained subjects generally present higher respiration-coupled heart rate (HR) variation [i.e., respiratory sinus arrhythmia (RSA)] (De Meersman 1992), higher resting high-frequency HR variability (HRV) (Silva et al. 2011; Bellenger et al. 2016) and faster HR recovery (HRR) after exercise (Bellenger et al. 2016; Imai et al. 1994) than sedentary counterparts. Altogether, these findings support better resting and post-exercise cardiac vagal control in endurance-trained as compared to sedentary subjects (Akselrod et al. 1981; Kannankeril et al. 2004; Imai et al. 1994). Another characteristic of endurance-trained subjects is that their cardiac vagal control may change during the course of exercise training programs (Buchheit 2014; Bellenger et al. 2016). For example, HRR after submaximal and maximal exercise increases throughout endurance training and such HRR increase is associated with the increase in endurance performance when there is no overreaching (Buchheit 2014; Vesterinen et al. 2016a; Rabbani et al. 2018; Daanen et al. 2012; Le Meur et al. 2017). In addition, prospective randomized controlled studies support endurance training prescribed according to acute changes in HRV after each training session induces further endurance performance improvement, with lesser high-intensity training sessions, than conventional fixed-planned endurance training (Kiviniemi et al. 2010; Vesterinen et al. 2016b). Therefore, cardiac vagal control indexes obtained at rest and post-exercise may be useful to track endurance performance improvement, monitor recovery from training sessions and adjust endurance training prescription (Buchheit 2014).

Given the prominent role of cardiac vagal control indexes in the context of exercise training, a method with the potential to acutely improve cardiac vagal control at rest and post-exercise could possibly enhance endurance athletes' readiness to cope training at high intensity, and perhaps could maximize endurance training adaptations (Machhada et al. 2017). In this sense, application of non-lethal brief cycles of ischemia and reperfusion, known as ischemic preconditioning (IPC), mediates powerful protection against ischemia–reperfusion injury (Turcato et al. 2006; Loukogeorgakis et al. 2005; Gourine and Gourine 2014). The protection is dependent on the vagal branch of the autonomic nervous system, since studies in rats showed vagotomy (Basalay et al. 2012), blockade of muscarinic receptors with atropine (Mastitskaya et al. 2012), or optogenetic silencing of vagal pre-ganglionic neurons (Mastitskaya et al. 2012) abolished the IPC protection against ischemia–reperfusion injury. Moreover, infusion of a ganglionic blocker in humans abolished the IPC protection against reduction of flow-mediated dilation induced by ischemia–reperfusion injury (Loukogeorgakis et al. 2005). Thus, IPC could be an option to acutely enhance cardiac vagal control in endurance athletes.

Some studies have already investigated the IPC effect on resting and post-exercise cardiac vagal control in humans (Enko et al. 2011; Zagidullin et al. 2016; Chen et al. 2018; Lopes et al. 2018). More specifically, Enko et al. (2011) reported IPC of one arm increased vagal-related HRV indexes in young sedentary men. Zagidullin et al. (2016) reported IPC of one forearm did not change vagal-related HRV indexes in patients with coronary heart disease and healthy controls. Chen et al. (2018) reported IPC of one arm, employed twice a day for 6 weeks, increased vagal-related HRV indexes in patients with ischemic heart failure. In addition, we recently showed that three daily sessions of IPC of both legs accelerated short-term recovery of cardiac autonomic control from repeated sprint exercise in moderately trained men (Lopes et al. 2018). Nevertheless, none of the mentioned studies strictly controlled placebo and nocebo effects possibly related to IPC application. Firstly, because IPC has been compared to a low-pressure control or no intervention, but subjects can clearly notice the difference between interventions (Sabino-Carvalho et al. 2015, 2017; Ferreira et al. 2016). Secondly, because possible IPC effects have not been informed to the subjects in an attempt of blinding, which however may have created either positive or negative expectations about IPC-related sensations (e.g., pain) (Sabino-Carvalho et al. 2017; Ferreira et al. 2016) and increased results' variability (Clark et al. 2000). Therefore, the specific IPC effect on cardiac vagal control in humans is still uncertain. In addition, no study has investigated the IPC effect on HRR after submaximal exercise, which may be more sensitive to monitor athletes' recovery from training sessions (Le Meur et al. 2017) and easier to implement in sports practice than HRR after maximal exercise (Rabbani

et al. 2018; Vesterinen et al. 2016a). Lastly, the IPC effect on cardiac vagal control in endurance athletes has not been investigated.

Given this background, the aim of the present study was to investigate the IPC effect on cardiac vagal control in endurance runners. To address this aim we compared IPC to a sham ultrasound intervention (SHAM), which was advanced by our group in an attempt to rule out IPC-related placebo and nocebo biases (Sabino-Carvalho et al. 2017). Cardiac vagal control was assessed at rest via RSA and HRV, and at post-exercise via HRR. We hypothesized IPC and SHAM would improve RSA, HRV and HRR as compared to an undisturbed resting control (CT). Additionally, we hypothesized the IPC effect on RSA, HRV and HRR would be superior to the SHAM effect.

Methods

Subjects

Fifteen subjects participated in the present study, 11 of whom were men [age = 23 ± 1 years; maximal oxygen consumption ($\dot{V}O_{2max}$) = 68 ± 1 ml kg^{-1} min^{-1}; body fat = 9 ± 1%; mean ± standard error of the mean (SEM)] and four women (age = 24 ± 2 years; $\dot{V}O_{2max}$ = 57 ± 2 ml.kg^{-1} min^{-1}; body fat = 24 ± 1%). These subjects took part in a broad study and some data have already been published (Sabino-Carvalho et al. 2017). Women were assessed between the seventh and twenty-fifth day of the menstrual cycle. All subjects were nonsmokers and were not taking medications, supplements, treating orthopedic injuries, or presented history of chronic diseases. They had been engaged on a supervised training routine, 6 times per week, for 5.0 ± 0.5 years, and had been competing in official middle and long distance races. The study was approved by the Ethics Committee of the Federal University of São Paulo (process No. 610.367) and all subjects signed an informed consent form before participating in the study.

Study design

The study was randomized, placebo- and nocebo-controlled, and crossed over. The experimental protocol consisted of four visits, conducted on non-consecutive days, at the same time of day for a given subject. The interval between visits was 7 days. The first visit was used for familiarization with interventions and execution of a continuous incremental test. In this visit, one of the researchers (J.L.S.) told subjects that (1) IPC and SHAM would similarly improve exercise performance compared to CT, in an attempt to induce similar placebo effect; and (2) IPC would be harmless despite circulatory occlusion sensations, in an attempt to avoid nocebo effect. On the other visits, subjects rested supine for 5 min and then cardiac vagal control was assessed at rest via RSA and HRV. Next, IPC, SHAM or CT was administered, in random order. RSA and HRV were reassessed after each intervention. Then, a maximal discontinuous incremental test was performed, in which HRR was assessed (Fig. 1). Assessments and interventions were performed at room temperature ranging from 21 to 23 °C and relative humidity from 45 to 65%. Subjects were asked to arrive at the laboratory well-hydrated, ingest a light meal 2 h before the tests, and avoid caffeine or alcoholic beverages for 24 h. Training intensity was reduced on the day before the testing sessions to allow adequate recovery from training. Subjects were assessed if they reported score of at least 15 (i.e., good recovery) in the total quality recovery scale (Kentta and Hassmen 1998). Only one subject's visit had to be postponed 1 day to allow adequate recovery.

