

# Acute cardiovascular and hemodynamic effects of set configuration of resistance training

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*A mis pequeños torbellinos*

*A mi fiel escudera, T.*

*A ti, 23 *





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*“Don't let anyone rob you of your imagination, your creativity, or your curiosity.*

*It's your place in the world; it's your life.*

*Go on and do all you can with it and make it the life you want to live.”*

*Mae Jemison*





## Abstract

Resistance exercise is characterised by a sharp rise in systolic blood pressure during exercise, and by reductions in cardiac parasympathetic control and baroreflex sensitivity with a concomitant hypotensive effect after exercise. This thesis aims to explore the effects of two moderate-intensity whole-body resistance training protocols differing in set configurations on those parameters. Long set configuration consisted of 4 sets of 10 repetitions with 2 min of rest between sets, while short set configuration consisted of 8 sets of 5 repetitions with a rest of 51 s between sets. Between exercises, both protocols rested 3 min. The results showed that during exercise, both structures produced similar increases in blood pressure. However, lower peaks of blood pressure were elicited in the last repetitions with the short configuration, also triggering a lower chronotropic response and less myocardial work. In addition, short sets promoted less lactatemia and smaller mechanical performance loss. Upon session completion, both designs promoted reductions in cardiac parasympathetic modulation, with a least withdrawal for the short set configuration. Neither design promoted changes in sympathetic vascular tone nor post-exercise hypotension. In conclusion, short set configurations result in a less cardiovascular compromise during and after exercise for healthy young individuals, resulting in safer designs.

**Keywords** set configuration, cardiac autonomic control, baroreflex sensitivity, post-exercise hypotension, hemodynamic.



## Resumen

Durante el ejercicio de fuerza se producen aumentos abruptos de la presión arterial sistólica, reportándose, junto con un efecto hipotensor, reducciones del control parasimpático cardíaco y sensibilidad barorrefleja tras su realización. Esta tesis busca examinar los efectos de dos protocolos compuestos por varios ejercicios de fuerza de intensidad moderada con diferente configuración de la serie sobre estos parámetros. La configuración de la serie larga consistió en 4 series de 10 repeticiones con 2 minutos de descanso entre series, mientras que la configuración corta en 8 series de 5 repeticiones con un descanso de 51 segundos. Entre ejercicios, ambos protocolos descansaron 3 minutos. Aunque los resultados muestran que ambas estructuras provocaron aumentos de presión arterial similares durante el ejercicio, en las últimas repeticiones se observaron picos más bajos de presión arterial con la configuración corta, la cual produjo una respuesta cronotrópica, trabajo miocárdico, implicación glucolítica y pérdidas de rendimiento mecánico menores. Tras la sesión, ambos diseños promovieron reducciones en la modulación parasimpática cardíaca; si bien la configuración corta causó una menor retirada. Ningún protocolo produjo hipotensión post-ejercicio ni cambios en el tono simpático vascular. En conclusión, las configuraciones cortas implican un menor compromiso cardiovascular durante y después del ejercicio en jóvenes sanos, lo que las convierte en más seguras.

**Palabras clave** configuración de la serie, control autonómico cardíaco, sensibilidad barorrefleja, hipotensión post-ejercicio, hemodinámica.





## Resumo

Durante o exercicio de forza prodúcense aumentos abruptos da presión arterial sistólica, reportándose, xunto cun efecto hipotensor, reducións do control parasimpático cardíaco e sensibilidade barorreflexa tras a súa realización. Esta tese busca examinar os efectos de dous protocolos compostos por varios exercicios de forza de intensidade moderada con diferente configuración da serie sobre estes parámetros. A configuración da serie longa consistiu en 4 series de 10 repeticións con 2 minutos de descanso entre series, mentres que a configuración curta en 8 series de 5 repeticións cun descanso de 51 segundos. Entre exercicios, ambos protocolos descansaron 3 minutos. Os resultados mostran que ambas estruturas provocaron aumentos de presión arterial similares durante o exercicio, aínda que coa configuración curta observáronse picos máis baixos de presión arterial nas últimas repeticións, a cal tamén produciu unha resposta cronotrópica, traballo miocárdico, implicación glicolítica e perdas de rendemento mecánico menores. Trala sesión, aínda que ambos deseños promoveron reducións na modulación parasimpática cardíaca, a configuración curta causou unha menor retirada. Ningún protocolo produciu hipotensión post-exercicio nin cambios no ton simpático vascular. En conclusión, as configuracións da serie curtas implican un menor compromiso cardiovascular durante e despois do exercicio en mozos sans, e por tanto, sendo deseños máis seguros.

**Palabras chave** configuración da serie, control autonómico cardíaco, sensibilidade barorreflexa, hipotensión post-exercicio, hemodinámica.



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## Abbreviations

$\Delta\%Lt$	Percentage change of lactatemia
15RM	15-repetition maximum load
5LFR	Last five to the first five repetition velocity ratio
ANOVA	Analysis of variance
ANS	Autonomic nervous system
AUC <sub>DBP</sub>	Analysis under the curve of diastolic blood pressure
AUC <sub>MAP</sub>	Analysis under the curve of mean arterial pressure
AUC <sub>SBP</sub>	Analysis under the curve of systolic blood pressure
BEI	Baroreflex effectiveness index
BMI	Body mass index
BP	Blood pressure
BPR	Bench press
BPV	Blood pressure variability
BRS	Baroreflex sensitivity
BRS <sub>count</sub>	Number of baroreceptor sequences detected
BRS <sub>slope</sub>	Magnitude of the baroreflex sensitivity
CON	Control session
CS	Cluster sets
CVDs	Cardiovascular diseases
DBP	Diastolic blood pressure
ECG	Electrocardiogram
HF	High frequency (in absolute values)
HF <sub>n.u.</sub>	High frequency in normalised units
HR	Heart rate
HRV	Heart rate variability
IRR	Beat-to-beat interval (R-R interval)
KE	Knee extension
LC	Leg Curl
LF	Low frequency
LF <sub>SBP</sub>	Low frequency of systolic blood pressure

LP	Lateral pull-down
LSC	Long set configuration session
Lt	Capillary blood lactate concentration
MAP	Mean arterial pressure
MMR	Average mean propulsive velocity to maximum velocity ratio
MPV	Mean propulsive velocity
PEH	Post-exercise hypotension
PNS	Parasympathetic nervous system
PP	Pulse pressure
PPG	Photoplethysmography
$\rho\eta^2$	Partial eta squared
r	Matched pair rank biserial correlation
RE	Resistance exercise
RM	Repetition maximum load
RMSSD	Root mean square of differences between adjacent pulse interval
RPE	Rating of perceived exertion
RPP	Rate pressure product
RRS	Rest redistribution set structure
RT	Resistance training
RTE	Relative treatment effect
SBP	Systolic blood pressure
SDNN	Standard deviations of normal-to-normal pulse intervals
SNS	Sympathetic nervous system
SQ	Parallel squat
SSC	Short set configuration session
TS	Traditional sets
TUT	Time under tension
ULF	Ultra-low frequency
VLF	Very low frequency



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# INTRODUCTION

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Cardiovascular diseases (CVDs) are globally the leading cause of death, achieving a total of 485.6 million cases and 17.8 million deaths in 2017 (1,2). Physical activity, specifically its absence, is in itself a major risk factor within core health behaviours, while it can modulate several other cardiovascular risk factors, such as cholesterol, blood pressure (BP) or glucose control (1).

Physical exercise, i.e. planned, structured, repetitive physical activity and with the objective of improving or maintaining physical fitness (3), given its powerful effectiveness in lowering BP (4), can be a non-pharmacological strategy to prevent (5) and/or treat CVDs (6). For this reason, as well as for the other benefits, exercise is part of most public policies. Although there are different types of physical exercise, concerning the cardiovascular component, aerobic exercise has been the most recommended for a long time. At the same time, it is the most studied for acute and chronic effects in both healthy and pathological populations. On the other hand, resistance exercise (RE) is currently also recommended as a significant component of a healthy fitness lifestyle and as a means of prevention and rehabilitation for several diseases, including for CVDs (5–9). As a matter of fact, the new guidelines for 2021 of the European Society of Cardiology already include RE among their recommendations for physical activity (10). Nonetheless, despite the large amount of evidence concerning the benefits of RE on general and disease populations, the position stands and guidelines are limited in this area, and with insufficient information or discordances between them regarding training parameters, due to the reduced evidence in comparison with aerobic training (11,12).

Moreover, although the health benefits outweigh the hazard (13), RE may trigger an acute cardiovascular event both during and shortly after the session in apparently healthy individuals (14) and specially in susceptible ones (15–18). These cardiovascular events, such as

artery dissection, subarachnoid haemorrhage (17) or sudden cardiac death and myocardial infarction (18) are due, on the one hand, to the RE pressor response characterized by a sharp rise of systolic blood pressure (SBP)(19), and on the other hand, to the reductions in cardiac autonomic modulation (20). Therefore, it is necessary to develop strategies that might diminish the cardiovascular impact during and after RE, while maintaining all its benefits.

In this context, cardiac autonomic modulation is not only a measure of clinical use. In recent years, due to technological progress, sports and exercise science has begun to use autonomic cardiac measurements to control sports performance and provide increasingly individualised training (21). In this area, it is a useful tool to monitor athletic training status (22), as indicators of fatigue and recovery, or as a marker to the effects of training in athletes (23) and, consequently, to promote greater adaptations and performance improvements (24). In this sense, knowing which designs will produce the greatest benefits with the least negative impact on the organism is key for coaches and athletes to be able to programme training as effectively as possible. The different loading parameters, including set configuration, are one of the main factors that can influence the different responses and adaptations to training. Hence, it is crucial to identify the effect of each parameter, and in particular how the set configuration can be a modulator of these effects.

Therefore, in order to allow evidence regarding the RE impact on the cardiovascular system and its control and how load parameters can be manipulated to manage these effects, the main objective of this thesis is to evaluate the cardiovascular, metabolic, and mechanical effects of two resistance training sessions differing in set configuration. Specifically, how set configuration can modulate the cardiac and BP dynamics during RE, and the autonomic and baroreflex control, the vasomotor tone modulation, and the post-exercise BP response after RE.



It is hypothesised that short set configurations would promote lower cardiac and pressure response during exercise and attenuate the reduction of cardiac parasympathetic modulation after session, improving the mechanical performance and decreasing the glycolytic involvement, without alterations regarding sympathetic vascular tone. Additionally, regarding post-exercise hypotension, it is expected that, although both protocols decrease BP to pre-exercise values, greater reductions would be observed following the long set configuration.



# THEORETICAL FRAMEWORK

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## 2.1. Cardiovascular system and resistance exercise

The cardiovascular system is responsible for responding to increased metabolic demand during exercise by supplying oxygenated blood and removing products from active muscles. This response involves some adjustments (i.e., an increase in cardiac output accompanied by a redistribution of blood flow from inactive organs to active skeletal muscle), which produce changes in different cardiac and haemodynamic parameters, including heart rate (HR) and BP. The changes in cardiovascular parameters will be different according to the type of muscle contraction.

During dynamic RE a combination of static and dynamic contractions of the muscles occurs (25). In general, at the beginning of the movement, a static contraction is produced to overcome the inertial resistance of the weight to be lifted. Once sufficient force is produced to defeat this resistance, a concentric dynamic contraction of the agonist muscles is produced to lift it. Then, after a lockout phase of the lift, dynamic eccentric contraction occurs to lower the weight, whereupon there is a relaxation phase until the next repetition is performed (26). Thus, at the initiation of each lift, the BP increases rapidly to maximum values during the lifting phase. The pressure then decreases in the lockout phase and increases again during the lowering phase, although not to the same extent as during the lifting. Once this phase is over, the BP values decrease again to the values before the execution. Concomitant with the BP rise, HR also increases, although - unlike BP - it maintains its values after the concentric phase (25–27) (Figure 1). After each repetition, during the relaxation phase, both BP and HR decline towards pre-exercise levels.

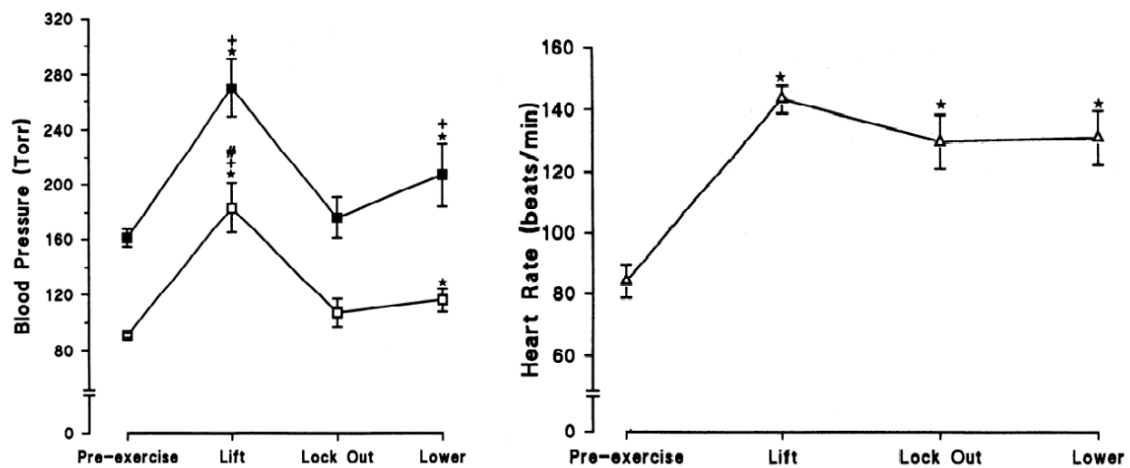


Figure 1. Blood pressure (left graph) and heart rate (right graph) responses at different phases of resistance exercise. In left graph, the upper line corresponds to systolic blood pressure and the lower line to diastolic blood pressure. From Lentini et al. (27)

This pattern of BP and HR response is replicated during each repetition performed during a set across the repetitions comprising a set. Nevertheless, it is important to highlight certain characteristics of the BP response during a set of RE. As previously described by de Sousa et al. (28), after an increase in the pressure response in the first repetition(s), there is a transient reduction in pressure until fatigue sets in. Once this point is passed, a progressive elevation of SBP is reached, showing maximum values in the last repetition(s) (Figure 2). This phenomenon, termed the “V-shape” pressure response, provides a cardiovascular benefit as it allows to perform some repetitions without BP increases and it may be explained by several factors. The effort required to overcome the load in the first repetition and the exacerbated intrathoracic pressure led to the increase in BP at the start of the set. In the following repetitions, due to the presence of a stretch-shortening cycle, the voluntary effort during the concentric contraction is reduced and the BP is lower. Once fatigue is present after several repetitions, a greater voluntary effort is again required, causing recruitment of accessory muscles, a greater metabolic demand (29) and increasing the need to perform the Valsalva manoeuvre (30) (boosting intrathoracic pressure). Coupled with the accumulation of metabolites caused by flow restriction, all these factors entail a higher BP response during the

last repetitions of the set (26). Regarding cardiac response throughout the set, HR increases progressively as the repetitions are carried out, reaching maximum values in function of the effort required.