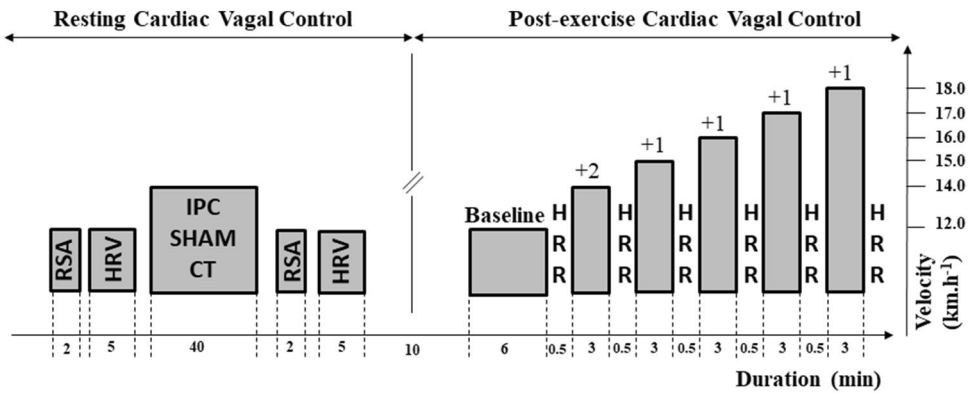

Fig. 1 Illustration of experimental procedures conducted on visits 2, 3 and 4. Subjects were assessed at pre- and post-ischemic preconditioning (IPC), sham ultrasound (SHAM) or resting control (CT), in random order. Then, they underwent a discontinuous incremental treadmill test. Baseline velocity was individualized. Thus, absolute velocities presented in the *Y* axis varied between individuals. *RSA* respiratory sinus arrhythmia, *HRV* heart rate variability, *HRR* heart rate recovery

Ischemic preconditioning, sham and control

IPC was administered via customized cuffs which characteristics were described in detail in previous publications from our group (Ferreira et al. 2016; Sabino-Carvalho et al. 2017; Lopes et al. 2018). One cuff was positioned per thigh, as proximal to the groin as possible. Subjects were placed supine for the IPC administration. Ischemia and reperfusion were achieved, respectively, with cuff inflation to 220 mmHg and cuff deflation to 0 mmHg. Inflation and deflation were alternated between thighs and lasted 5 min each (Sabino-Carvalho et al. 2017). Four inflation/deflation cycles were performed on each thigh (Sabino-Carvalho et al. 2017), so the IPC administration lasted 40 min. Ischemia was confirmed with a vascular Doppler (Doppler vascular 610B, MEDMEGA, Brazil) at the posterior tibial artery. Arterial pulse was not detected in any subject during cuffs inflation.

SHAM procedure consisted of sham therapeutic ultrasound administration on the lower limbs. Physical therapists regularly use ultrasound aiming to treat musculoskeletal lesions. All subjects had been treated with ultrasound and had positive impression about its beneficial effects regarding musculoskeletal lesions. To induce placebo effect, one of the researchers (J.L.S.) informed the subjects that the beneficial effects of ultrasound administration could include enhancement of exercise performance, via imperceptible deep tissue heating. If subjects had doubts about it, the researcher showed a scientific paper to strengthen the justification (Draper et al. 1995). During sham ultrasound administration, the device was turned on, but instead of pushing the button to start ultrasound delivery, the researcher pushed another inactive button without subjects noticing. Of note, active administration of therapeutic ultrasound does not generate any important sensation than that generated by gel application and probe rubbing on the skin. Thus, subjects could not notice the device was not delivering ultrasound. The researcher slid the ultrasound probe for 5 min over each of the four following regions: anterior thigh, posterior thigh, anterior leg and posterior leg. Ultrasound administration was alternated between limbs and totaled 40 min.

In the CT intervention, subjects rested supine during 40 min without falling asleep. After the administration of interventions, subjects were instrumented for the discontinuous incremental exercise test while standing on a treadmill. At the end of instrumentation, subjects answered the question: "Do you think your performance today will be equal, better or worse than the performance on the previous visit(s)?". They were instructed to contrast their performance with the CT day. More specifically, if CT was employed on visit two, subjects contrasted IPC and SHAM with CT (e.g., IPC better than CT). If CT was used on visit four, subjects were asked on this visit to contrast their expected performance with the performance on previous visits, and later responses were reversed for statistical analyses (e.g., the answer CT worse than SHAM was analyzed as SHAM better than CT). These queries were employed to verify placebo induction and nocebo avoidance. The same researcher performed all interventions (J.L.S). Furthermore, this researcher questioned about exercise performance expectation. Just one researcher executed these methods, in a systematic manner, to homogenize placebo induction and nocebo avoidance (Benedetti 2013).

Resting cardiac vagal control

Subjects rested supine for 5 min prior to assessments. After that, beat-by-beat HR was recorded during 2 min of RSA, 1 min of interval and 5 min of HRV. Next, IPC, SHAM or CT was administered, and then, RSA and HRV were reassessed. Breathing rate was controlled during RSA and HRV assessments. Subjects were instructed to breathe according to sounds emitted by a metronome set to yield 6 breaths min^{-1} during RSA and 15 breaths min^{-1} during HRV. Subjects were instructed to adjust their tidal volume at a magnitude they felt comfortable for each breathing rate. Of note, the breathing pattern herein used in the RSA is assumed to maximize the cardiac vagal control (Grossman et al. 1991). In addition, the breathing rate set for the HRV assessment has been shown to center respiratory-related HRV at the high-frequency spectral band (Medigue et al. 2001), and limit confounding effects of cardiac sympathetic control and variations in the respiratory pattern (Medigue et al. 2001).

Post-exercise cardiac vagal control

The continuous incremental test, executed on visit 1, yielded data to determine stages of the discontinuous incremental test, executed on visits 2, 3 and 4. Both tests were conducted on a treadmill (Super ATL, Inbrasport, Brazil) with grade set at 1% to simulate energy expenditure of outdoor running. The continuous incremental test started at 8 km h^{-1} for 3 min, and then, velocity was increased 1 km h^{-1} per minute until voluntary exhaustion. The discontinuous incremental test began at velocity 1 km h^{-1} inferior to the velocity in which ventilatory threshold was observed during the continuous incremental test (Sabino-Carvalho et al. 2017). Velocity was then increased by 2 km h^{-1} for 3 min and next increased 1 km h^{-1} each 3 min until voluntary exhaustion. After each 3-min stage, velocity was reduced to zero and, as soon as possible, subjects stepped off the treadmill belt and stood still for HRR assessment and capillary blood sampling from an ear lobe. The researcher responsible to encourage the subjects during the test (T.R.L. or T.N.F.) was identical for a given subject and was blinded about all collected

data and administered interventions. Subjects were similarly blinded about all collected data during the study.

Measurements

R–R intervals (RRi) were acquired at 1000 Hz via a one-lead electrocardiogram (Powerlab, AD Instruments, Australia). RRi were automatically detected in the electrocardiogram tracing (Labchart 7, AD Instruments, Australia). However, occasionally, automatic detection failed due to noise and/or shift in the electrocardiogram signal during running, particularly at high velocities. Thus, undetected RRi were manually quantified by one of the researchers (T.O.F.) using the device's software. Onset of each inspiration and expiration was manually marked in the electrocardiogram file during the RSA assessment. Twenty-five microliters of blood were collected from an earlobe, during breaks of the discontinuous test. A vasodilator ointment was used to arterialize blood samples (Finalgon, Boehringer Mannheim, Germany). Blood was drawn using heparinized and calibrated capillaries, and later stored in Eppendorf's containing 50 µL of 1% NaF (i.e., anticoagulant) at − 20 °C, until analysis of lactate concentration (YSI 1500 SPORT, Yellow Springs Instruments, USA).

Data analyses

RSA was quantified via two different methods using RRi data from 6 respiratory cycles. One method consisted of a ratio between the longest RRi among all expirations and the shortest RRi among all inspirations (E/I_{max} index) (Paiva et al. 2011; de Castro et al. 1992). Another consisted of a ratio between the mean of the longest RRi of each expiration and the mean of the shortest RRi of each inspiration (i.e., E/I_{mean} index) (de Castro et al. 1992). HRV was quantified in time and frequency domains from 5-min continuous RRi data (Kubios HRV Pro 2.0, University of Kuopio, Finland). In the time domain, data were analyzed by the square root of the mean squared differences between consecutive RRi (RMSSD) (Task Force 1996). The natural logarithm of the RMSSD was divided by the mean RRi (LnRMSSD/RRi) in an attempt to circumvent possible HRV saturation (Buchheit 2014). In the frequency domain, data were analyzed by the fast Fourier transform (Task Force 1996). Data were divided into two overlapping segments (256-s windows with 50% overlap). Trend component was removed from the time series using the smoothing prior approach. Then, a 4-Hz cubic spline interpolation was applied. Power spectral density of the low-frequency (LF; 0.04–0.15 Hz) and high-frequency (HF; 0.15–0.4 Hz) bands were expressed in absolute values (ms^2) and normalized units (n.u.) (Task Force 1996). Of note, both RMSSD and HF are mostly determined by the cardiac vagal control (Task Force 1996; Akselrod et al. 1981).

RRi were converted to beats min^{-1} and HRR was calculated via the following indexes: (1) T30—negative reciprocal of the slope of the linear regression between the natural logarithm of beat-by-beat HR throughout 30-s recovery (Imai et al. 1994; Kannankeril et al. 2004); (2) HRR30s—HR data were averaged using 5-s windows and then we calculated the absolute difference between HR at the end of a given stage of the discontinuous incremental (HRex) and HR at the end of the succeeding 30-s recovery period (Imai et al. 1994; Kannankeril et al. 2004). Importantly, both indexes are predominantly determined by the fast component of cardiac vagal reactivation (Imai et al. 1994; Kannankeril et al. 2004). Data obtained during the discontinuous incremental test were linearly interpolated to allow comparison at similar exercise intensities (Origin 6.0, Microcal, USA). The highest common velocity among interventions for a given subject was set as 100% effort (i.e., maximal effort). Then, interpolated data equivalent to 70%, 75%, 80%, 85%, 90% and 95% of maximal effort were identified and used for statistical analyses. Lactate threshold was automatically identified via a mathematical model which determined the intersection point between two linear regressions that best fitted the data (Newell et al. 2007).

Statistical analyses

Sample size was calculated taking into account a mean difference of 3% among interventions (Sabino-Carvalho et al. 2017). *P* value was set at 0.05 and power at 0.80. These parameters indicated 15 subjects would be needed in a repeated measures ANOVA (G*Power, 3.1 version, Dusseldorf University, Germany). After data were collected, we calculated the observed (i.e., actual) power of our sample size and results, which was 0.85 for the HRR30s two-way ANOVA interaction. Subjects' expectancy about interventions was compared via the Chi-square test. Only HRV data did not show normal distribution in the Shapiro–Wilk's test. HRV data were then natural logarithm-transformed for inferential analyses. Pre-values were compared among days via one-way ANOVA to assess whether baseline was the same before the experiments. In addition, inter-day reproducibility was assessed via calculation of interclass correlation coefficient (ICC) and coefficient variation (CV). Two-way repeated measures ANOVA was employed to compare IPC, SHAM and CT [3 interventions (IPC vs. SHAM vs. CT) and 2 measurements (pre vs. post), or 3 interventions (IPC vs. SHAM vs. CT) and 7 measurements (70–100% maximal effort)]. The Greenhouse–Geisser's correction was employed to adjust ANOVA results, whenever sphericity was violated in the Mauchly's test. If necessary, the Fisher's post hoc was employed after ANOVA. Results are presented as

mean ± SEM. All analyses were two-tailed and statistical significance was set at $P < 0.05$. Percent change was calculated as: [(IPC − SHAM)·SHAM^{-1}]·100. Smallest worthwhile change (SWC) was taken into account to interpret the practical implication of the IPC effect on the HRR30s. The SWC was considered as the CV for the HRR30s, which was 22.6% in the study conducted by Boullosa et al. (2014). Statistical analyses were conducted in the software STATISTICA (version 12, Statsoft, USA).

Results

Score on the total quality recovery scale was similar among interventions (IPC: 16.5 ± 0.3 vs. SHAM: 16.3 ± 0.3 vs. CT: 16.3 ± 0.39 a.u., $P = 0.52$). Most of the subjects expected exercise performance would better after IPC than CT (better, 87%; equal, 13%; worse, 0%) and after SHAM than CT (better, 80%; equal, 20%; worse, 0%). Of note, IPC and SHAM produced similar positive expectation (IPC: 87% vs SHAM: 80%, $P = 0.62$). All RSA and HRV pre-values were similar among experimental days (Table 1). All variables presented significant ICC and RSA indexes presented the lowest CV.

IPC, SHAM and CT did not change RSA indexes (Table 2), as well as RMSSD, LnRMSSD/RRi, HF (ms^2) and TP (Table 2). HRrest, HF (n.u.) and LF/HF decreased post all interventions, without difference among interventions. LF (ms^2) and LF (n.u.) increased post all interventions, without difference among interventions.

The highest velocity achieved during the discontinuous incremental test was similar among interventions (IPC: 18.0 ± 0.4 vs. SHAM: 18.1 ± 0.4 vs. CT: 18.2 ± 0.3 km h^{-1}, $P = 0.32$). HRex and T30 increased, whereas HRR30s decreased throughout the discontinuous incremental exercise test (Fig. 2).

IPC increased HRR30s vs. SHAM and CT at 70% and 75% of maximal effort. Such IPC effect on the HRR30s remained statistically significant after removal of women's data from the ANOVA analysis. HRR30s percent change corresponded to 39.5 ± 16.5% and 33.4 ± 17.2%. Seven subjects (50% of the study's sample) presented HRR30s percent change superior than the SWC at 70 and 75% of maximal effort (Fig. 3). Of note, one man presented HRR30s change higher than 200% at both 70% and 75% of maximal effort. These were the unique data points that lied beyond 3 standard deviations of the group's mean, which could be considered as outlier data. Thus, we removed all HRR30s data from this man and redid the ANOVA analysis. HRR30s remained significantly higher at 70% and 75% of maximal effort in the IPC as compared with SHAM and CT.

Velocity at the lactate threshold was similar among interventions (IPC: 15.3 ± 0.4 vs. SHAM: 15.4 ± 0.4 vs. CT: 15.5 ± 0.4 km h^{-1}, $P = 0.74$). Lactate threshold velocity corresponded to 85 ± 4% of maximal effort.