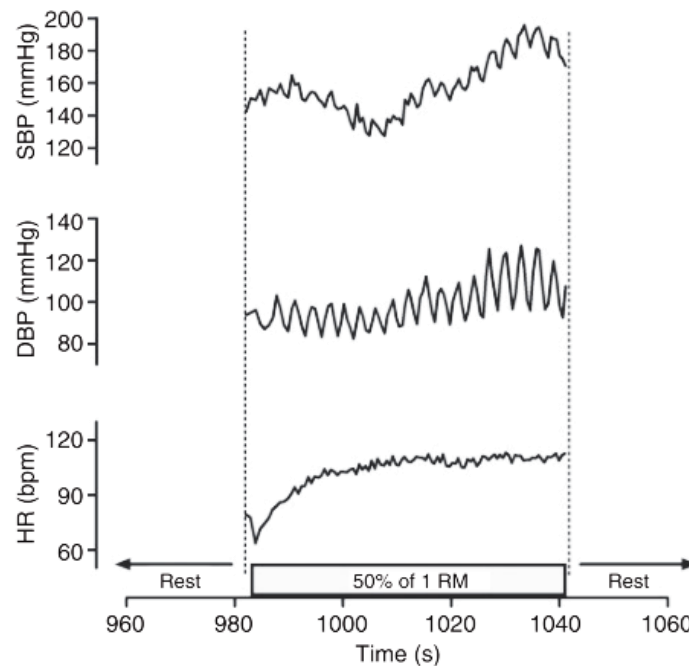


Figure 2. Blood pressure and heart rate response during a set of leg press exercise. SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: hear rate. From de Sousa et al. (28).

After completion of RE, the cardiovascular system must again make changes to maintain the homeostasis of the organism, decreasing HR values. This cardiac deceleration is commonly referred to as heart rate recovery and it has been established as a simple cardiac and ecological cardiac autonomic index (31). Post-exercise HR recovery can be divided into two phases: a fast phase and a slow phase. The fast phase comprises the first minute of recovery and is characterised by a rapid and abrupt decrease in HR; the slow phase extends after the first minute until HR returns to resting values, decreasing in a more gradual pattern as can be appreciated in Figure 3.

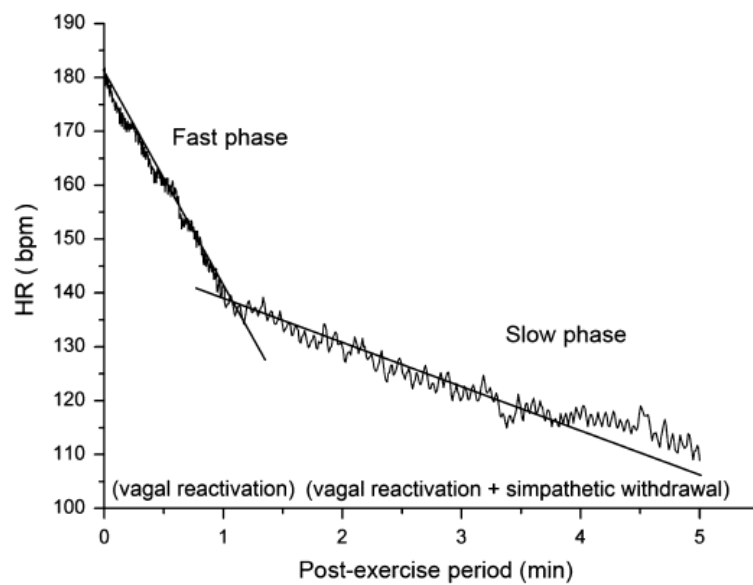


Figure 3. Heart rate recovery after exercise. From Peçanha et al. (32)

Concurrent to the recovery of the FC, a transient but sustained reduction in BP below baseline levels are often observed after exercise is completed. This drop has been termed post-exercise hypotension (PEH) (33) and it has been reported in response to different types of exercise. Aerobic protocols, also the most extensively studied (12), has reported large and lasting BP reductions after exercise (34), whereas RE has shown slightly post-exercise effects. However, the differences between these types of exercises are not consistent across the scientific evidence (35–38). Likewise, as Casonatto et al. (39) have reported in their meta-analysis, the potential hypotensive effect of RE can be influenced by multiple factors, noting that greater reductions occurred when, for example, a session of RE involved large muscle groups or recovery was performed in the supine position. These assertions will be discussed in a greater detail in a succeeding below.



### 2.1.1. Neural cardiovascular control and exercise

The autonomic nervous system (ANS) regulates several physiological processes to maintain homeostasis during internal or external stimuli. Regarding the cardiovascular system, the ANS modulates, via the sympathetic nervous system (SNS) and parasympathetic nervous system (PNS), the cardiac (i.e., the chronotropic, inotropic, dromotropic, and lusitropic properties of the heart) and the vascular function (i.e., peripheral vascular resistance) in order to preserve the correct blood perfusion to the organs when metabolic requirements are modified, such as during exercise (40). In general terms, the SNS produces an increase in HR (positive chronotropic effect), as well as in contractile force (positive inotropic effect) and increases conduction velocity (positive dromotropic effect) through the atrioventricular node. As for the PNS, a constant vagal tone slows the heart rate. When this tone is increased, the HR can be reduced (negative chronotropic effect) and, in turn, when this tone is blocked, the HR increases. In addition, the PNS also reduces the speed of conduction through the atrioventricular node. During exercise, as previously noted, HR increases, which is mainly mediated by a drop in parasympathetic activity (commonly referred to as parasympathetic withdrawal) and subsequently by an increase in sympathetic activity. Once the exercise is concluded, HR returns to basal values. In the fast phase of HR recovery, it is mainly caused by parasympathetic reactivation, whereas the slow phase entails parasympathetic reactivation and sympathetic withdrawal (32,41) (Figure 4). The cardiac response is the responsibility of both the SNS and the PNS, but peripheral vascular adjustments are essentially the responsibility of the SNS. In this sense, sympathetic activity is tonically activated during rest, being the main regulator of vasomotor tone in the peripheral circulation and essential involved in BP regulation through reflex mechanisms.

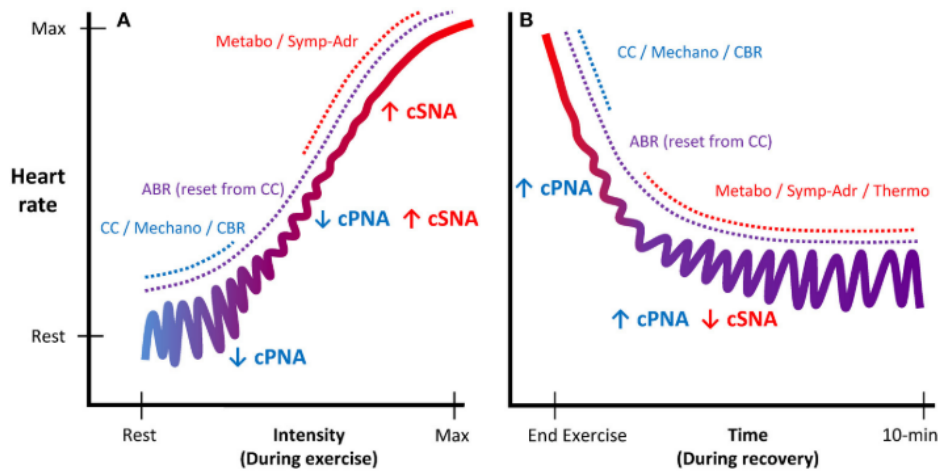


Figure 4. Heart rate (HR) dynamics during exercise (A) and recovery (B) and the neural mechanisms involved. Graph A illustrates the HR regulation during exercise according to intensity. Graph B shows time-dependently HR regulation during recovery. Cardiac control shifts from predominantly parasympathetic to predominantly sympathetic as exercise intensity increases. During recovery, the mechanisms that produce the HR increases during exercise are reversed, gradually returning to predominantly parasympathetic control. cPNA: cardiac parasympathetic neural activity; cSNA: cardiac sympathetic neural activity; CC: central command; Mechano: mechanoreflex; CBR: central baroreflex; ABR: arterial baroreflex; Metabo: metaboreflex; Symp-Adr: sympathetic-adrenal; Thermo: thermoregulatory influences. From Michael et al. (41).

Various adjustments occur in order to maintain homeostasis in response to an internal or external stimulus. These adjustments require an integrated action of multiple neural, cardiovascular, renal, endocrine and local tissue control systems (42). In the present thesis, the focus is on the cardiovascular neural control.

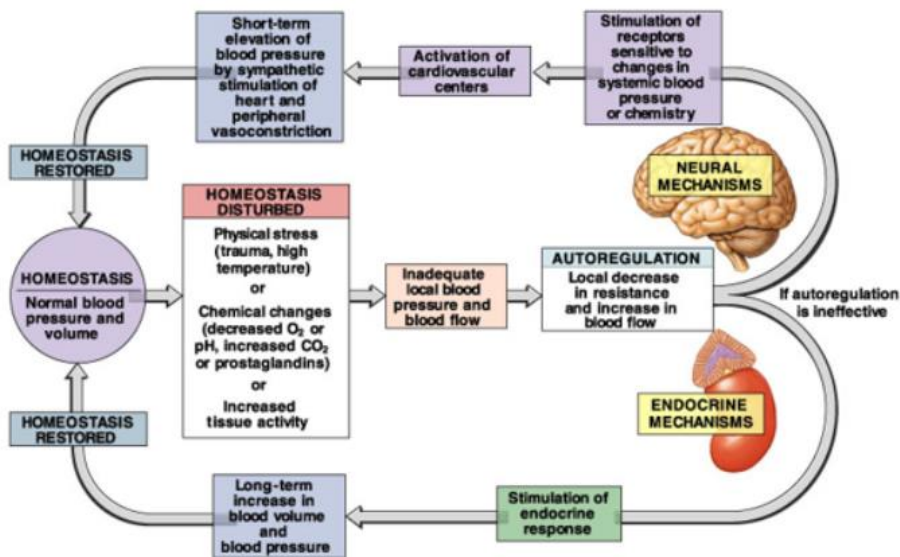


Figure 5. Cardiovascular adjustments to maintain homeostasis to external (physical stress) or internal stimulus. From Martini et al. (43).

In this sense, during and after exercise, several neural mechanisms are involved to produce autonomic adjustments, and it is the integration of them all that allows the autonomic nervous system to respond appropriately to the requirements of the exercise performed (Figure 6). These mechanisms are both central and peripheral. The central command (i.e., neural signals originating from higher brain centres that activate cardiovascular and somatomotor systems) is the central neural mechanism, while the peripheral mechanisms correspond to reflexes activated by different sensory receptors. Peripheral reflexes can be classified according to different criteria such as the type of receptor (i.e., mechanoreceptors - baroreceptors and proprioceptors- and chemoreceptors) or their location (i.e., placed in the vessels or the muscle). Thus, different reflex mechanisms can be established. As regards the type of receptor, mechanical and chemical reflexes can be defined. Concerning the mechanical ones, these can be mediated by baroreceptors, including the high-pressure baroreflex (or *arterial baroreflex*, pressure receptors placed in the carotid sinus and in the aortic arch that regulate changes in BP) and the low-pressure baroreflex (or *cardiopulmonary baroreflex*, pressure receptors involved with the regulation of blood volume), or by proprioceptors located in the muscle (*muscle mechanoreflex*). About chemical reflexes, these can respond to changes in the concentration of different metabolites in the muscle (*muscle metaboreflex*) or the blood vessels (*carotid or arterial chemoreflex*). On the other hand, depending on the origin of the reflex, the receptors can be located in the vessels (high- and low-pressure baroreflex, and *carotid or arterial chemoreflex*) or in the muscles (muscle metabo- and mechanoreflex of the exercise pressor reflex, and *respiratory metaboreflex*). The below is a brief description of each mechanism.

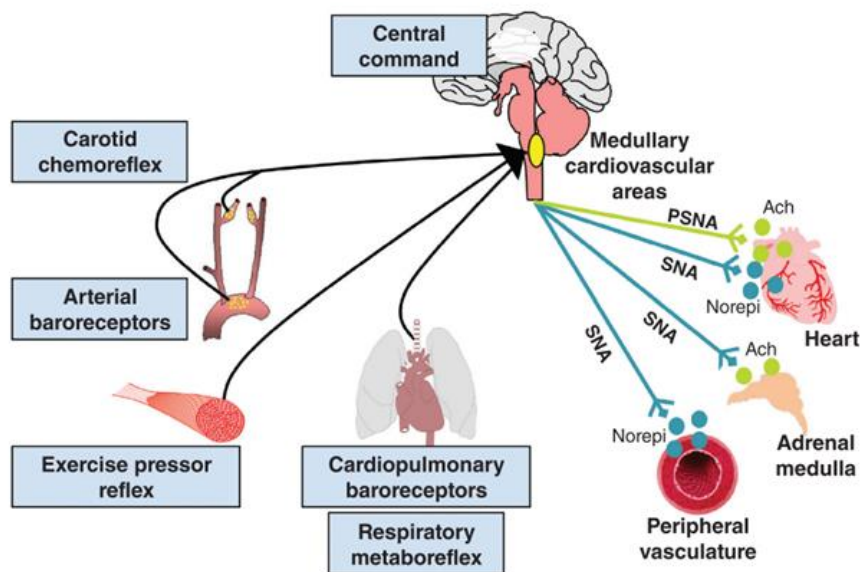


Figure 6. Mechanisms involved in the cardiovascular autonomic adjustments to exercise and recovery. Ach: acetylcholine; Norepi: norepinephrine; PSNA: parasympathetic neural activity; SNA: sympathetic neural activity. From Fisher et al.(40)

### 2.1.1.1. Central command

The central command refers to the descending “feed-forward” neural inputs from the higher brain centres to the cardiovascular centre. These cause the contraction of skeletal muscle and, concomitantly, activate the central nervous system centres that participate in the control of cardiac autonomic activity.

This mechanism was first enunciated in 1886 by Zuntz and Geppert (44) and proposed for circulation control by Johansson in 1893 (45). Subsequent studies at the University of Copenhagen by Krogh and Lindhard (in collaboration with Miss Buchanan from Oxford (46)) concluded that the immediate increase in HR and ventilation at the onset of exercise was related to a central control mechanism termed by the authors as "cortical irradiation". The term central command was used for the first time by Goodwin et al. in 1972 (47). The authors applied an electrical vibration to the tendon of agonist or antagonist muscles during a voluntary static muscle contraction in order to decrease or increase the contribution of the

central command, respectively. They concluded that BP, HR, and ventilation increased to a greater or lesser extent when the central command contribution was increased or decreased, respectively, demonstrating that downstream signals from higher brain centres play a role in the cardiovascular and ventilatory responses during exercise in humans. Other studies subsequently corroborated these findings using other assessment methods (48–54), allowing to establish the anticipatory action of the central command, as well as the involvement of perceived effort in its response and the additional influence of feedback inputs (55,56).

### 2.1.1.2. Baroreceptor reflex

#### 2.1.1.2.1. Arterial baroreflex or high-pressure baroreflex

The arterial baroreflex is the main mechanism involved in the short-term homeostatic control of BP, based on a negative feedback mechanism (57–59). This reflex is initiated by pressure receptors, called baroreceptors (or pressoreceptors), located in the aortic arch and carotid sinus (60). Baroreceptors have a tonic (constant) activity, which translates into a basal frequency of action potentials in their sensory neurons. In response to changes in BP, the walls of the aortic and carotid sinuses distend or relax, resulting in an increase or decrease in the frequency of afferent neuronal firing. A branch of the glossopharyngeal nerve and Hering's nerve carry these impulses from the carotid baroreceptors, while small branches of the vagus nerve carry impulses from the aortic baroreceptors. These afferents are centrally integrated into the nucleus tractus solitarius of the medulla oblongata and involve reflex changes in parasympathetic and sympathetic efferent activity towards the heart and blood vessels, modulating HR and peripheral vasoconstriction (57,58,61), to return BP to the original operating point values. The Figure 7 shows a schematic representation of the arterial baroreflex operation.

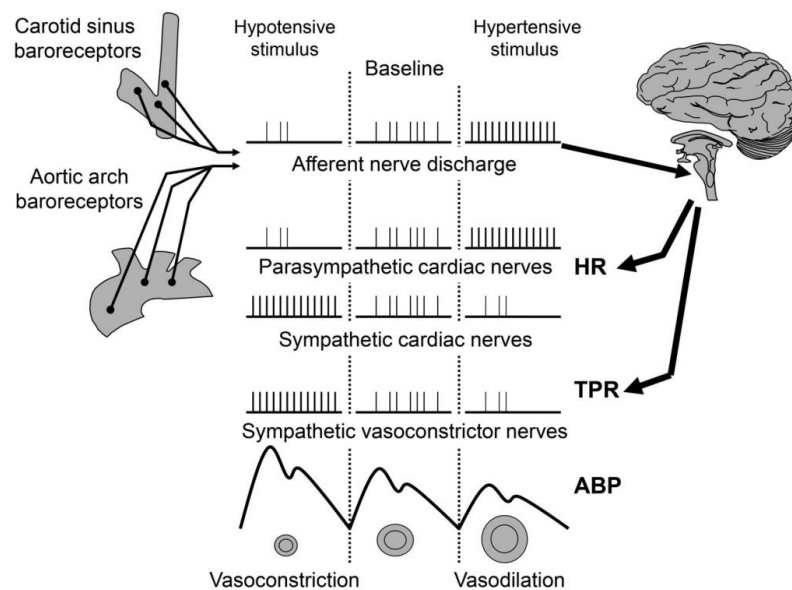


Figure 7. Afferent and efferent neural responses of arterial baroreceptors. HR: heart rate; TPR: total peripheral resistance; ABP: arterial blood pressure. From Fisher et al. (40)

In response to a hypotensive stimulus, baroreceptors become relaxed and send impulses less frequently, which decreases parasympathetic stimulation and increases sympathetic stimulation, leading to an increase in blood pressure due to increased heart rate and contractility and vasoconstriction. Conversely, when there is an increase in BP, the frequency of impulses emitted by afferent neurons increases, leading to an increase in parasympathetic nervous activity and a decrease in sympathetic nervous activity. This results in reflex bradycardia and peripheral vasodilatation (57,58,61).

The inverse relationship between HR and BP, which establishes the fundamental principle of the baroreflex system, was first described in 1863 by Marey (62). Although historically there has been some controversy about the role of the arterial baroreflex, findings from David Donald's and Peter Raven's research groups have demonstrated that it remains operational during exercise. Indeed, a properly functioning arterial baroreflex is essential for a correct cardiovascular neural response during exercise (63). Likewise, the findings of both research groups have established the characteristics of the arterial baroreflex and its function.

Thus, as postulated by Melcher & Donald (64) with the stimulus-response curves of carotid baroreceptors during exercise, the baroreflex efficacy is not constant, acting most effectively between certain pressure limits (where it will be most needed), and with greater activation at rapid pressure changes compared to a stationary pressure. That is, the BP regulation occurs around a preset value determined operating point (65). Likewise, the operating point of the baroreflex is not fixed but varies over a range of pressures. The modulation of the response of barosensitive neurons, which is determined by different inputs from the peripheral and central nervous system (66), shifts the operating point to a new BP value upon BP changes (65). This variation or readjusting of the operant point was termed arterial baroreflex resetting (67). This mechanism justifies the possibility of concomitant increases in BP and HR (as occurs during exercise – see Figure 8) or the reason for normal BRS values in individuals with mild or moderate hypertension (68,69).

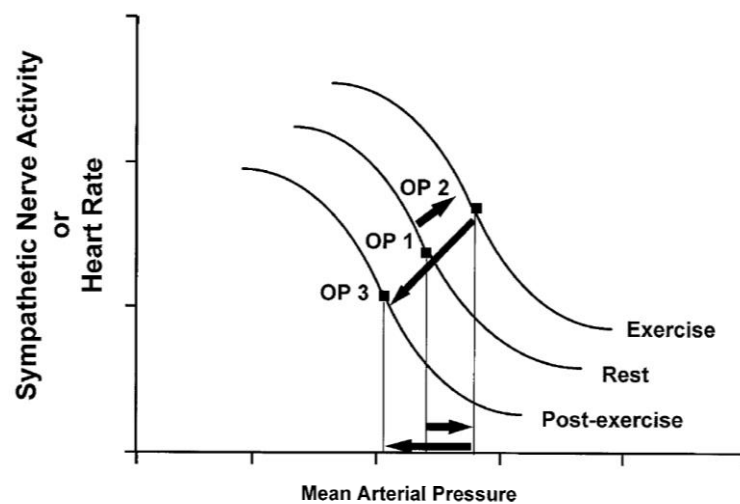


Figure 8. Arterial baroreflex resetting during and after exercise. Blood pressure is regulated around a preset value (operating point - OP 1). Upon exercise, the operating point is raised to a higher pressure (OP 2), shifting it upwards and to the right. After exercise, the operating point is readjusted again, shifting it downwards and to the left (OP 3), allowing to reach a lower pressure than the operating point at rest (OP 1). From DiCarlo & Bishop (68).

#### *2.1.1.2.2. Cardiopulmonary baroreflex or low-pressure baroreflex*

Fluctuations in central venous pressure and blood volume are detected by low-pressure, mechanically sensitive stretch receptors located in the atria, ventricles, and pulmonary vessels, which carry afferent information via the vagus nerve to the nucleus tractus solitarius (Fadel & Raven, 2012). Thus, upon an elevation in central blood volume (e.g., during supine positioning), cardiopulmonary baroreceptors reflexively increase parasympathetic nervous activity and inhibit sympathetic nervous activity, lowering HR and BP. Conversely, with a reduction (e.g., during orthostatic stress), cardiopulmonary afferent fibres reduce the parasympathetic activity and produce a sympathetic excitation, increasing HR and BP (Fadel & Raven, 2012).

Although the cardiopulmonary baroreflex is relatively less studied compared to other mechanisms previously mentioned, evidence has shown that it is an important mediator of cardiovascular responses during exercise, specifically modulating the cardiovascular response as a function of the position adopted. (40,67,70–74).

#### *2.1.1.3. Exercise pressor reflex*

The exercise pressor reflex is a feedback mechanism arising from contracting skeletal muscle that functions to increase cardiovascular and ventilatory function in response to mechanical and metabolic stimuli produced during muscle contraction. The afferent arm of the reflex is composed of myelinated type III and unmyelinated type IV fibres that are depolarised in response to mechanical (muscle mechanoreflex) and metabolic (muscle metaboreflex) stimuli during exercise. The muscle mechanoreflex is predominantly mediated by type III fibres, which tend to discharge an explosive burst of impulses at the onset of contraction, decreasing as muscles fatigue. In contrast, the muscle metaboreflex is mainly mediated by type



IV fibres (Figure 9). These fibres do not discharge vigorously at the onset of contraction, responding with some latency but maintaining their unloading as the muscle fatigues. However, as has been reported (73–75), both fibres exhibit polymodal qualities, meaning that certain type III fibres will respond to metabolic changes in the muscle while type IV fibres will respond to mechanical stimuli. Thus, through the activation of both afferent neurons of the pressor exercise reflex, an efferent response of decreased parasympathetic activity and increased sympathetic nervous activity is produced, leading to an increase in BP, HR, and myocardial contractility (47,76–78).

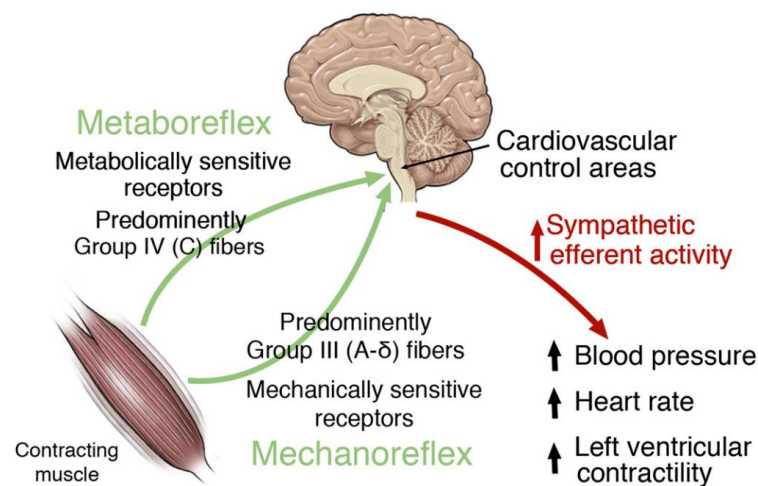


Figure 9. Exercise pressor reflex. From Mitchell (77).

The influence of a skeletal muscle reflex on the cardiorespiratory response to exercise was initially investigated by Krogh and Lindhard in 1917, but it was not until 20 years later that Alam and Smirk demonstrated that the accumulation of metabolites during muscle contraction plays an important role in the reflex regulation of cardiovascular system during exercise. These researchers found that BP and HR increased significantly greater during an isometric exercise of both upper (79) and lower limbs (80) with ischaemia, and remained elevated when exercise was ceased (Figure 10). From these studies onwards, several new insights have been found on the metabolic component, including the differences between the two branches of this reflex (81–86).

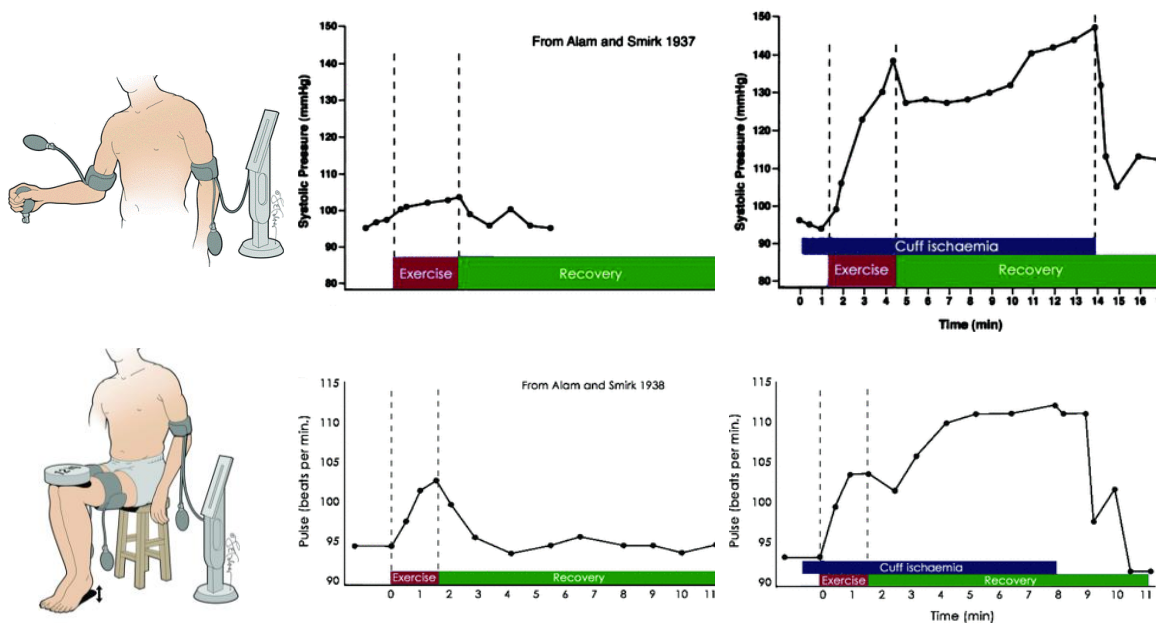


Figure 10. Alam and Smirk protocols representation with systolic blood pressure (top) and heart rate (above) response during exercise performed without and with circulatory occlusion. From Mitchell (87).

Furthermore, similar to the metaboreflex, several investigations have evaluated the ability of the mechanoreflex to elicit a cardiovascular response. Although in humans it is more complex to isolate this branch (as muscle contraction is accompanied by both central command and metaboreflex activation (75), research studies like that performed by Nóbrega & Araújo (88) investigated the independent action of the muscle mechanoreflex through passive limb movement, reporting similar increases in HR compared to voluntary movement. Similarly, other studies were developed that corroborated the relevance of mechanoreflex receptors located in striated skeletal muscles in cardiovascular responses. Mainly, the activation of this branch produces an increase in HR at the onset of exercise (cardiac vagal withdrawal), independently of the concomitant activation of the central command and muscle metaboreflex. (46,89–91).

#### 2.1.1.4. Arterial chemoreflex

Chemical changes in the blood are detected by chemosensitive receptors located in the carotid sinus and aortic arch. These are considered peripheral chemoreceptors, as receptors with the same function are located in the central nervous system (central chemoreceptors). While peripheral chemoreceptors are activated and inhibited by hypoxia and hyperoxia, respectively, central chemoreceptors are activated and inhibited by hypercapnia and hypocapnia. Particularly, carotid chemoreceptors have been considered the main oxygen sensor in humans. Both chemoreceptors are responsible for transmitting this information to the cardiovascular and respiratory control centre, thereby regulating in parallel the autonomic and respiratory activity (46).

Different situations can trigger hypoxia and hypercapnia in both healthy and diseased individuals and both at rest and during exercise, triggering the involvement of central and peripheral chemoreceptors (92). Recent studies have also shown that during normoxic exercise, carotid chemoreceptors are also involved, counteracting sympathetic vasoconstrictor flow and thus participating in the neural control of the circulation during exercise (93,94).

#### 2.1.2. Assessment of cardiovascular function and its control

For the assessment of cardiovascular response, some parameters can be measured in order to analyse these responses and the physiological adjustments involved, either during or before exercise. Briefly, two variables are the main inputs for the assessment of cardiovascular function: HR and BP. Besides, the processing of these two signals provides information about other cardiovascular parameters, as well as the physiological processes that regulate them. The following is a summary of the different assessment methods that will be used in the development of this thesis, as well as their alternative or gold standard techniques.

### 2.1.2.1. Heart rate

Several devices provide beat-to-beat HR recordings, which are obtained by tracking the time elapsed between two consecutive R waves (called RR intervals - IRR). The “gold standard” for the quantification of RR intervals is electrocardiogram (ECG), which records each electrical impulse of the heart (95). Additionally, there are other reference methods within the ambulatory clinical context such as the Holter ECG monitor (96), as well as sensors for auscultation of the heart, or blood pressure measurement. However, nowadays, several instruments and techniques have been developed to facilitate the assessment of HR in different contexts, such as sport. These devices are mainly based on single-lead ECG, photoplethysmography (PPG) or pulse oximetry, which allow for more economical, accessible, and practical assessments, while maintaining reliability and accuracy of measurement (97,98). Thus, wearable devices such as HR straps (chest or wrist) and watches, PPG devices (e.g., wrist-worn devices or smartphones) and adhesive single-lead ECG recorders, implantable loop recorders, have been developed. Specifically, in this thesis, the ECG was used to obtain the HR and IRR values.