Discussion

The vagal branch of the autonomic nervous system plays a role in the IPC-induced protection against ischemia–reperfusion injury (Basalay et al. 2012; Loukogeorgakis et al. 2005; Mastitskaya et al. 2012). Some studies have consequently investigated whether IPC increases resting cardiac vagal control in healthy subjects (Enko et al. 2011; Lopes et al.

Table 1 Comparison of baseline data and inter-day reproducibility

	IPC	SHAM	CT	ANOVA *P* value	ICC Coefficient	CV (%)
I/E_{max}	1.58 ± 0.04	1.61 ± 0.05	1.58 ± 0.04	0.81	0.79	6.2
I/E_{mean}	1.43 ± 0.04	1.48 ± 0.05	1.46 ± 0.03	0.38	0.83	5.5
HRrest, bpm	61.0 ± 4.0	61.0 ± 3.0	60.0 ± 3.0	0.83	0.89	9.3
RMSSD, ms	88.9 ± 12	92.7 ± 11	96.3 ± 13	0.80	0.81	21.0
LF, ms^2	890 ± 226	1021 ± 191	1011 ± 204	0.79	0.75	48.6
HF, ms^2	4837 ± 1276	4987 ± 944	5892 ± 1405	0.65	0.75	36.0
LF, n.u.	20 ± 4	21 ± 4	19 ± 3	0.82	0.79	43.5
HF, n.u.	80 ± 4	79 ± 4	81 ± 3	0.82	0.79	10.7
LF/HF	0.3 ± 0.1	0.3 ± 0.1	0.3 ± 0.1	0.74	0.75	50.3
LnRMSSD/RRi	4.4 ± 0.2	4.5 ± 0.2	4.4 ± 0.2	0.83	0.92	7.4

Values are means ± SEM

IPC ischemic preconditioning, *SHAM* sham ultrasound, *CT* resting control, *RMSSD* square root of the mean squared differences between consecutive R–R intervals (RRi), *LF/HF* ratio between low- and high-frequency powers of heart rate variability, *TP* total power, E/I_{max} ratio between the longest RRi among all expirations and the shortest RRi among all inspirations, E/I_{mean} ratio between the mean of the longest RRi of each expiration and the mean of the shortest RRi of each inspiration, *ICC* intra-class correlation coefficient, *CV* coefficient of variation

Table 2 Effect of interventions on heart rate variability (HRV) and respiratory sinus arrhythmia (RSA) indexes

	IPC		SHAM		CT		*P* value		
	Pre	Post	Pre	Post	Pre	Post	Condition	Time	Interaction
RSA indexes									
E/I_{max}	1.58 ± 0.04	1.56 ± 0.06	1.61 ± 0.05	1.60 ± 0.04	1.58 ± 0.04	1.54 ± 0.04	0.38	0.49	0.82
E/I_{mean}	1.43 ± 0.04	1.43 ± 0.05	1.46 ± 0.03	1.42 ± 0.04	1.48 ± 0.05	1.45 ± 0.04	0.34	0.28	0.69
HR variability									
HRrest, bpm	61 ± 4	56 ± 3	61 ± 3	57 ± 2	60 ± 3	57 ± 2	0.97	0.01	0.42
RMSSD, ms	89 ± 12	94 ± 11	93 ± 11	99 ± 10	96 ± 13	96 ± 11	0.75	0.20	0.82
LF, ms^2	890 ± 226	1342 ± 229	1021 ± 192	1253 ± 298	1011 ± 204	1510 ± 259	0.52	0.01	0.23
HF, ms^2	4837 ± 1276	5194 ± 1397	4987 ± 944	5537 ± 1192	5892 ± 1405	5347 ± 1210	0.69	0.99	0.67
LF, nu	20 ± 4	29 ± 6	21 ± 4	27 ± 5	19 ± 3	25 ± 4	0.85	0.01	0.53
HF, nu	80 ± 4	71 ± 6	79 ± 4	73 ± 5	81 ± 3	75 ± 4	0.53	0.01	0.69
LF/HF	1.74 ± 0.3	1.18 ± 0.3	1.58 ± 0.2	1.22 ± 0.3	1.64 ± 0.2	1.33 ± 0.2	0.92	0.01	0.59
TP, ms^2	5782 ± 1345	6664 ± 1426	6103 ± 1042	7215 ± 1228	7022 ± 1501	6722 ± 1417	0.80	0.43	0.41
LnRMSSD/RRi	4.4 ± 0.2	4.2 ± 0.3	4.5 ± 0.2	4.3 ± 0.2	4.4 ± 0.2	4.3 ± 0.2	0.86	0.02	0.83

Values are means ± SEM

IPC ischemic preconditioning, *SHAM* sham ultrasound, *CT* resting control, *RMSSD* square root of the mean squared differences between consecutive R–R intervals (RRi), *LF/HF* ratio between low- and high-frequency powers of heart rate variability, *TP* total power, *E/Imax* ratio between the longest RRi among all expirations and the shortest RRi among all inspirations, *E/Imean* ratio between the mean of the longest RRi of each expiration and the mean of the shortest RRi of each inspiration

2018) and patients with cardiovascular diseases (Chen et al. 2018; Zagidullin et al. 2016). However, results have been heterogeneous and placebo and nocebo effects have not been strictly controlled. No study had investigated the IPC effect on HRR after submaximal exercise. Furthermore, the IPC effect on cardiac vagal control in endurance athletes had not been investigated. Our study therefore used a randomized, placebo-controlled, nocebo-controlled and crossed over experimental design to test the hypothesis that IPC could enhance cardiac vagal control in endurance runners. Our data showed IPC did not have an effect on RSA and HRV indexes. On the other hand, IPC increased HRR30s at exercise intensities below lactate threshold. Collectively, these results indicate IPC did not change resting cardiac vagal control, but boosted the fast phase of post-exercise cardiac vagal reactivation at exercise intensities below lactate threshold in endurance runners.

Placebo and nocebo

Most of the subjects answered both IPC and SHAM would improve exercise performance vs. CT, which indicates the study's methods produced the intended positive expectation about IPC and SHAM administration. Yet, SHAM did not change any of the cardiac vagal control endpoints. In our previous related study (Sabino-Carvalho et al. 2017), SHAM yielded positive expectation and enhanced exercise performance (i.e., longer time to exhaustion at supramaximal exercise intensity), whereas it did not change aerobic metabolic parameters and perceived effort during exercise. Thus, our previous and present findings indicate the effect of subjects' positive belief about an intervention seems to vary according to the endpoint under investigation. Of note, Beedie et al. (2006) corroborate that positive belief about an intervention may not necessarily translate into improved objective physiological and performance measurements. Altogether, the presented evidence supports the complex neurophysiological basis of placebo and nocebo effects (Benedetti 2013), as well as highlights that placebo and nocebo effects should continue to be controlled in IPC studies to strengthen the interpretation about specific IPC effects.