### 2.1.2.2. Blood pressure

BP can be assessed using different methodologies adapted to the requirements and the context of the measurement. The methods can be classified into intermittent and continuous, according to the type of registration. The former, mainly auscultatory and oscillometric methods, are techniques that allow for simple and direct BP assessment in the healthcare setting and day-to-day use with home monitors. However, for sports and scientific applications, these methods are sometimes not sufficiently appropriate. This is first because of the possible artefacts related to movement. Secondly, due to the characteristics of the

methodology, it may underestimate SBP values in some situations, e.g., during and after exercise cessation (99–101). Among these types, the auscultatory method with mercury sphygmomanometer is considered the "gold standard". For continuous methods (i.e., beat-to-beat BP assessment), the "gold standard" is the intra-arterial measurement. This consists of inserting a catheter into a peripheral artery (mostly the radial or femoral artery), and the intra-arterial space is connected to the measuring device via a column of fluid (19). Although this methodology allows accurate assessment of BP, it presents some disadvantages, including potential adverse effects due to its invasive nature, as well as its cost and lack of feasibility in areas such as sport. Alternatively, non-invasive methods have been developed based on two different techniques, namely arterial applanation tonometry and the volume clamp method (or vascular unloading technique)(102). The former consists of pulse wave analysis by applying a pressure sensor perpendicularly to the arterial wall, allowing BP calculation, as well as other information regarding vessel characteristics. The second, based on the work of Penaz in the 1970s (103), involves the measurement of BP at the finger employing an inflatable cuff combined with a photodiode. The diameter of the artery in the finger is measured by the photodiode while the pressure in the cuff is adjusted to keep the diameter of the artery constant. Based on the pressure changes in the cuff, the BP of the brachial artery is calculated and computed (102). Specifically, in this thesis, the BP values were recorded using a device based on the volume clamp method.

### 2.1.2.3. Heart rate variability

Heart rate variability (HRV), defined as the oscillation between consecutive IRR and influenced by continuous modulation of PNS and SNS (95), is a novel, inexpensive, useful and non-invasive tool for evaluating cardiac autonomic modulation. In this sense, HRV has been reported as a strong predictor of mortal risk, sudden cardiac death, or cardiac arrhythmias (104–107). Additionally, it was evidenced the proper use of HRV to monitor acute responses and chronic adaptations to different situations, such as exercise (22,108–114), since it was evidenced the use of HRV as an indicator of stress, recovery or overreaching (115,116). Several parameters can be used for the HRV output according to the techniques used for the processing of the IRR signals, as described in the following paragraphs.

#### 2.1.2.3.1. Heart rate variability measurements

HRV analysis can be performed by several methods: time domain, frequency domain, and non-linear methods that will be described below.

##### *Time-domain method*

The time-domain method provides the simplest index of HRV based on statistical and geometrical approaches, quantifying the amount of variability in measurements of the time period between successive heartbeats (95). For time-domain indices, periods of at least 1 minute up to more than 24 hours must be recorded, although different minimum acceptable time periods have also been proposed for each metric (117). The time-domain measures are described in Table 1.

Table 1. Time domain measures of heart rate variability (HRV) (95,118).

Variable	Units	Description	Physiological origin
<b>Statistical measures</b>			
		Standard deviation of all NN intervals.	
<b>SDNN</b>	ms	* Gold standard for medical stratification of cardiac risk in 24h recordings	Cyclic components responsible for HRV.
<b>SDANN</b>	ms	Standard deviation of the averages of NN intervals in all 5 min segments of the entire recording.	
<b>RMSSD</b>	ms	The square root of the mean of the sum of the squares of differences between adjacent NN intervals.	Vagal modulation
<b>SDNN index</b>	ms	Mean of the standard deviations of all NN intervals for all 5 min segments of the entire recording.	
<b>SDSD</b>	ms	Standard deviation of differences between adjacent NN intervals.	
<b>NN50 count</b>		The number of pairs of adjacent NN intervals differed by more than 50 ms in the entire recording. Three variants are possible counting all such NN intervals pairs or only pairs in which the first or the second interval is longer.	
<b>pNN50</b>	%	NN50 count divided by the total number of all NN intervals.	Vagal modulation
<b>Geometric measures</b>			
<b>HRV triangular index</b>		The total number of all NN intervals is divided by the height of the histogram of all NN intervals measured on a discrete scale with bins of 7·8125 ms (1/128 s).	
<b>TINN</b>		Baseline width of the minimum square difference triangular interpolation of the highest peak of the histogram of all NN intervals.	

HRV: heart rate variability; NN intervals: time between two consecutive normal to normal beats.

### Frequency domain methods

Frequency domain measurements estimate the absolute or relative power distribution in four frequency bands: ultra-low frequency (ULF), very low frequency (VLF), low frequency (LF) and high frequency (HF) bands, where power is the signal energy for each frequency bands. Frequency domain measurements can be expressed in both absolute and relative power. While absolute power is calculated as milliseconds squared divided by cycles per second ( $\text{ms}^2/\text{Hz}$ ), relative power is estimated as the percentage of the total HRV power or in normal units (nu). For the calculation of the normal units, the absolute power for a specific frequency band must be divided by the summed absolute power of the LF and HF bands, thus allowing the comparison of measurements from different people (95). In order to decompose

the HRV signal in the different frequency ranges, some models can be used. The most important and noteworthy are the Fast Fourier Transformation or autoregressive method.

The spectral analysis can be established for two recording patterns: short-term recordings and long-term recordings. The formers are set between 2 to 5 minutes, while the latter corresponds to 24-hour recordings, and certain methodological considerations must be addressed. For short-term recordings, only three main spectral components (i.e., VLF, LF and HF) are observed in contrast with the four components in 24h recordings (95,117). The frequency-domain measures are described in Table 2.



Table 2. Frequency domain measures of heart rate variability (HRV) (95,118)

Analysis of short-term recordings (5 min)				Analysis of entire 24 h				Physiological origin
Variable	Units	Description	Frequency range	Variable	Units	Description	Frequency range	
<b>5 min total power</b>	ms <sup>2</sup>	The variance of NN intervals over the temporal segment	≈ ≤ 0.4 Hz	<b>Total power</b>	ms <sup>2</sup>	The variance of all NN intervals over	≈ ≤ 0.4 Hz	
				<b>ULF</b>	ms <sup>2</sup>	Power in very-low-frequency range	≤ 0.003 Hz	Circadian oscillations, core body temperature, metabolism, and the renin-angiotensin system
<b>VLF</b>	ms <sup>2</sup>	Power in very-low-frequency range	≤ 0.04 Hz	<b>VLF</b>	ms <sup>2</sup>	Power in very low frequency range	0.003 - 0.04 Hz	Long-term regulation mechanisms, thermoregulation, and hormonal mechanisms
<b>LF</b>	ms <sup>2</sup>	Power in the low-frequency range	0.04 - 0.15 Hz	<b>LF</b>	ms <sup>2</sup>	Power in the low-frequency range	0.04 - 0.15 Hz	Mix of sympathetic and vagal activity, baroreflex activity
<b>LF norm</b>	n.u.	LF power in normalised units LF/(Total Power–VLF) x 100						
<b>HF</b>	ms <sup>2</sup>	Power in low-frequency range	0.15 – 0.4 Hz	<b>HF</b>	ms <sup>2</sup>	Power in low-frequency range	0.15 - 0.4 Hz	Vagal modulation
<b>HF norm</b>	n.u.	HF power in normalised units HF/(Total Power–VLF) x 100						
<b>LF/HF</b>		Ratio LF [ms <sup>2</sup> ]/HF [ms <sup>2</sup> ]						Mix of sympathetic and vagal activity
				<b>α</b>		The slope of the linear interpolation of the spectrum in a log-log scale	≈ ≤ 0.4 Hz	

HF: high frequency; LF: low frequency; ULF: ultra-low frequency; VLF: very low frequency.

*Non-linear methods*

Non-linear methods are relatively recent and provide a more sensitive approach to characterising the autonomic nervous system function. These methods are based on the premise that a relationship between variables is not tractable as a straight line, (i.e., they are unpredictable) and are the result of the complex interaction of the mechanisms that regulate a signal, in this case, IRR. Several non-linear methods exist, such as attractors, 1/f behaviour of the power spectrum, fractal dimension and correlation dimension, Poincaré and higher-order moment plots, approximate and sample entropy, pointwise correlation dimension, detrended fluctuation analysis and Lyapunov exponents (95,118). Thus, the most relevant indices are described in table 3.

Table 3. Non-linear indices of heart rate variability (HRV) (95,118).

Variable	Units	Description	Physiological origin
<b>S</b>	ms	Area of the ellipse which represents total HRV	
<b>SD<sub>1</sub></b>	ms	Poincaré plot standard deviation perpendicular to the line of identity	Unclear, depicts quick and high frequent changes in heart rate variability. Correlated with HF (vagal tone)
<b>SD<sub>2</sub></b>	ms	Poincaré plot standard deviation along the line of identity	Unclear, depicts long-term changes in heart rate variability. Correlated with LF (mix of sympathetic and vagal activity, baroreflex activity)
<b>SD<sub>1</sub>/SD<sub>2</sub></b>	%	Ratio of SD <sub>1</sub> /SD <sub>2</sub>	Correlated with LF/HF
<b>ApEn</b>		Approximate entropy, which measures the regularity and complexity of a time series	
<b>SampEn</b>		Sample entropy, which measures the regularity and complexity of a time series	
<b>DFA α1</b>		Detrended fluctuation analysis, which describes short-term fluctuations	
<b>DFA α2</b>		Detrended fluctuation analysis, which describes long-term fluctuations	
<b>D<sub>2</sub></b>		Correlation dimension, which estimates the minimum number of variables required to construct a model of system dynamics	

HF: high frequency; LF: low frequency.

#### 2.1.2.3.2. *Physiological interpretation of HRV indices*

HRV indices, whether time-domain, frequency-domain or non-linear, correlate with each other and their calculation allows estimation of cardiovascular modulation by the autonomic nervous system. Although some controversy for physiological interpretation of some indices remains (119–122), other HRV metrics present extensive evidence to support their use for the estimation of autonomic modulation. Tables 1, 2 and 3 describe, as applicable, the physiological interpretation of each index.

#### 2.1.2.4. **Baroreflex sensitivity**

The efficiency with the baroreflex is able to respond to alterations in blood pressure, i.e., the capacity with which it can modify heart rate in response to alterations in SBP is known as baroreflex sensitivity (BRS) (123). This has been extensively studied since, as La Rovere et al. (124) state, BRS is, together with HRV, one of the autonomic markers of greatest clinical interest.

There are different methodologies to assess BRS, ranging from the use of drugs to non-invasive procedures such as the use of suction collars, the Valsalva manoeuvre or the analysis of spontaneous BP and IRR variations. Within the latter method, there are two types of techniques: the spectral method and the sequence method.

The spectral method, outlined by Mulder (125), evaluates the BRS by means of the moduli of the transfer function between the variabilities of the IRR and the SBP. From the simultaneous analysis of both variabilities, the  $BRS_{LF}$  and  $BRS_{HF}$  indices are obtained according to the following procedures. Firstly, the cross spectra are calculated, consisting of the magnitude-squared coherence spectrum and the phase spectrum. Subsequently, the LF and HF powers for two bands are obtained from the IRR and SBP variabilities with a magnitude-

squared coherence spectrum greater than 0.5. Finally, the  $BRS_{LF}$  and  $BRS_{HF}$  powers were calculated, without a normalisation procedure, using the following equations:  $BRS_{LF} = [(PR(LF)/PS(LF))]^{0.5}$  and  $BRS_{HF} = [(PR(HF)/PS(HF))]^{0.5}$ , where PR(-) and PS(-) represented the power of IRR or SBP, respectively (126–129).

The sequence method, described by Parati et al. (130), is based on the identification of at least three or more consecutive beats in which SBP and IRR increase progressively (+IRR/+SBP, up-events) or decrease (-IRR/-SBP, down-events) in a linear fashion (131) (Figure 11). The threshold change is established at 1 mmHg for SBP and 6 ms for the RRI.

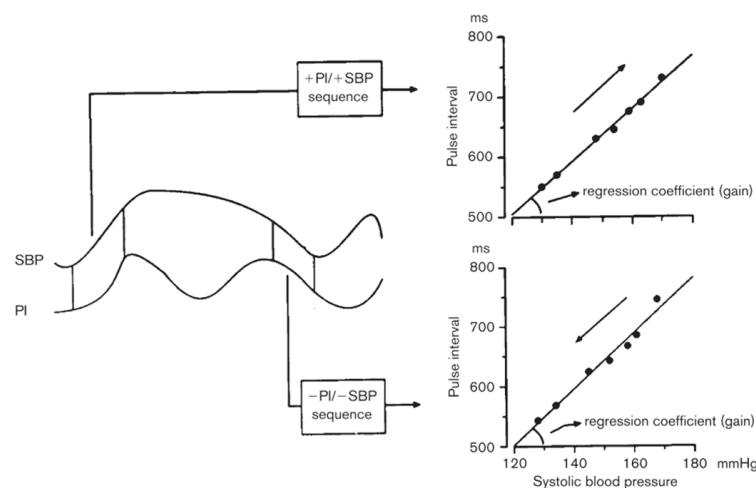


Figure 11. Baroreflex sensitivity assessment by sequences method. Up- and down-event analysis. PI: pulse interval; SBP: systolic blood pressure. Plus (+) and minus (-) symbols represent, respectively, increases and decreases of PI and SBP. From Parati et al. (138).

A baroreceptor event can be calculated using the same ramps for IRR and SBP, i.e., in the detected event, there is no shift between blood pressure beats and heart rate. This is called Lag0, but there are other ways of calculating BRS, such as Lag1 and Lag2. These calculate a baroreceptor event with one or two shifts, respectively, between the SBP and IRR beats, i.e., the event is detected when the IRR ramp is considered temporarily one or two beats (depending on whether it is Lag1 or Lag2) later than the SBP ramp started (132–134). The BRS is usually evaluated as the mean slope of all sequences detected ( $BRS_{slope}$ ). It is obtained by

computing all the slopes of the regression obtained from the function that relates changes in SBP and changes in RRI for each event detected, and their subsequent averaging (135). Additionally, other variables related to the sequence method can be used in order to improve the analysis of baroreflex activity. Firstly, the total number of events ( $BRS_{count}$ ), as it reflects the number of times that concomitant SBP and RRI changes, and therefore baroreceptor response, are identified. Secondly, the Baroreceptor Effective Index (BEI). It is a novel measurement regarding baroreflex activity that provides information on how well the baroreceptors are responding to oscillations in BP. BEI is calculated as the proportion of baroreflex events (i.e., the number of SBP ramps followed by the respective reflex IRR ramps) divided by the total number of BP changes (including those instances with no associated IRR change) in a given time window (136), and it is usually presented as a percentage. Moreover, BEI can be used to identify if there is an amount or frequency of activity at which the baroreceptors are unable to continue to adjust to respond to blood pressure changes since they remain refractory to further stimuli (134). Likewise, this index is also an indicator of the severity and duration of several diseases, such as renal failure (137).

The sequence method has several advantages over other techniques, as the calculations are automatic and standardised, which virtually eliminates intra- and inter-subject variability. In addition, these calculations are obtained for both increases and decreases in blood pressure. This is because the devices that determine spontaneous baroreceptor activity by this method allow sequences to be evaluated and represented, separating ascending sequences (increases in SBP and elongated IRR) from descending sequences (decreases in SBP and shortened IRR) (133), which allows the asymmetry of the baroreceptor response to be taken into account (135). Another advantage is that the results obtained, which are recorded over periods of about 10-15 minutes and with a standardised protocol, are highly reproducible

(138). In the present thesis, the sequence method is the technique that will be used for the assessment of baroreflex sensitivity before and after the resistance session.

#### 2.1.2.5. Blood pressure variability

BP is not constant and suffers spontaneous variations over time. These oscillations are referred to as blood pressure variability (BPV) and can be assessed in different ways about the time scale assumed. Thus, there is a very short-term (i.e., beat to beat changes), short-term (changes over 24 hours), medium-term (day-to-day changes) and long or very long term (visit-to-visit alterations) BPV (139–142). Likewise, it has been evidenced that BPV is an indicator of cardiovascular risk. Higher BPV is associated with cardiac, vascular and renal damage, increasing the risk of suffering a cardiovascular event (139). Moreover, compared to normotensive individuals, the hypertensive population usually exhibit increases in BPV values, becoming a critical factor in the treatment of hypertension (143).

In the context of the purpose of this thesis, the assessment of very short-term BPV, i.e., that able to estimate the neural and humoral response to blood pressure control, will be used to evaluate the acute response to resistance exercise training. For this purpose, beat-to-beat BP recording is required over a period of time. As with HRV (see above), BP oscillations can be analysed by different methods, among which the spectral method stands out. In particular, the analysis of the low-frequency SBP (LFSBP) is an indicator of the modulation of sympathetic vasomotor tone, which is closely associated with arterial stiffness (144–147). Although there is some controversy about its use, this index has been used in different fields for the assessment of sympathetic vascular tone (148–152).

### 2.1.3. Acute effects of resistance exercise on cardiovascular system

Cardiovascular responses to resistance exercise, as explained at the outset of this chapter, occur to match the rise in metabolic demand of the working muscles. In general terms, resistance exercise results in a modest increase in cardiac output, an increase in HR, little change or a decrease in stroke volume, and a large increase in BP during exercise, followed by a reduction after exercise cessation (153). These responses are influenced by many factors, ranging from the characteristics of the athlete and his or her context to the exercise characteristics. These include the different load parameters (intensity, volume, rest, etc.), the type of contraction, the posture, the velocity of execution, the muscle mass involved, the execution of the Valsalva manoeuvre, and others (28,154–163). The following is a summary of the evidence on the different responses related to these parameters.

#### 2.1.3.1. Heart rate and blood pressure response

##### *2.1.3.1.1. Heart rate and blood pressure during exercise*

The HR and BP rise at the onset of RE until the cessation of exertion (19,164–166). Increases in these two cardiovascular parameters (as well as other related variables) occur in response to different factors. The intensity (i.e., the weight lifted), directly affects cardiovascular responses, with greater impact as load increases (28,99,167–173). For example, a study by Wescott and Howes (172) showed that performing the biceps curl at a higher intensity (10RM) produced greater increases in BP responses compared to a medium and a light intensity session. Likewise, as demonstrated by Rozenek et al. (173), HR was higher when five sets of ten repetitions of bench press were performed at an intensity of 70% of 1RM compared to 50%. In this line, a later work conducted by de Sousa et al. (28) compared the SBP, diastolic blood pressure (DBP) and HR increases throughout the 20, 25, 30, 35, 40, 50, 60,

70, and 80% of 1RM or until exhaustion during the leg press exercise. Conclusions corroborated the effect of intensity in increasing HR and BP responses across loads. On the other hand, volume (i.e., the number of repetitions and sets performed) is another variable that affects cardiovascular response. Thus, as greater volume is performed, higher HR and BP values are registered (163,174). In this sense, evidence has established that the number of sets and their length determines the pressure response to a greater extent than the load intensity (154,156–158,175,176).

Another important training variable that can affect cardiovascular response is the characteristics of the exercise. In this regard, the muscle mass involved has been identified as a key factor (155,177,178). Thus, Matos-Santos et al (155) compared the cardiovascular impact of performing 4 sets of 12 repetitions at 70% of 12RM of bilateral knee extensions with unilateral knee extensions. The authors reported greater increases in SBP (35% vs 23%), diastolic BP (DBP, 36% vs 23%), HR (40% vs 26%), rate pressure product (RPP, 90% vs 53%) and cardiac output (55% vs 39%). Different responses were also observed when comparing exercises performed by lower and upper limbs (159,177), or even in different lower limb exercises (178). Machado et al. (159) compared different intensity protocols to muscular failure in leg press and bench press exercises. Although they found no differences between intensities (10RM vs. 20RM), they reported that BP was higher in the leg press in both conditions. Finally, investigating the effect of the muscle mass involved and the type of exercise collectively, Moreira et al (177) concluded that, after performing three strength exercises with different body segments (biceps curls, barbell rows, and knee extension exercises) bilaterally, unilaterally and alternatively, all designs in all exercises are safe for apparently healthy individuals although the exercises that elicited the greatest cardiovascular response were the bilateral exercises performed mainly on the upper limbs.



Another factor that can modulate the impact on the cardiovascular system is the type of contraction executed) and the velocity or cadence of the movement (158,161,162,179,180). Okamoto et al. and Huggett et al. conclude that eccentric contractions produce a lower response compared to concentric (161) or isometric contractions (179). On the other hand, the velocity of movement analysis has shown that higher speeds produce lower cardiovascular impact (158,162,180).

Finally, the posture in which the RE is performed is another variable that has demonstrated effects on cardiovascular involvement, although the evidence for this factor is scarce. Thus, a study compared the cardiac and pressor response (along with other haemodynamic variables) in three upper limb exercises in the supine position (bench press), in the upright position above the heart (seated shoulder press), and the upright position at the heart level (seated biceps curl). Exercises in the upright position resulted in greater responses compared to the supine position (160).

Set configuration, the independent variable of this thesis, is another component that can affect the cardiovascular response. Despite divergences in the literature, most studies suggest that traditional or long set configurations produce the greatest increases during exercise compared to short sets, except for inter-repetition rest protocols, which also promote a high arterial response. The literature on this topic will be developed in more detail below.

#### *2.1.3.1.2. Post-exercise hypotension*

The acute effect of RE upon cessation of exercise on BP has been repeatedly analysed by the literature over the decades. Thus, the transient reduction of BP values below those recorded prior to exercise has been reported in the literature to a considerable extent, although there are also some studies showing the absence of this effect. Several mechanisms

by which this hypotensive effect occurs have been previously suggested: baroreflex resetting, a reduction in peripheral sympathetic activity, a worsened transduction of sympathetic activity into vasoconstriction and activation of histamine receptors (181). Although this model is based on the stipulations proposed for aerobic training (which has been more investigated), RE seems to promote the same mechanisms. Therefore, RE is also a potential tool to promote short-term BP reductions, which will generate long-term adaptations (182,183).

It is important to note that the hypotensive effect of RE can be described both in terms of magnitude and duration, i.e., how much BP is reduced from pre-exercise values and for how long. Furthermore, as with most physiological responses, there is a percentage of the population that is "non-responder" to the PEH. Specifically, Forjaz et al. (184) described that only 67% of normotensives and 65% of hypertensive individuals experienced significant BP reductions after cycling exercise in their study. Authors also concluded that some individual characteristics, regardless hypertension diagnosis, may affect this response such as sex, age, maximal oxygen consumption and overweight or obesity (assessed by weight or body mass index (BMI)). Thus, normotensive women showed greater reductions compared to men, while those with lower peak oxygen consumption, overweight or obesity indices or older people (whether normotensive or hypertensive) showed smaller reductions in BP.

Reviews have been conducted for RE, summarising the acute effects on BP after resistance exercise (12,39,185,186). These works confirm this PEH effect after RE, as well as different aspects that may affect this response. In terms of intensity, several comparisons between protocols have been made (187–191) concluding that this parameter is not a modulating factor of PEH. However, it is important to highlight the findings of Figueiredo et al (192). Although they showed that their trained men experienced a hypotensive effect after exercise regardless of the intensity of the load worked, the session at 70% intensity (compared

to 60% and 80%) resulted in a longer duration of PEH (up to 60 minutes). By other authors, the BP reduction after exercise in older hypertensive subjects was also greater when a high-intensity protocol was performed compared to a moderate intensity protocol, being the characteristics of the subjects the possible reason for these differences (193). In terms of volume, i.e., the number of sets, repetitions and exercises performed, there is a great diversity of protocols in the literature. Although some studies do not find significant differences (189,194), others have found that a greater number of sets implies a higher PEH (195,196). Thus, both Figueiredo et al. and Mediano et al. claim that performing three sets versus a single set results in greater decreases in BP compared to pre-exercise values in normotensive (195) and controlled hypertensive (196) individuals. However, as Casonatto et al. (39) state in their meta-analysis, more research is needed to clearly define the effect of volume on post-exercise BP response, due to the non-significant differences found between protocols involving more or less total repetitions.

One variable that has been shown to have a significant effect on HPE is the amount of muscle mass involved in the exercise(s). Protocols with multi-joint workouts or those involving large muscle groups result in greater decreases in BP compared to those involving less muscle mass (197–199). Related to muscle mass, a study only found a hypotensive effect in sessions performed with lower limb or whole-body exercises (so larger muscle mass), compared to an upper limb protocol (198). Lastly, some studies have investigated how different types of resistance training sessions may promote greater or lesser PEH. In this sense, longer post-exercise BP reductions were observed after superset or paired set sessions in comparison with a traditional one (200) and, in older women, PEH was only reported when they completed a power-oriented session and not for a resistance training protocol (201).

The monitoring period, as well as the methodology employed for BP assessment, may also influence the significance of the PEH. Although the measurement instrument has not revealed clear significant differences, the beat-to-beat method for measuring BP changes is more accurate than non-continuous techniques. Regarding the measurement conditions, posture has been demonstrated to have a significant effect on post-exercise BP behaviour. To the assessment conditions, posture has been shown to have a significant effect on post-exercise BP behaviour (39), although discrepancies are surrounding this factor. The supine position allows a reduction in peripheral vascular resistance due to better redistribution of blood in this position compared to the seated position, which may require greater vascular compression of the lower limbs due to gravity (202). This might be the possible explanation for the greater hypotensive effect observed with supine recoveries.

#### 2.1.3.2. Cardiac autonomic modulation

Cardiac autonomic modulation is a useful marker of recovery status and can be assessed by various HRV indices (see above). Extensive research has been published on the effect of resistance exercise on HRV, summarised in some reviews (203,204), and concluded that following a RT session a withdrawal of cardiac parasympathetic modulation occurs up to approximately 30 minutes after cessation of exercise.

Similar to the cardiac and pressor responses reviewed above, different loading parameters can modulate the autonomic response. The factor that has been shown to have the greatest impact on the autonomic response (both RMSSD and HFn.u.) after exercise is the total volume of the session, i.e., the number of repetitions, sets and exercises performed (203). However, when each variable that defines the volume of an RE session was analysed independently, significantly different reductions in RMSSD were only observed for the number of sets and exercises. These data, which resulted from meta-analysing all existing studies on

HRV, show that a higher volume during a RT session results in a greater cardiac parasympathetic control loss compared to lower volumes. This has also been reported by different controlled randomised trials such as that conducted by Figueiredo et al (195). Authors showed that sessions with a higher number of sets (and therefore higher volume) led to a higher cardiac parasympathetic withdrawal. Regarding load intensity, some studies found differences between performing a session at 50% compared to one at 70% (205) or 30% vs. 80% (187). Nevertheless, other researchers reported that this factor did not produce changes in autonomic response when 40 vs. 80% (206) or between 60, 70 and 80% (192) sessions were compared. Similar conclusions to the latter have been attained by Marasingha-Arachchige et al. (203). They found only a significant effect of intensity for HFn.u.. However, as the authors pointed out, these differences may be due to the duration of the session rather than the load intensity itself, since, contrary to what was expected, an effect was only found for sessions with low intensity. In this sense, to compare protocols with equal total volume is required to conclude more appropriate assertions regarding load intensity.

Another parameter that may influence parasympathetic withdrawal after exercise is recovery time. Shorter rest periods have resulted in greater reductions in HFn.u., with standardised mean differences twice as large for protocols with inter-set rests of less than 2 minutes compared to RE sessions of 2 or more minutes (203). For instance, although both sessions resulted in reductions in parasympathetic indexes, resting for 1 minute between sets resulted in lower HFn.u. up to 20 minutes post-exercise in comparison with a 2 minute rest protocol (207). Additionally, when the rest time was auto-suggested (with a range of 128 to 155 seconds), it did not differ from the standardised structures with 1 and 2 rest periods (208). Thus, at least 2 minutes of rest is recommended when performing an RE session, so as not to delay parasympathetic recovery (203,208).

The type of exercises performed may influence autonomic modulation after exercise, albeit not extensively investigated. For example, a study by Kingsley et al. (209) compared three RT sessions consisting of upper-, lower- and whole-body exercises. The authors reported reductions for RMSSD and HFn.u. compared to baseline in the lower limb and whole-body protocols, while the upper limb sessions only reflected decreases (and smaller) for RMSSD. Nonetheless, it is important to note that the whole-body session included double the number of exercises, and this might be the main reason for these results. By contrast, another study observed similar decreases in parasympathetic indices between whole body, upper and lower limb protocols (199). On the other hand, the order of the exercises in a session composed of several RE may affect the parasympathetic response after exercise, as it has been observed that beginning the session with lower limb exercises and progress to upper limb exercises resulted in lower reductions in RMSSD and HF after exercise (210). Finally, the training method has shown no effect on cardiac autonomic recovery. A recent study shows that both hypertrophy and a maximal strength session acutely produced similar withdrawals of cardiac parasympathetic control (211). However, the literature on this factor is also scarce.

### 2.1.3.3. Cardiac baroreflex control

Multiple studies have demonstrated a reduction in baroreflex sensitivity after resistance exercise (38,187,212–214). These changes have been observed in both normotensive and hypertensive individuals (213), with lower values already at rest for the latter (215). Furthermore, when a resistance training session was compared with an anaerobic training session, the RE protocol exhibited a more pronounced BRS loss (214). To the best of our knowledge, most studies that have analysed BRS before and after an RE session conducted trials for comparison with non-exercise control situations. Only the work by Niemelä et al. (187) and those performed for the evaluation of the set configuration (described below)

provide information on the effect of different loading parameters on post-exercise baroreflex activity. Niemelä et al (187) demonstrated that a protocol with a higher loading intensity resulted in a longer reduction in BRS compared to a protocol with a lower loading intensity. From these results, it can be hypothesised that the more demanding an RE session is, the greater BRS losses will be experienced. Therefore, protocols with higher volume, shorter total rest time, greater muscle involvement or closer to muscle failure could be expected to produce a greater reduction in BRS. These speculations would be supported by the greater glycolytic involvement of these sessions, due to the relationship between neural control of the cardiovascular system and the concentration of metabolites during exercise (216,217). However, further research into the load parameters is needed to confirm these conjectures.