IPC effect on RSA and HRV

IPC changed neither RSA nor HRV, indicating IPC was not capable of enhancing resting cardiac vagal control in endurance athletes. Our results corroborates findings reported by Zagidullin et al. (2016), who found IPC of one forearm did not change vagal-related HRV indexes in patients with coronary heart disease and healthy controls. In contrast, our results are dissimilar from those reported by Enko et al. (2011) and Chen et al. (2018). The former found IPC of one arm increased vagal-related HRV indexes in young sedentary men (Enko et al. 2011). The latter found IPC of one arm, employed twice a day for 6 weeks, increased vagal-related HRV indexes in patients with ischemic heart failure (Chen et al. 2018). Multiple factors may explain the heterogeneity among our and others' findings. For example, endurance

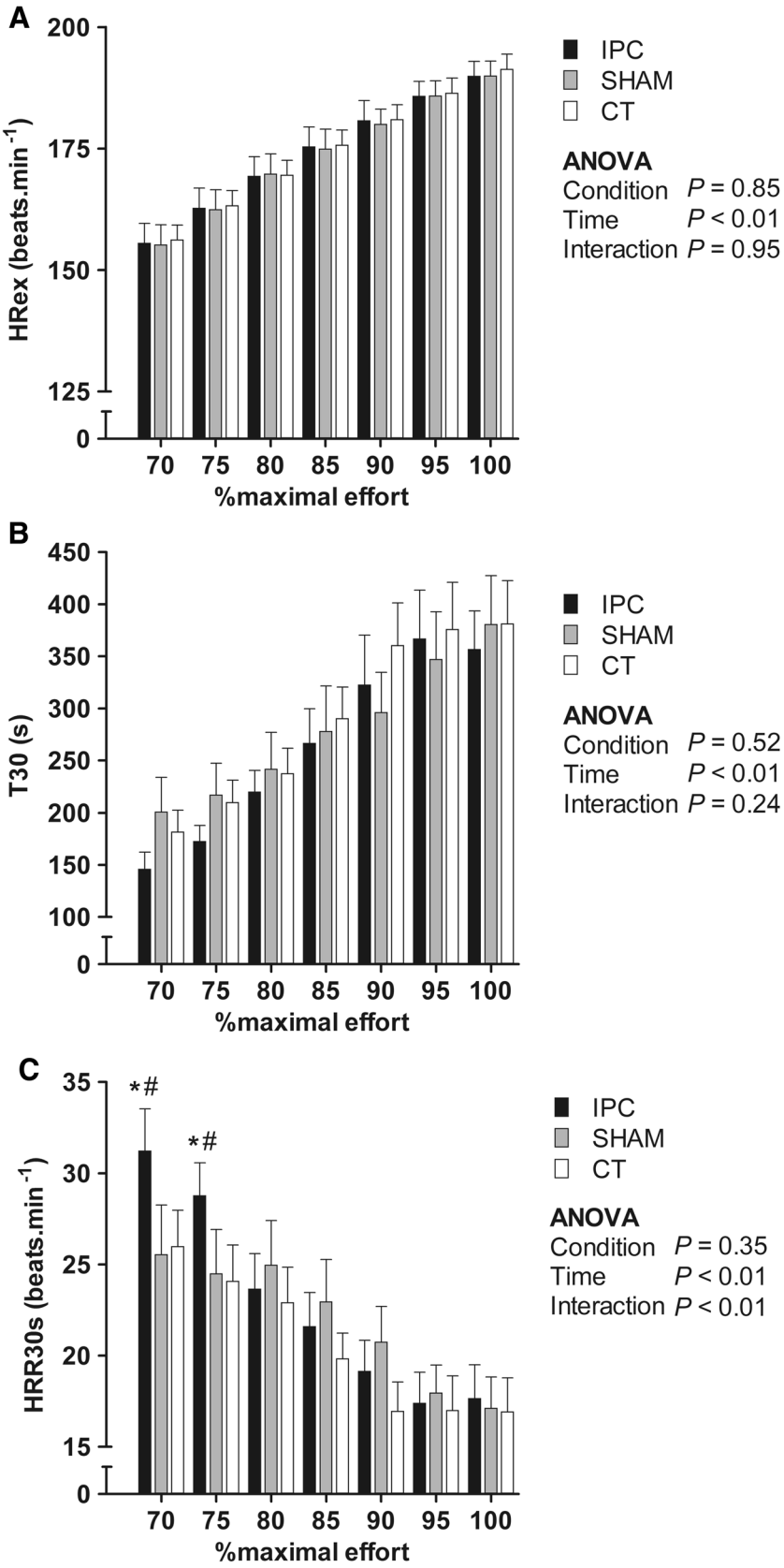

Fig. 2 Post-exercise cardiac vagal control assessed by heart rate recovery (HRR). Results reported as mean ± SEM, $n = 15$. The highest common velocity among interventions was considered 100%, and based on that, interpolated data corresponding to 70, 75, 80, 85, 90 and 95% were identified. Data are heart rate at the end of each exercise stage (HRex), time constant of heart rate decay (T30) and absolute HR change between HRex and HR recovery at 30 s post-exercise (HRR30s). Note that HRex and T30 increased, whereas HRR30s decreased as exercise intensity increased. Moreover, ischemic preconditioning (IPC) increased HRR30s vs. sham ultrasound (SHAM; $^{*}P < 0.01$) and resting control (CT; $^{\#}P < 0.01$) at 70% and 75% of maximal effort

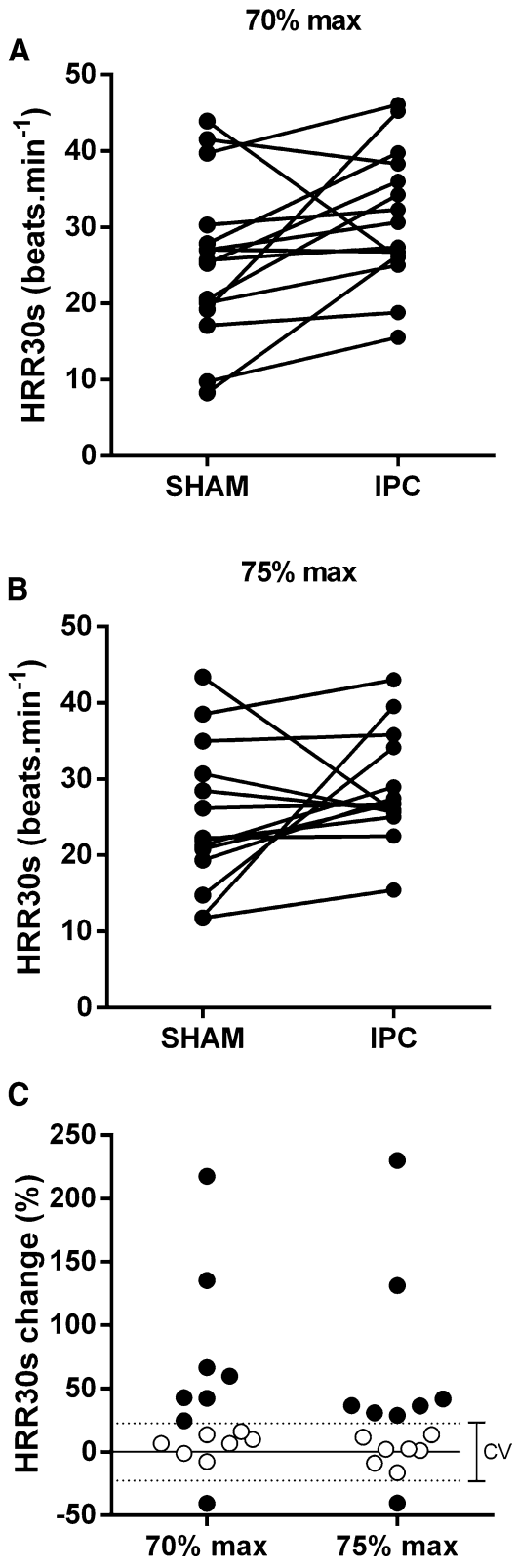

Fig. 3 Individual data of heart rate recovery at 30 s post-exercise (HRR30s). Panels A and B show HRR30s post 70 and 75% of maximal effort, respectively, in the sham ultrasound (SHAM) and ischemic preconditioning (IPC) interventions. Panel C shows IPC-induced percent change in HRR30s post 70% and 75% maximal effort. Closed circles represent data that surpassed the HRR30s coefficient of variation (CV). Open circles represent data that did not surpass the HRR30s CV