#### 2.1.3.4. Sympathetic vascular tone

Similar to baroreflex activity, sympathetic vascular tone activity has not been as well studied as other autonomic markers. Some studies have observed increases following a RE session (38,187,212–214). For example, a study comparing the autonomic response of men and women to RE showed that both sexes experienced an increase in  $LF_{SBP}$  values, which persisted well into recovery. In addition, the authors observed that, although both men and women experienced statistically significant increases, men enlarged their  $LF_{SBP}$  values percentage-wise more than women. Although this was not assessed in the study, it was suggested that hormonal differences between the sexes, and the consequent difference in nitric oxide bioavailability, could be the reason for these differences (212). Partially contrary to these studies, Queiroz et al. only found significant increases in hypertensive participants, while healthy individuals maintained similar  $LF_{SBP}$  values after exercise (215).

In terms of load parameters, only the study by Niemelä et. al. compared two different RE sessions and an aerobic session, observing that only increased sympathetic vasomotor tone was observed after the high-intensity RE session (187). Further research is needed to establish which factors modulate the sympathetic activity of vascular tone.

Set configuration, the independent variable of this thesis, is another component that can affect the cardiovascular and autonomic response after session. Scientific evidence suggest that traditional or long set configurations produce the greatest reductions in cardiac parasympathetic modulation and post-exercise hypotension responses after RT session. The literature on this topic will be developed in more detail in a separate section below.



## 2.2. Set configuration

Resistance training design is composed of several parameters, such as type of exercise, load, number of series and repetitions, frequency, recovery, or velocity of execution. The adjustment and control of these parameters allows generating the different effects and adaptations according to the objective to be achieved. Recently, a novel variable has begun to be studied in order to manipulate the set structure, and therefore, manage the intensity of effort (218). This variable is the set configuration, and it refers to the number of repetitions performed in each set in relation to the maximum number of feasible repetitions of such set (219).

### 2.2.1. Traditional vs cluster configurations

Traditionally, resistance training has been designed with a continuous fashion of performing repetitions during the sets with a fixed time rest between them and without any rest between repetitions. These structures, commonly referred to as traditional (TS) sets or long set configurations (LSC), are usually close to or lead to muscular failure since fatigue appears quickly during these structures as repetitions are performed. The phosphocreatine and adenosine triphosphate depletion and the concomitant increase in metabolite concentrations are the causes for the fatigue onset. In contrast to traditional structures, cluster sets (CS), or also named short set configuration (SSC), is a novel structure based on the idea of breaking the sets into small groups of repetitions with pauses between them (220). Although there are different types of cluster configurations regarding the management of set structure (basic cluster, inter-set rest redistribution, equal work-to-rest ratio, and rest-pause method) (220), the more frequent rest periods during all of them allow the maintenance of phosphocreatine stores, the adenosine triphosphate resynthesis and a higher clearance of metabolites in active muscles, resulting in enhanced recovery and, therefore, reduce fatigue

(221,222). In brief, basic cluster protocols consisted in maintain the inter-set rest duration and introducing an additionally intra-set rest or inter-repetition rest time (usually between 15 to 45 seconds). It implicated a longer training duration compared to traditional protocols. An example of this type of configuration could be a protocol of 4 sets of 10 repetitions with 2 minutes inter-set rest and an additionally 30 seconds of intra-set rest. However, a set configuration does not always imply the addition of more rest time. In order to accomplish it, inter-set rest redistribution protocols involve an equalisation and readjustment of the rest periods. In this type of configuration, the rests between sets become shorter and more frequent, allowing the total rest time to remain equal. For instance, if the previous example were modified to be an inter-set rest redistribution, one possibility could be 8 sets of 5 repetitions with 1 minute of rest between sets. Another type of cluster configuration stated in the review conducted by Tufano et al. (220) is the equal work-to-rest ratio. In this case, the traditional structure is used as a model to calculate the work-to-rest ratio and develop the new cluster designs. An example, 10 sets of 4 repetitions with 40 seconds of rest between sets in contrast with a traditional protocol of 4 sets of 10 repetitions with 2 minutes between sets. Although in practice both inter-set rest redistribution and work-to-rest ratio seem similar strategies, it is noteworthy that the latter are predominantly used in the research context, to better control the load parameters. Lastly, although the scientific literature does not include the rest-pause method as a type of group training, this method has been considered in the review by Tufano et al. (220) as it involves performing single repetitions with short rest periods between each repetition for limited sets of repetitions or sets with short rest intervals of increasing duration between each pair of repetitions, to lift a near-maximal load several times.

Due to the large possibilities of cluster structures, there are multiple acute and chronic effects of the different cluster structures. However, as previously mentioned, the set configuration allows modulating the intensity of effort. In this sense, all types of cluster configurations are characterised for a lower intensity of effort in comparison with traditional structures. Therefore, it is important to establish the differences that exist between these configurations in the short- and long-term effects.

### 2.2.2. Acute effects of set configuration

There is a lot of evidence that support the differences in acute responses regarding set configuration. For clarity, they are classified below according to the different systems involved.

#### 2.2.2.1. Mechanical performance

Mechanical performance refers to the different parameters expression of strength. Velocity, force and, consequently, power are some of the parameters that inform about mechanical performance during RT. The first study that investigated the effect of set configuration on these variables was by Haff et al. (221), which analysed the effects of three types of set configurations (cluster, traditional and undulating) on bar kinematics during power clean exercise. Thereafter, several investigations have aimed to analyse the effect of different set configurations on these variables. Moreover, some works have also studied different protocols without using the term set configuration. One example is the study by Sanchez-Medina & Gonzalez-Badillo (223), who examined the velocity loss in the different bench press and squat protocols using the ratio between the fastest and lowest repetition. They concluded that velocity loss can be used as an indicator of neuromuscular fatigue and that it can be modulated by set configuration.

Two recent meta-analyses by Latella et al. (224) and Jukic et al. (225) have reviewed the acute neuromuscular effect of CS versus TS. Both works summarised that CS positively affects mechanical performance during RT compared to TS, being in most parameters higher for cluster structures with additional rest time compared to rest redistribution protocols. Specifically, CS allow for higher absolute velocity, power, and peak force during RT. Moreover, as suggested by these authors (224,225), several factors may affect the differences between configurations such as the exercise performed, the intensity and volume managed, whether protocols achieved the muscle failure, among others. Furthermore, according to the different mechanical parameters analysed and their evolution throughout the repetitions, the management of the set configuration can lead to different results.

Thus, a study by Tufano et al. (226) investigated the effect of three different set configurations with the 60% of 1RM on back squat performance. For the traditional session, they proposed 3 sets of 12 repetitions with 120 seconds of rest between sets, and for the cluster sessions, they provided two structures: grouping the repetitions in sets of 4 or 2 repetitions (i.e., 3 sets of 3 groups of 4 repetitions and 3 sets of 6 groups of 2 repetitions, respectively) and adding 30 seconds of intra-set rest. These authors concluded that introducing 30 seconds of rest between every two repetitions allowed the maintenance of velocity and power. In line with these results, other recent research on full squat exercise compared 6 types of configurations equated by total volume (30 repetitions), intersets rest (5 minutes) and load (10 RM)(227). Specifically, they conducted two traditional sessions (i.e., no rest between repetitions) with two different levels of effort (3 sets of 10 repetitions and 6 sets of 5 repetitions), another 3 cluster sessions with a 3x 10 repetition structure with 10-, 15- and 30-seconds rest between repetitions and a final one consisting of performing all 30 repetitions within a single set with 15 seconds rest between repetitions. In this case, the 15 and 30 seconds of inter-repetition rest set configurations were the best at maintaining velocity losses.

Similar work was conducted by Garcia-Ramos et al. (228) with the bench press exercise. The authors compared the velocity losses when 30 repetitions with the 10RM load were performed with 5-minute rests between sets with five different structures: two with traditional structures (i.e., 3x10 and 6x5), and the other three with an inter-repetition rest design with 5-, 10- and 15- seconds of rest between repetitions. They reported that the 6x5 structure and the inter-repetition rest configuration with 10- and 15-seconds rest between repetitions are the most effective in maintaining high mechanical outputs. Other studies on the kinematics of bench press investigated how grouping the repetitions in single, double or triple sets with their respective 20, 50 and 100 seconds of repetition between sets, did not produce differences in power output between sessions but did when compared to a continuous structure (in this case, the 6RM test) (229).

When the effect of the set configuration was analysed in different intensity protocols, the different studies have reported that regardless of the intensity of the session, cluster configurations produce lower power (230) and velocity (231) losses compared to traditional configurations. At the same time, the cluster configuration allows maintaining the power throughout more repetitions, being able to work for more time at optimal power (230). Moreover, Mora-Custodio et al. (231), compared a continuous design with two protocols with 10- and 20-second rests between repetitions, reported no differences between the inter-repetition structures. Hence, the authors recommended the protocol with 10-second inter-repetition rest, as it requires less total training time, since it implicates less rest time, and is, therefore, more efficient.

However, as previously commented, a shorter set configuration does not always imply the addition of more rest time. In this regard, several studies have reported that when comparing structures with equal work-to-rest ratio, continuous or longer protocols involve

lower mean velocity and produce higher velocity losses and/or lower velocity maintenance throughout the session (232–234). In particular, the study by Rial-Vázquez et al (234) investigated two protocols with the same intensity (10RM), volume (32 repetitions) and total rest time (15 minutes) but with different set configurations for the bench press and parallel squat. The protocols were 4 sets of 8 repetitions with 5 minutes rest between sets and 16 sets of 2 repetitions with 1 minute recovery. The authors reported lower velocity losses in the shorter configuration for both exercises, although they noted that the differences in velocity loss were not the same for BP (39% and 13% for TT and CT, respectively) and SQ (15% and 5% in TT and CT, respectively). Lastly, must be noted the work conducted by Torrejón et al. (235). They did not report significant differences in the percentage of velocity loss between their three protocols (traditional, cluster and inter-repetition set configuration sessions) although the repetition-to-repetition session tended to exhibit higher velocities during some repetitions compared to the other ones. The authors suggested the use of longer rest (beyond the 15 seconds of their study) to maintain the velocity during exercise execution. In addition, this work stands out for being the first to analyse the differences between men and women, showing similar values for velocity losses in both sexes.

#### 2.2.2.2. Metabolic response

During RE, different metabolic processes occur that lead to a depletion of phosphocreatine and adenosine triphosphate reserves, as well as increases in the accumulation of metabolites (such as lactate, ammonia, or uric acid) (29,236). This process results in a performance drop, and due to the inverse relationship between them, the assessment of these markers can be used to determine the level of fatigue produced by exercise (223) or the training status of an athlete (237).

For this matter, the set configuration can modulate the metabolic responses. During traditional set configurations, the phosphocreatine concentration in the muscle is drastically reduced whereas shorter sets maintained it due to the additional rest periods. In addition, exercising with a continuous design lead to a higher glycolytic involvement compared to short sets, in which no or only slight metabolites concentration increases are observed (223,236).

In this sense, blood lactate concentration is one of the most studied metabolites in resistance training and several studies have compared its response after different set configuration protocols. Goto et al. (238) compared the acute lactate response of two whole-body RT sessions performing 3-5 sets of 10 repetitions at 10RM load with one minute rest between sets. One session was completed under a continuous regimen throughout the sets, while the other session included 30 seconds of recovery between the fifth and sixth repetition of each set. Authors reported lower lactate production in the intra-set rest regimen. Similar results were described by Denton & Cronin (239), who observed that completing the protocol with a continuous pattern promoted a greater lactate response and a slower recovery to baseline values than with an intra-set rest design.

Furthermore, as established by Jukic et al. (225) in their review, despite all cluster types promoting lower lactatemia than continuous protocols, the differences in post-exercise lactate response are greater when comparing basic cluster protocols (i.e. rest between repetitions or set of repetitions is included) (227,228,231,240) than when comparing protocols in which the rest time is redistributed (232,234,241–243). This is because phosphocreatine and adenosine triphosphate stores are replenished to a greater extent due to the additional rest time (222). Finally, when different cluster configurations with equal loads, number of repetitions and total rest duration were tested for lactate production during exercise and recovery, no differences were observed between them (244). All this suggests that cluster configurations allow for

reduced glycolytic involvement compared to a traditional session regardless of how rest periods are distributed within the protocol but being lower when rest times are incorporated within the sets.

### 2.2.2.3. Hormonal response

Resistance exercise produces an acute hormonal response, which appears to be critical for growth and tissue remodelling (245). Previous studies suggest that the magnitude of the hormonal response is partly conditioned by metabolic involvement during exercise (246). Thus, Goto et. al., who reported higher concentrations of lactate in the continuous design, observed that it caused greater elevations of growth hormone and norepinephrine concentrations compared to the protocol with 30 seconds of rest in the middle of the set. However, they found no differences in testosterone concentrations. Contrary to them, other studies found no differences in growth hormone concentrations between protocols (240,242). Besides, Girman et al. (240) also described no difference between performing repetitions continuously or in doubles with 15 seconds of rest between pairs for cortisol, whereas Oliver et al. (242) did find lower post-exercise cortisol values after their cluster protocol. As well, these authors did not observed differences for testosterone hormone. The disagreements between studies may be due to variations in total rest, as when cluster protocols are equated for work and total rest, they produce similar hormone increases, in their case in concentrations of the growth hormone, total testosterone and sex hormone-binding globulin (244).

A recent study conducted in resistance trained women revealed that a rest redistribution protocol did not modify the hormonal response compared to a traditional protocol (247). Lastly, Pareja-Blanco et al. (248) compared the post-exercise hormonal response (i.e., cortisol, testosterone, growth hormone, insulin-like growth factor and prolactin) of 10 sessions composed of 3 sets of bench press and 3 sets of squat exercises differentiated in



the intensity of the load and the intensity of the effort. That is, the participants lifted the load corresponding to their 70, 75, 80, 85 and 90% of their 1RM, with effort intensities of 50% and 100% (to muscular failure). They reported only differences in certain hormonal concentrations for RE sessions performed to failure.

#### 2.2.2.4. Perceive exertion response

Rating of perceived exertion (RPE) are scales used to subjectively measure the intensity of exertion and consequently the fatigue that an exercise produces in an individual (249). In resistance exercise, the OMNI-RES scale is commonly used, which categorises the perception of effort between a numerical response range between 0 and 10 (250). Myriad research has studied the effects of different load parameters on RPE, and in this sense, it has been observed that the configuration of the series can modulate this response. Thus, short set configurations or clusters would produce a lower RPE compared to long or traditional configurations. To illustrate, Hardee et al. (251) compared three power clean protocols of three sets of six repetitions and found that performing with 40-second rest between repetitions produced the lowest RPE responses compared to resting for 20 seconds or performing continuously. In addition, some works of Mayo et al. analysed different types of configurations for the bench press, parallel squat, and leg press exercises. These authors concluded that the RPE is higher for the traditional sessions and that it is higher for the parallel squat than for the bench press (252). For the leg press exercise, they observed lower values of perceived exertion in the inter-repetition rest design compared to the cluster (sets of 4 repetitions) and traditional (sets of 8 repetitions) designs, all presenting the same work-rest ratio (253). Similar results have been reported by other studies with different types of squat (227,254,255), free weight bench press (243) or upper body RT session (256), except those of Vasconcelos et al. These authors suggest that strength training experience may affect the perception of exertion, as trained men who

completed their experimental sample showed no differences between a cluster and a traditional session. Lastly, when different cluster structures are compared between them, no differences were observed for RPE responses.