athletes generally present higher cardiac vagal control than sedentary subjects (Buchheit 2014; Bellenger et al. 2016) and patients with cardiovascular diseases (Imai et al. 1994). As a result, endurance athletes may be close to or at the limit of vagal influence toward the resting HR, which has been named saturation phenomenon (Buchheit 2014). Thus, enhancing their resting cardiac vagal control may be more difficult or not possible (Buchheit 2014). Moreover, in the present study we administered the IPC immediately before the cardiac vagal control assessment, whereas Chen et al. (2018) repeated the IPC administration for 6 weeks, which may have summed early and late effects of IPC (Loukogeorgakis et al. 2005). Thus, perhaps a more intensive administration may be required to increase the resting cardiac vagal control in endurance athletes whose resting cardiac vagal control is not yet saturated.

IPC effect on HRR

Although IPC did not change RSA and HRV, it increased HRR30s. Such dissimilar IPC effect is corroborated by evidence that assessments of cardiac vagal control at rest and post-exercise may not be associated in endurance athletes (Lee and Mendoza 2012; Buchheit 2014). The lack of association is probably attributed to two factors. On the one hand, resting cardiac vagal control is likely more vulnerable to saturation (Buchheit 2014; Lee and Mendoza 2012). On the other hand, different mechanisms are involved in vagal regulation at rest and post-exercise. At rest, cardiac vagal control is predominantly coupled to the respiratory cycle (Grossman et al. 1991), apparently due to respiratory-induced hemodynamic changes and synchronized activation of respiratory and autonomic neurons in the brainstem (Yasuma and Hayano 2004). At post-exercise, in addition to respiratory coupling (Arai et al. 1989), deactivation of central command and muscle mechanoreflex (Carter et al. 1999), as well as activation of metabolite-sensitive (i.e., muscle metaboreceptors and carotid chemoreceptors) (Buchheit et al. 2007) and temperature-sensitive (i.e., thermoreceptors) (Pecanha et al. 2017) afferents may influence the cardiac vagal control.

The IPC effect on HRR30s was not accompanied by change in both HRex and T30. The lack of effect on HRex suggests IPC may selectively improve post-exercise cardiac vagal control, rather than the autonomic control of HR during exercise. The lack of T30 change may be explained by its poor reproducibility (Dupuy et al. 2012). In our study and others (Buchheit et al. 2007; Imai et al. 1994), HRR30s

progressively decreased as exercise intensity increased. This finding possibly suggests that the mechanisms that influence the fast component of cardiac vagal reactivation change according to the increase in exercise intensity. In this sense, mechanisms activated by the buildup of metabolites reasonably do not play a major role for the regulation of cardiac vagal reactivation at exercise intensities below the lactate threshold, whereas recruitment of anaerobic pathways for ATP resynthesis are possibly linked with smaller and slower cardiac vagal reactivation at higher exercise intensities (Buchheit et al. 2007). The fact that the IPC effect on HRR30s occurred at exercise intensities below lactate threshold possibly indicates the IPC effect on HRR30s was unrelated to changes in metabolic responses to exercise. Data from our previous related study support this interpretation (Sabino-Carvalho et al. 2017), since IPC did not change blood lactate concentration, oxygen uptake and carbon dioxide output throughout the discontinuous incremental exercise test. In addition, in another study we showed that IPC accelerated short-term recovery of cardiac autonomic control from repeated sprint exercise, but did not change peak pulmonary oxygen uptake, peak carbon dioxide output, peak respiratory exchange ratio, kinetics of pulmonary oxygen uptake decay within 360 s of recovery and blood lactate concentration (Lopes et al. 2018). Collectively, these findings suggest that the IPC effect on the cardiac autonomic control is not linked to changes in energy metabolism responses to exercise (Lopes et al. 2018; Sabino-Carvalho et al. 2017). Alternatively, IPC has been linked to local activation of nociceptors and release of substances in the circulation (Gourine and Gourine 2014). Neural and humoral mechanisms have thus been considered triggers of increased cardiac vagal activity during ischemia–reperfusion injury protocols (Gourine and Gourine 2014). Therefore, IPC activation of both neural and humoral mechanisms likely underlies the present findings, rather than IPC-mediated change in metabolic responses to exercise.

Limitations

Firstly, RSA, HRV and HRR are indirect measures of the cardiac vagal control, as these methods rely on HR measurements rather than direct neural recording of cardiac vagal activity. Nevertheless, systemic blockade of muscarinic receptors in humans support the variables taken into consideration in the present study are largely determined by the cardiac vagal activity (Akselrod et al. 1981; Imai et al. 1994; Kannankeril et al. 2004; Grossman et al. 1991; Task Force 1996). Secondly, we had only 30 s to analyze the HRR between stages, which did not allow the calculation of the commonly reported HR recovery at 60 s post-exercise (HRR60s). However, both HRR30s and HRR60s are assumed to represent the fast phase of post-exercise cardiac vagal reactivation and are highly associated after submaximal exercise (Imai et al. 1994). Thus, our results can probably be translated to the HRR60s after submaximal exercise. In turn, HRR after 60 s post-exercise is determined by both slow vagal reactivation and progressive sympathetic withdrawal (Kannankeril et al. 2004; Imai et al. 1994). Thus, the IPC effect herein observed should not be extrapolated to HR data after 60 s of recovery. At last, the IPC-induced protection against ischemia–reperfusion injury seems to be modulated by gender (Turcato et al. 2006). We assessed both men and women, but our women sample size was not big enough to dissect whether gender modulated the IPC effect on HRR30s. Noteworthy, results remained the same when women were removed from data analysis, which indicates that women's data did not compromise the interpretation of men's data.

Practical implications

The IPC effect on HRR30s surpassed the SWC in half of the subjects. This corroborates the view that there may be responders and non-responders to the IPC (Incognito et al. 2016) and indicates that factors associated with the IPC responsiveness deserve further investigation in an attempt to translate the IPC to the sports practice. The IPC effect on HRR30s occurred at submaximal exercise intensities. This is relevant because submaximal measures of post-exercise cardiac vagal control seem to be more sensitive to athletes' recovery status than maximal measures (Le Meur et al. 2017) and are more practical to be implemented in the routine of training monitoring (Buchheit 2014; Rabbani et al. 2018; Vesterinen et al. 2016a). The HRR30s increase occurred at a non-intensified phase of the athletes' training season. According to previous evidence, HRR increase at such phase probably represents an increased readiness to train at high-intensity (Buchheit 2014; Vesterinen et al. 2016b; Kiviniemi et al. 2010). Thus, if the IPC could repeatedly boost the post-exercise cardiac vagal control before training sessions, athletes could possibly tolerate more high-intensity training sessions, culminating with amplified chronic aerobic adaptations (Buchheit 2014; Vesterinen et al. 2016b; Kiviniemi et al. 2010). In our previous related study (Sabino-Carvalho et al. 2017), the IPC effect on time to exhaustion at a constant supramaximal velocity did not surpass the SHAM effect. However, this endpoint does not resemble a training session. In another study, we showed repeated IPC administration for 3 consecutive days improved exercise performance on a repeated sprint swimming task (Ferreira et al. 2016), which simulated a high-intensity training session. Therefore, the association of IPC and exercise training deserves investigation by future studies. Of note, however, HRR paradoxically increases in endurance athletes who develop functional overreaching (Aubry et al. 2015).