#### 2.2.2.5. Other parameters

As Sánchez-Medina and González-Badillo (223) demonstrated, velocity loss can be used as an indicator of neuromuscular fatigue. However, other parameters can be used to examine the fatigue: the loss of jump performance (i.e., reductions in height or distance executed), the velocity loss against fixed load, the reductions in maximal voluntary isometric contraction or the changes in the force-velocity (231,235,257).

Some investigations reported for CS structures reduce the height losses in the CMJ after session (231,241), better maintenance of jump performance (240), or even only differences in CMJ height for the traditional sessions (258). Likewise, Mora-Custodio et al. (231) also revealed higher loss of velocity against the load that elicits a velocity of 1 m·s<sup>-1</sup> before protocols for continuous design at 60% of 1RM. A recent study comparing different protocols at failure and without failure (at 50% of intensity of effort) agrees that the losses in both CMJ height and velocity at a fixed load are greater when long set configurations are performed (i.e., to muscle failure), especially in the protocols with higher volumes (8-12 repetitions per set) (248). Furthermore, in the protocols performed up to failure, both parameters of fatigue were not fully restored until 48 hours after the session. In line with these results, a study by Iglesias-Soler et al. (232) reported that only the muscle failure session (3 repetitive sets of high maximal power with 4RM load and 3 min rest between sets) produced changes in mean propulsive velocity with the load corresponding to the mean maximal propulsive power after protocol. Also, these authors noted that the Not Failure protocol (a work-to-rest ratio structure which repetitions were performed individually) resulted in a higher maximum

isometric force when it was expressed as a percentage of data before training (Failure session:  $94.75 \pm 5.62$  % vs. Not Failure session:  $99.14 \pm 3.99$  %). Regarding isometric evaluation, the study of Río-Rodríguez et al. (257), after two isometric knee extension sessions (traditional vs. intra-set rest configurations) results demonstrated a superior loss of maximal voluntary contraction after traditional sets.

On the other hand, the technique is a very important aspect of resistance training and can be greatly affected by fatigue. Several studies have investigated how set configuration can alter kinematics (221,259,260). They reported that introducing between 20 and 40 seconds of rest between single and double reps allows for reduced horizontal bar displacement and/or increased vertical displacement and momentum compared to traditional sessions and, therefore, less detriment to technique in exercises such as the clean pull, power clean or deadlift.

Furthermore, it has also been demonstrated that due to the lower accumulation of fatigue during exercise, cluster configurations allow increasing the total volume that can be performed during a session (219,232,239,261). On this matter, Denton & Cronin (239) found that a cluster session permitted to increase the number of repetitions to be completed in each set compared to the continuous session, where not even all the participants managed to perform the number of repetitions prescribed. Similarly, some work by Iglesias-Soler et al. (219,261) has also reported that when training to muscular failure, an inter-repetition rest structure enables increasing the total volume compared to a traditional design in both upper and lower limb exercises and can even increase the number of repetitions fivefold in the parallel squat.

Finally, although less well researched, the effects on muscle protein synthesis induced by strength exercise have also been investigated concerning set configuration. A recent study showed that there was no difference between protocols 5 hours after exercise, albeit a significant trend was observed in the early phases for a traditional squat exercise session compared to a cluster session with redistributed rest time. So the authors concluded that cluster structures are a useful strategy for preserving power production (as reported in previous sections) while maintaining protein stimulation levels comparable to the traditional designs (254).

#### 2.2.2.6. Cardiovascular and autonomic response

As previously commented, RE produces some cardiovascular adjustments, orchestrated - among others- by the autonomic nervous system, in order to perform the exercises. The cardiovascular involvement during exercise and the cardiovascular and autonomic response after exercise cessation can be modulated by the set configuration.

The effect of set configuration during exercise has been studied by different researchers so far, reporting different results. To a large extent, the possible discrepancies between them are largely due to methodological issues, such as the design of the protocols (i.e., the loading parameters set, the equating of variables, the type of execution performed, etc.), the methodology used for the assessment of cardiovascular parameters or the evaluation conditions.

To the best of our knowledge, the first studies that analysed different set structures during RE were conducted in 2003. The most relevant one was published by Baum et al (262), who analysed the response of HR, BP and RPP during two leg press protocols. Both protocols consisted of performing 12 repetitions at 50% of 1RM, 10 repetitions at 70% of 1RM and 8

repetitions at 80% of 1RM, respectively, with 2.5 minutes between intensities and a cadence of 1.5 s for both the concentric and eccentric phases. While one protocol consisted of performing the repetitions in a continuous mode, the other was performed intermittently, incorporating 3 s of rest between each repetition. Thus, the authors observed that the intermittent session produced a lower cardiovascular response (i.e., HR, BP and RPP) in comparison to the continuous structure, with no effect of age. At the same time, two studies were published investigating different discontinuous versus continuous structures. Thus, Coelho et al (201) observed that performing a session composed of six RE in a continuous fashion elicited a higher HR response than a discontinuous session composed of 2 sets of 6 repetitions with 15 seconds rest. On the other hand, the study conducted in older women by Veloso et al (263), showed that performing 2 sets of 12 repetitions (continuous sets) produced greater cardiovascular stress than 4 sets of 6 repetitions (intermittent sets).

Divergent results were described by da Silva et al. (264). Their continuous design produced similar SBP but lower HR and RPP values compared to two discontinuous structures: one with 5 s and one with 15 s rest in the middle of the sets. Quite contrary to the results of preceding research, some studies reported that the inclusion of 2 seconds in the unilateral knee extension exercise (265) or 5 to 10 seconds in the bilateral version of the same exercise (266) produced a higher arterial response than performing it continuously, with HR being equal or lower when resting for 10 seconds between sets of repetitions. It is important to note that the above studies all include designs where rest time is not equalised between protocols. In this sense, discontinuous protocols also showed longer total rest times with the inclusion of the respective intra-set rests. This does not allow to isolate the strategy of set structure as an independent variable, being the results affected by other variables such as, for example, resting time.

Thus, more recent articles have been conducted with the different loading parameters matched. Studies have been carried out on healthy people (257,267–269), as well as on people with pathologies (270,271). Both Iglesias-Soler et al. (267), with high-intensity squat exercise, and Río-Rodríguez et al. (257) and Paulo et al. (269), with their respectively isometric and dynamic leg extension exercises, have demonstrated that short set configurations were less cardiovascular demanding than longer structures in healthy participants. Specifically, the study by Iglesias-Soler et al. (267) revealed that two equated high-intensity protocols differing in the set configuration (i.e., traditional set reaching muscular failure session vs. inter-repetition rest session) achieved differences regarding overall SBP, as only the traditional protocol increased the BP values across the sets and RPP. However, no overall differences were detected compared to the repetition-to-repetition sets for HR response, even though the session to failure resulted in greater increases in HR from the second set onwards. In line with the findings by Massaferri et al and Polito et al, Mayo et al (268) stated that performing repetition-to-repetition leg presses with 18.5 seconds of rest resulted in a greater peak blood pressure response compared to a continuous design with the same work-to-rest ratio and performing 5 sets of 8 repetitions with 3 minutes of rest between repetitions. This is in line with the findings of Paulo et al. (269). Authors reported that even though protocols with an intensity of effort of 75% produced the highest peak of SBP and DBP changes during exercise compared to protocols with shorter structures (25% and 5%), performing the exercise repetition by repetition (5% intensity of effort) resulted in a higher pressor response than the 25% protocol.

Lastly, two recent researchs analysed the HR response to different set configuration structures. One study showed that the maximal HR was lower in the short set configuration compared to a traditional one when a deep back squat is performed, but with a higher mean HR response throughout the session (272). The other study (256), comparing different set structures (traditional training, 4 x 6 repetitions with 120 s of rest between sets, 4 x 2+2+2

repetitions with 15 s of intra-rep rest and 80 s between sets, and 1 x 24 repetitions with 15 s of inter-set recovery), showed that when a session is composed of several exercises, both peak and average HR values are similar for all protocols.

On the other hand, the effect of set configuration on the cardiovascular and autonomic response after an RE session has been focused on the analysis of single exercise sessions. Only one study did not report differences in HRV measurement after two protocols with different set structures (267). Contrary, several works demonstrated that long set configurations elicited higher reductions of cardiac parasympathetic modulation in comparison with a short structure or an inter-repetition rest set. Mayo et al (233) investigated how three set configurations reduced parasympathetic activity to a greater or lesser extent, concluding that sessions with more than one repetition per set (i.e., 4 or 8 repetitions) produced a loss of cardiac parasympathetic control while performing the leg press exercise repetition by repetition produced no significant changes. Likewise, in other work, Mayo et al. (273) demonstrated that a failure protocol resulted in a greater loss of cardiac vagal control compared to an inter-repetition protocol. The authors also determined that the type of exercise performed (in their case, squat, or bench press exercise) can be affected by the set configuration. Lastly, the recent study by Kassiano et al. (274) showed similar results after comparing four squat sessions (one traditional session to muscle failure, one traditional session without reaching muscle failure, one repetition-to-repetition session with a 10-second rest and one session with the rest-pause method). Except for the session with rest between repetitions, all experimental conditions decreased parasympathetic tone up to 30 minutes after the end of the session, with the protocols that reached muscle failure reducing it most drastically, and the rest-pause method promoting the greatest losses.

Therefore, attending the preceding evidence, cluster or short set configurations may be an alternative to reduce the cardiac and vascular stress during exercise and mitigate the reduction of cardiac autonomic control, maintaining the other benefits of RE.

In summary, the cluster configuration can modulate acute mechanical, metabolic, hormonal, perceptual and cardiovascular responses, making cluster or short set configurations less fatiguing compared to traditional or longer ones. In this sense, higher velocities, as well as better maintenance and lower losses of velocity are reported for cluster configurations, with consequent lower glycolytic involvement. In addition, a lower perceived exertion and the cardiovascular response has been reported for these structures, except for the inter-repetition rest protocols, which promote a greater arterial response. Finally, shorter protocols produce a similar hormonal response than traditional regimens.



### 2.3. Background resume

Resistance exercise improves muscle strength and endurance, physical function, and quality of life (275). These improvements are associated with a reduction in all-cause mortality and cardiovascular disease incidence (8). Several investigations have studied the acute effect of RE on the cardiovascular system and its control both during and immediately after exercise cessation. Cardiovascular response through exercise is characterised by a sharp rise of SBP (19), potentially increasing the risk of an acute cardiovascular event (e.g. rupture of an aneurysm), especially in people with systemic hypertension or at an older age (17). In addition, whilst the acute effects of RE on some outcomes remain unclear, the review by Kingsley and Figueroa (204) summarised that RE induces parasympathetic withdrawal after exercise, also leading to an increased risk of a cardiac event (such as cardiac arrest or sudden death) in apparently healthy individuals (14) and especially in people at elevated cardiac risk (15–18), due to these reductions in cardiac autonomic modulation (20). Notwithstanding these risks, the health benefits of regular RE outweigh the hazards (13). Even so, it is necessary to develop effective strategies to diminish the cardiovascular demands during this type of exercise.

Cardiovascular response during and after resistance training can be modulated by several load parameters. In this sense, set configuration, is an alternative approach to reduce the cardiovascular demand during exercise (201,257,262–264,267–271) and minimising the cardiac parasympathetic withdrawal (233,267,273,274). Nevertheless, the cluster structure to be managed to reduce exacerbated BP rises is not yet well defined and studies that analyse the set configuration on cardiac autonomic modulation have used a single exercise model, inaccurately reflecting a conventional and suitable RT session composed of multiple upper- and lower-body RT exercises (276).

Therefore, this thesis is going to investigate the acute cardiovascular -both during and after the session-, metabolic and mechanical response of two moderate-intensity whole-body RT protocols composed by several whole-body exercises and involving all the major muscle groups and that differed in the set configuration.

# HYPOTHESIS AND PURPOSES

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### 3.1. Hypothesis

- A short set configuration below 50% intensity of effort, potentially associated with the lowest portion of the v-shape pressure response, can benefit from this advantage, and provides lower BP responses during a single moderate-intensity RE (knee extension) compared to long set configurations with an intensity of effort above 50%.
- A short set configuration below 50% intensity of effort promotes a lower chronotropic response and less myocardial work, estimated by rate pressure product, during a single moderate-intensity RE (knee extension) in comparison with a long structure with an intensity of effort above 50%.
- After a whole-body moderate-intensity RT session composed by several exercises, a short set configuration protocol under 50% of intensity of effort attenuates the reduction in cardiac parasympathetic activity after session, evaluated by heart rate variability and baroreflex sensitivity, in comparison with a long set configuration over 50% of intensity of effort.
- After a whole-body moderate-intensity RT session composed by several exercises, a long set configuration protocol over 50% of intensity of effort promotes a greater reduction on post-exercise BP compared to shorter sets under 50% of intensity of effort.
- Regardless of the set configuration, after a whole-body moderate-intensity RT session composed by several exercises, there are no changes in sympathetic vasomotor modulation, evaluated by spectral analysis of BPV.

- A whole-body RT session composed by several exercises with a short set protocol with an intensity of effort under 50% reduces the glycolytic involvement in comparison with a longer set configuration with an intensity of effort over 50%, due to lower lactate production resulting from more frequent recovery periods in the session with the short set protocol.
- Long set configuration protocol with an intensity of effort above 50% produces greater velocity loss moderate-intensity RE for both upper (bench press) and lower (knee extension and parallel squat) body exercises in comparison with a short set configuration below 50% intensity of effort.

## 3.2. Purposes

### 3.2.1. Main purposes

- To compare the hemodynamic responses during two single moderate-intensity RE protocols (knee extension) differing in the set configuration.
- To assess the effect of set configuration on cardiac parasympathetic activity (i.e., heart rate variability and baroreflex sensitivity) after a whole-body moderate-intensity RT session composed by several exercises and, therefore, to identify the protocol with the least impact.
- To evaluate the post-exercise BP response and sympathetic vasomotor modulation (i.e., blood pressure variability) after two whole-body moderate-intensity RT session composed by several exercises differing in set configuration.

### 3.2.2. Secondary purposes

- To examine the blood lactate concentration to contrast the glycolytic involvement of two after a whole-body moderate-intensity RT session differing in set configuration.
- To analyse and examine the effect of two RE protocols differed in set configuration on mechanical performance (i.e., mean propulsive velocity, velocity maintenance and velocity loss).





## METHODS

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## 4.1. Participants

Thirty-three healthy (24 men, 9 women), moderately trained sport science students (age= $23.03 \pm 2.05$  yr.; height= $1.73 \pm 0.08$  m; body mass= $70.58 \pm 9.67$  kg; body mass index (BMI) =  $23.50 \pm 2.10$  kg·m<sup>-2</sup>) were recruited to participate in this cross-sectional study. No participants presented any medical contraindications for lifting weights, had not a prior history of cardiovascular disease and were not using any controlled medications. All participants signed an informed consent form to participate in this study, which was approved by the local Institutional Ethics Committee (University of Coruña ethics committee: CE 01/2016), in accordance with the Declaration of Helsinki.