Thus, additional tools should be taken into consideration along with cardiac vagal control measures, like psychometric measures and neuromuscular performance (Buchheit 2014), to interpret athletes' overall recovery status.

Conclusion

IPC did not change RSA and HRV, but increased HRR30s at exercise intensities below lactate threshold. Thus, the results support IPC did not change resting cardiac vagal control, but boosted the fast phase of post-exercise cardiac vagal reactivation at exercise intensities below lactate threshold in endurance runners.

Acknowledgements The time and effort expended by all the volunteer subjects is greatly appreciated.

Author contributions JLS, TRL and BMS conceived and designed research. JLS, TO, TRL and THNF conducted experiments. JLS, TO, MP and TRL analyzed data. All authors interpreted the results of experiments. JLS and BMS prepared the figures and tables. JLS, BMS drafted the manuscript. All authors edited, revised and approved the manuscript.

Funding J.L.S. and M.P. received scholarship from the Coordination for Improvement of Higher Education Personnel (CAPES). J.L.S., M.P. and T.O. received scholarship from the São Paulo Research Foundation (FAPESP; grants: 2014/15877-8, 2015/22198-2 and 2015/03572-0, respectively). B.M.S received funding from FAPESP (Grant: 2014/25683-6) and CNPq (Grant: 461516/2014-4) to conduct the study.

Compliance with ethical standards

Conflict of interest None of the authors declares a conflict of interest.

References

Akselrod S, Gordon D, Ubel FA, Shannon DC, Berger AC, Cohen RJ (1981) Power spectrum analysis of heart rate fluctuation: a quantitative probe of beat-to-beat cardiovascular control. Science 213:220–222. https://doi.org/10.1126/science.6166045

Arai Y, Saul JP, Albrecht P, Hartley LH, Lilly LS, Cohen RJ, Colucci WS (1989) Modulation of cardiac autonomic activity during and immediately after exercise. Am J Physiol 256:H132–H141. https://doi.org/10.1152/ajpheart.1989.256.1.H132

Aubry A, Hausswirth C, Louis J, Coutts AJ, Buchheit M, Le Meur Y (2015) The development of functional overreaching is associated with a faster heart rate recovery in endurance athletes. PLoS One 10:e0139754. https://doi.org/10.1371/journal.pone.0139754

Basalay M, Barsukevich V, Mastitskaya S, Mrochek A, Pernow J, Sjoquist PO, Ackland GL, Gourine AV, Gourine A (2012) Remote ischaemic pre- and delayed postconditioning—similar degree of cardioprotection but distinct mechanisms. Exp Physiol 97:908–917. https://doi.org/10.1113/expphysiol.2012.064923

Beedie CJ, Stuart EM, Coleman DA, Foad AJ (2006) Placebo effects of caffeine on cycling performance. Med Sci Sports Exerc 38:2159–2164. https://doi.org/10.1249/01.mss.0000233805.56315.a9

Bellenger CR, Fuller JT, Thomson RL, Davison K, Robertson EY, Buckley JD (2016) Monitoring athletic training status through autonomic heart rate regulation: A systematic review and meta-analysis. Sports Med 46:1461–1486. https://doi.org/10.1007/s40279-016-0484-2

Benedetti F (2013) Placebo and the new physiology of the doctor-patient relationship. Physiol Rev 93:1207–1246. https://doi.org/10.1152/physrev.00043.2012

Boullosa DA, Barros ES, del Rosso S, Nakamura FY, Leicht AS (2014) Reliability of heart rate measures during walking before and after running maximal efforts. Int J Sports Med 35:999–1005. https://doi.org/10.1055/s-0034-1372637

Buchheit M (2014) Monitoring training status with HR measures: do all roads lead to Rome? Front Physiol. https://doi.org/10.3389/fphys.2014.00073

Buchheit M, Laursen PB, Ahmaidi S (2007) Parasympathetic reactivation after repeated sprint exercise. Am J Physiol Heart Circ Physiol 293:H133–H141. https://doi.org/10.1152/ajpheart.00062.2007

Carter R 3rd, Watenpaugh DE, Wasmund WL, Wasmund SL, Smith ML (1999) Muscle pump and central command during recovery from exercise in humans. J Appl Physiol 87:1463–1469. https://doi.org/10.1152/jappl.1999.87.4.1463

Chen L, Zhou Q, Jin H, Zhu K, Zhi H, Chen Z, Ma G (2018) Effects of remote ischaemic conditioning on heart rate variability and cardiac function in patients with mild ischaemic heart failure. Heart Lung Circ 27:477–483. https://doi.org/10.1016/j.hlc.2017.03.164

Clark VR, Hopkins WG, Hawley JA, Burke LM (2000) Placebo effect of carbohydrate feedings during a 40-km cycling time trial. Med Sci Sports Exerc 32:1642–1647

Daanen HA, Lamberts RP, Kallen VL, Jin A, Van Meeteren NL (2012) A systematic review on heart-rate recovery to monitor changes in training status in athletes. Int J Sports Physiol Perform 7:251–260. https://doi.org/10.1123/ijspp.7.3.251

De Meersman RE (1992) Respiratory sinus arrhythmia alteration following training in endurance athletes. Eur J Appl Physiol Occup Physiol 64:434–436. https://doi.org/10.1007/BF00625063

de Castro CL, de Nobrega AC, de Araujo CG (1992) [Autonomic cardiovascular tests. A critical review. I]. Arq Bras Cardiol 59:75–85

Draper DO, Castel JC, Castel D (1995) Rate of temperature increase in human muscle during 1 MHz and 3 MHz continuous ultrasound. J Orthop Sports Phys Ther 22:142–150. https://doi.org/10.2519/jospt.1995.22.4.142

Dupuy O, Mekary S, Berryman N, Bherer L, Audiffren M, Bosquet L (2012) Reliability of heart rate measures used to assess post-exercise parasympathetic reactivation. Clin Physiol Funct Imaging 32:296–304. https://doi.org/10.1111/j.1475-097X.2012.01125.x

Enko K, Nakamura K, Yunoki K, Miyoshi T, Akagi S, Yoshida M, Toh N, Sangawa M, Nishii N, Nagase S, Kohno K, Morita H, Kusano KF, Ito H (2011) Intermittent arm ischemia induces vasodilatation of the contralateral upper limb. J Physiol Sci 61:507–513. https://doi.org/10.1007/s12576-011-0172-9

Ferreira TN, Sabino-Carvalho JL, Lopes TR, Ribeiro IC, Succi JE, da Silva AC, Silva BM (2016) Ischemic preconditioning and repeated sprint swimming: a placebo and nocebo study. Med Sci Sports Exerc 48:1967–1975. https://doi.org/10.1249/mss.0000000000000977

Gourine A, Gourine AV (2014) Neural mechanisms of cardioprotection. Physiology 29:133–140. https://doi.org/10.1152/physiol.00037.2013

Grossman P, Karemaker J, Wieling W (1991) Prediction of tonic parasympathetic cardiac control using respiratory sinus arrhythmia: the need for respiratory control. Psychophysiology 28:201–216. https://doi.org/10.1111/j.1469-8986.1991.tb00412.x

Imai K, Sato H, Hori M, Kusuoka H, Ozaki H, Yokoyama H, Takeda H, Inoue M, Kamada T (1994) Vagally mediated heart rate recovery after exercise is accelerated in athletes but blunted in patients with

chronic heart failure. J Am Coll Cardiol 24:1529–1535. https://doi.org/10.1016/0735-1097(94)90150-3
Incognito AV, Burr JF, Millar PJ (2016) The effects of ischemic preconditioning on human exercise performance. Sports Med 46:531–544. https://doi.org/10.1007/s40279-015-0433-5
Kannankeril PJ, Le FK, Kadish AH, Goldberger JJ (2004) Parasympathetic effects on heart rate recovery after exercise. J Investig Med 52:394–401. https://doi.org/10.1136/jim-52-06-34
Kentta G, Hassmen P (1998) Overtraining and recovery. A conceptual model. Sports Med 26:1–16. https://doi.org/10.2165/00007256-199826010-00001
Kiviniemi AM, Hautala AJ, Kinnunen H, Nissila J, Virtanen P, Karjalainen J, Tulppo MP (2010) Daily exercise prescription on the basis of HR variability among men and women. Med Sci Sports Exerc 42:1355–1363. https://doi.org/10.1249/MSS.0b013e3181cd5f39
Le Meur Y, Buchheit M, Aubry A, Coutts AJ, Hausswirth C (2017) Assessing overreaching with heart-rate recovery: what is the minimal exercise intensity required? Int J Sports Physiol Perform 12:569–573. https://doi.org/10.1123/ijspp.2015-0675
Lee CM, Mendoza A (2012) Dissociation of heart rate variability and heart rate recovery in well-trained athletes. Eur J Appl Physiol 112:2757–2766. https://doi.org/10.1007/s00421-011-2258-8
Lopes TR, Sabino-Carvalho JL, Ferreira TN, Succi JE, Silva AC, Silva BM (2018) Effect of ischemic preconditioning on the recovery of cardiac autonomic control from repeated sprint exercise. Front Physiol 9:1465. https://doi.org/10.3389/fphys.2018.01465
Loukogeorgakis SP, Panagiotidou AT, Broadhead MW, Donald A, Deanfield JE, MacAllister RJ (2005) Remote ischemic preconditioning provides early and late protection against endothelial ischemia-reperfusion injury in humans: role of the autonomic nervous system. J Am Coll Cardiol 46:450–456. https://doi.org/10.1016/j.jacc.2005.04.044
Machhada A, Trapp S, Marina N, Stephens RCM, Whittle J, Lythgoe MF, Kasparov S, Ackland GL, Gourine AV (2017) Vagal determinants of exercise capacity. Nat Commun 8:15097. https://doi.org/10.1038/ncomms15097
Mastitskaya S, Marina N, Gourine A, Gilbey MP, Spyer KM, Teschemacher AG, Kasparov S, Trapp S, Ackland GL, Gourine AV (2012) Cardioprotection evoked by remote ischaemic preconditioning is critically dependent on the activity of vagal preganglionic neurones. Cardiovasc Res 95:487–494. https://doi.org/10.1093/cvr/cvs212
Medigue C, Girard A, Laude D, Monti A, Wargon M, Elghozi JL (2001) Relationship between pulse interval and respiratory sinus arrhythmia: a time- and frequency-domain analysis of the effects of atropine. Pflugers Arch 441:650–655. https://doi.org/10.1007/s004240000486
Newell J, Higgins D, Madden N, Cruickshank J, Einbeck J, McMillan K, McDonald R (2007) Software for calculating blood lactate endurance markers. J Sports Sci 25:1403–1409. https://doi.org/10.1080/02640410601128922
Paiva VC, Santana KR, Silva BM, Ramos PS, Lovisi JC, Araujo CG, Ricardo DR (2011) Comparison of assessment methods of cardiac vagal modulation. Arq Bras Cardiol 97:493–501. https://doi.org/10.1590/S0066-782X2011005000109
Pecanha T, Forjaz CLM, Low DA (2017) Passive heating attenuates post-exercise cardiac autonomic recovery in healthy young males. Front Neurosci 11:727. https://doi.org/10.3389/fnins.2017.00727
Rabbani A, Kargarfard M, Twist C (2018) Reliability and validity of a submaximal warm-up test for monitoring training status in professional soccer players. J Strength Cond Res 32:326–333. https://doi.org/10.1519/jsc.0000000000002335
Sabino-Carvalho JL, Barbosa TC, Silva BM (2015) What is the effect of ischemic preconditioning on the kinetics of pulmonary oxygen uptake and muscle deoxygenation during exercise? Physiol Rep. https://doi.org/10.14814/phy2.12540
Sabino-Carvalho JL, Lopes TR, Obeid-Freitas T, Ferreira TN, Succi JE, Silva AC, Silva BM (2017) Effect of ischemic preconditioning on endurance performance does not surpass placebo. Med Sci Sports Exerc 49:124–132. https://doi.org/10.1249/mss.0000000000001088
Silva BM, Neves FJ, Negrao MV, Alves CR, Dias RG, Alves GB, Pereira AC, Rondon MU, Krieger JE, Negrao CE, Nobrega AC (2011) Endothelial nitric oxide synthase polymorphisms and adaptation of parasympathetic modulation to exercise training. Med Sci Sports Exerc 43:1611–1618. https://doi.org/10.1249/MSS.0b013e3182152197
Task Force (1996) Heart rate variability: standards of measurement, physiological interpretation and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Circulation 93:1043–1065. https://doi.org/10.1161/01.CIR.93.5.1043
Turcato S, Turnbull L, Wang GY, Honbo N, Simpson PC, Karliner JS, Baker AJ (2006) Ischemic preconditioning depends on age and gender. Basic Res Cardiol 101:235–243. https://doi.org/10.1007/s00395-006-0585-4
Vesterinen V, Nummela A, Ayramo S, Laine T, Hynynen E, Mikkola J, Hakkinen K (2016a) Monitoring training adaptation with a submaximal running test under field conditions. Int J Sports Physiol Perform 11:393–399. https://doi.org/10.1123/ijspp.2015-0366
Vesterinen V, Nummela A, Heikura I, Laine T, Hynynen E, Botella J, Hakkinen K (2016b) Individual endurance training prescription with heart rate variability. Med Sci Sports Exerc 48:1347–1354. https://doi.org/10.1249/mss.0000000000000910
Yasuma F, Hayano J (2004) Respiratory sinus arrhythmia: why does the heartbeat synchronize with respiratory rhythm? Chest 125:683–690. https://doi.org/10.1378/chest.125.2.683
Zagidullin N, Scherbakova E, Safina Y, Zulkarneev R, Zagidullin S (2016) The impact of remote ischemic preconditioning on arterial stiffness and heart rate variability in patients with angina pectoris. J Clin Med 5. https://doi.org/10.3390/jcm5070060