Of all participants, data of 32 (23 men, 9 women; age =  $23.06 \pm 2.08$  yr.; height =  $1.73 \pm 0.08$  m; body mass =  $70.04 \pm 9.30$  kg; BMI =  $23.38 \pm 2.01$  kg·m<sup>-2</sup>) were treated for the acute effect analysis, while data from 24 participants (18 men, 6 women; age= $23.21 \pm 2.13$  yr.; height= $1.72 \pm 0.07$  m; body mass= $69.33 \pm 8.20$  kg.; BMI=  $23.26 \pm 1.74$  kg·m<sup>-2</sup>) were utilized for the during exercise analysis. The participant characteristics are described in Table 4 and Table 5 in the RESULTS section.

## 4.2. Study design

Participants visited the laboratory a total of six times separated at least by 72 h. The first and second sessions were conducted to familiarise them with the exercises. In the third session, 15-repetition maximum load (15RM) was determined for all the exercises. After assigning the participants into different experimental sequences, following a randomised block design to warrant an equated regarding the sex distribution, the final three sessions consisted

of two experimental (LSC and SSC) and one control protocol. Participants were assessed before and after each session for cardiovascular and metabolic variables. Additionally, cardiovascular, and mechanical performance was collected during three exercises: knee extension (KE), bench press (BPR) and parallel squat (SQ). A schematic representation of the study is presented in Figure 1.

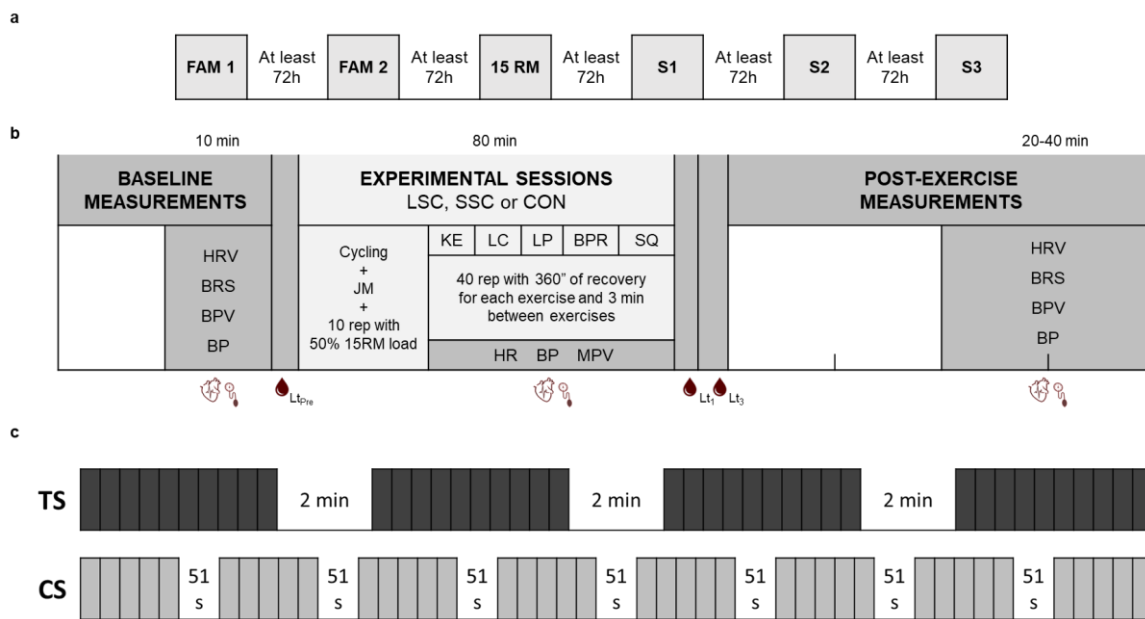


Figure 1. (a) Schematic representation of the study. FAM: familiarisation session; S: experimental session. (b) Graphical simplification assessment. Cardiovascular measurements during exercise were conducted for knee extension, whereas mechanical parameters were registered for knee extension, bench press and parallel squat. (c) Representation of the experimental sessions. All sessions consisted of 40 repetitions and 360 s of total rest with the 15RM load for each exercise and with 3 min between exercises. LSC: 4 sets of 10 repetitions with 2 min of rest between sets. SSC: 8 sets of 5 repetitions with 51 s of rest between sets. FAM: familiarisation; LSC: long set configuration session; SSC: short set configuration session; CON: control session; HR: heart rate; HRV: heart rate variability; BRS: baroreflex sensitivity; BPV: blood pressure variability; BP: blood pressure; Lt: Capillary blood lactate concentration; MPV: mean propulsive velocity; JM: joint mobilisation; KE: knee extension; LC: leg curl; LP: lateral pull-down; BPR: bench press; SQ: parallel squat

The sessions were composed of five resistance exercises performed in the same order: KE, leg curl (LC), lateral pull-down (LP), BPR and SQ. Participants were encouraged to produce the maximal intended velocity during the concentric phase of the exercises and the eccentric phase was performed in a controlled manner. The full range of motion for each repetition of

each exercise was required and was objectively determined by the investigator for all exercises, except for SQ, in which an external device was used.

The KE exercise was performed in a KE machine (Technogym, Gambettola, Italy) where participants were fixed to it by a strap positioned at the hip level. Leg position and ankle angle were standardised for all sessions. Since cardiovascular measurements were performed during the KE exercise, participants were positioned as follows: the right arm - on which the continuous BP assessment device was placed- was supported on an armrest to raise it to the level of the fourth intercostal space. The left arm - on which the oscillometric BP assessment device was placed- rested on the thigh. Gripping the machine was forbidden. Participants were instructed to avoid hip flexion, to produce the maximal intended velocity during the concentric phase of the exercise, to control the eccentric phase, and to complete the full range of motion for each repetition ( $80^\circ$ , i.e., from  $90^\circ$  to  $10^\circ$  of knee flexion;  $0^\circ$  knees fully extended).



*Figure 12. Knee extension exercise*

For the LC, participants were placed in a prone position on the machine (Biotech Fitness Solutions, Brazil) with both shinbones parallel to the floor and hands gripping the handles. The position of the legs was standardised for all sessions. The movement started with the heels in contact with the padding placed on the lever and participants were instructed to flex their knees until the padding touched the buttocks to complete the full range of motion. The concentric phase was performed in an explosive manner, while the eccentric phase was performed in a controlled manner.



*Figure 13. Leg curl exercise*

LP was performed on a seated LP machine (Biotech Fitness Solutions, Brazil). The bar grip and seat height were standardised for all participants. The movement started with the arms extended, performing the concentric phase as fast as possible. The bar should be directed diagonally towards the chest, and once it touched it, the controlled eccentric phase was performed.

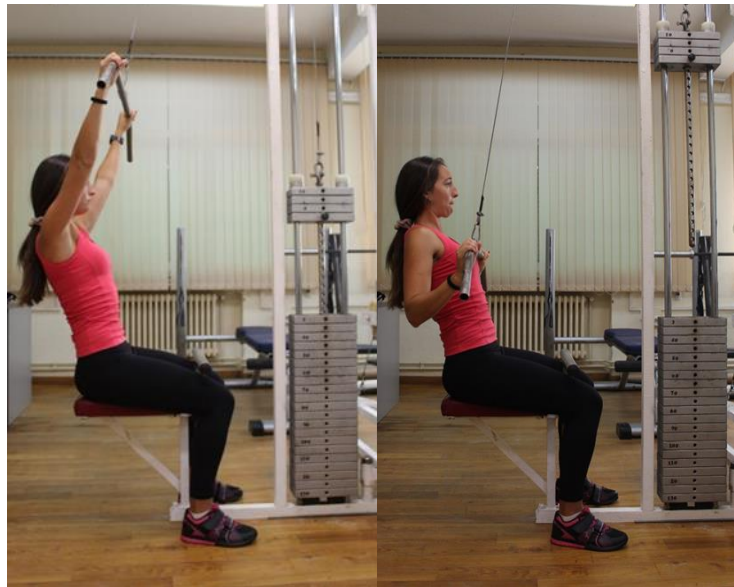


Figure 14. Lat pull down exercise

Regarding BP, it was performed on a Smith machine (Telju Fitness, Toledo, Spain) with the participants lying on a flat bench. The exercise was performed in an eccentric-concentric fashion. Participants started with their elbows fully extended, performed the eccentric phase in a controlled manner and once the bar touched the chest, the concentric phase was performed as fast as possible. To avoid bouncing the barbell on the chest, participants were instructed to wait 1 second between the eccentric and concentric phases.



Figure 15. Bench press exercise



Lastly, for the SQ, the participants used the Smith machine (Telju Fitness, Toledo, Spain), choosing the bar grip width and leg position themselves, which were standardised. The exercise started in a standing position with the barbell over the shoulders and they performed the controlled eccentric phase until the upper thighs were parallel to the floor. Then, they performed the concentric phase as fast as possible to the standing position maintaining contact with the ground. To control the range of motion, an adjustable bench was placed at the height necessary to achieve a parallel squat. Participants were instructed to perform the repetitions in a continuous manner (i.e., without pauses between phases).



*Figure 16. Parallel squat exercise*



### 4.2.1. Familiarisation sessions

In the familiarisation sessions, the participants were instructed on how to perform each exercise. In this regard, the individual position references for each exercise were registered to standardise the execution conditions across the study. The first session started with a 5 min warm-up in a cycle ergometer at 60-80 revolutions per min (Monark 828E; Monark Exercise AB, Vansbro, Sweden) as well as joint mobilisation, followed by 2 sets of 15 repetitions with approximately 50% of perceived maximum load and 2 min of recovery between sets and exercises. In the second session, participants were instructed to perform the same warm-up, joint mobilisation and 2 sets at 75% of perceived maximum load. In the last set of each exercise, participants were encouraged to perform the maximal number of repetitions, to get more experience reaching muscular failure.

Additionally, height was measured by a stadiometer (Seca 202; Seca Ltd., Hamburg, Germany) and body mass measured with a bioelectric impedance scale (Omron BF-508, Omron Healthcare Co., Kyoto, Japan). BMI was calculated as body mass in kilograms divided by height in meters squared ( $\text{kg} \cdot \text{m}^{-2}$ ).

### 4.2.2. 15RM test

In the third session, the 15RM test was conducted to assess the maximum load that each participant could lift no more than 15 times for each exercise. The session started with the general warm-up previously described, followed by 10 repetitions of each exercise performed with the 50% of load from the last set of the second familiarisation session. Then, after 5 min of rest, participants performed a set with approximately 110% of load from the last set of the second familiarisation session. If participants performed 16 repetitions, the load was increased, whereas if they could not complete 15 repetitions, the load was reduced. The first

load which they performed no more than 15 repetitions was considered the 15RM. The test comprised a maximal of 2 attempts interspersed with at least 5 min of rest. Participants were instructed to perform the concentric portion of each repetition as fast and explosive as possible. Muscle failure was defined when the participants could not complete the full range of movement of the exercise, or the load could not be moved. The order of evaluation of the exercises was the one previously described.

### 4.2.3. Experimental sessions

Each participant completed the two experimental sessions and one control session (CON) in a random order. In all the sessions, the participants were instructed to refrain from exercise, alcohol, and caffeine for 24 h prior to the testing sessions and keep hydration and feeding habits stable. Participants were 3 h postprandial upon arrival to the laboratory. Sessions were separated by at least 72 h and were performed at the same time of the day ( $\pm 1.5$  h) and a temperature and humidity-controlled room (23°C and 50% respectively). Both experimental sessions consisted of performing a total of 200 repetitions (40 per exercise) with the 15RM load and with a total rest of 42 min (360 s between sets for each exercise and 3 min between exercises) and differed in the set configuration. LSC consisted of 4 sets of 10 repetitions (an intensity of effort of 66%, 10/15RM) with 2 min of rest between sets and 3 min between exercises. SSC consisted of 8 sets of 5 repetitions (an intensity of effort of 33%, 5/15RM) with 51 sec of rest between sets and 3 min between exercises. After a baseline assessment and prior to experimental protocols, the general warm-up previously described was performed and, in addition, a specific warm-up consisting of 10 repetitions with 50% of 15RM was carried out before each exercise. In the CON, after and before the measurements, the participants remained in the laboratory for 80 min refrain from physical activity.

## 4.3. Procedures

### 4.3.1. Cardiovascular recording

Cardiovascular parameters were registered using the Task Force® Monitor (TFM, CNSystems, Graz, Austria). A three-lead electrocardiogram obtained continuous heart rate with a sampling frequency of 1,000 Hz. Beat-by-beat monitoring of SBP, DBP, and mean arterial pressure (MAP) was obtained by photoplethysmography. The finger cuffs were placed on the proximal phalange of the index and the middle fingers of the right hand, sited on the fourth intercostal space. Additionally, an oscillometric device transformed automatically and continuously absolute values of the finger pressure into the values of the brachial artery. The oscillometric device consisted of an arm cuff tightly attached to the left arm with the compressed air outlet on the brachial artery and the lower edge of the cuff approximately 2.5 cm from the elbow crease (Figure 17). The validity and verification of this device have been previously reported (277).

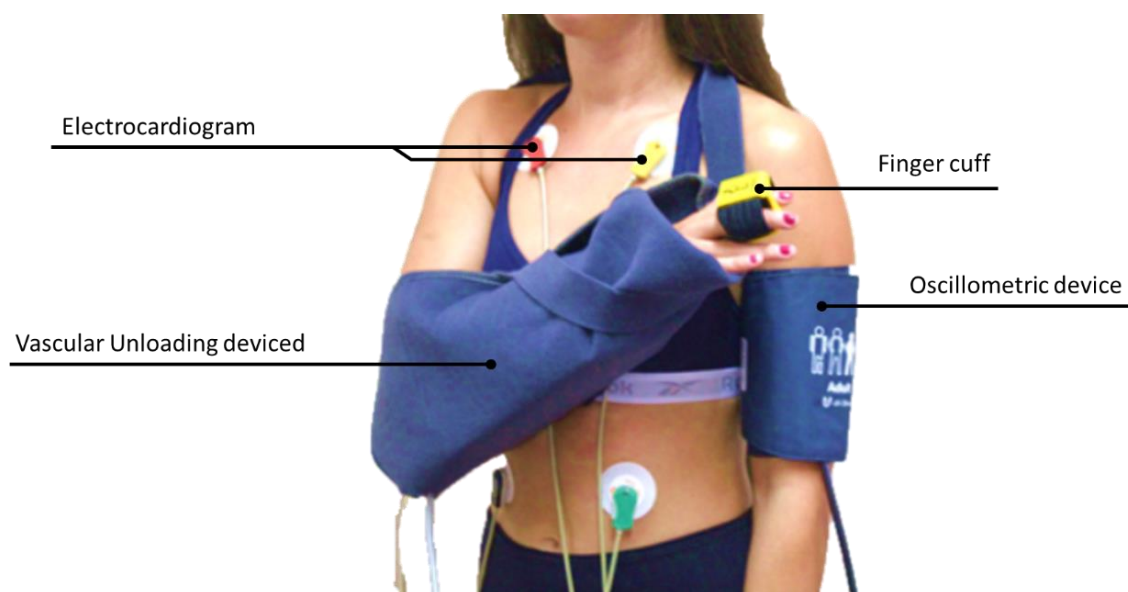


Figure 17. Cardiovascular equipment

Cardiovascular data were obtained 10 min before each session (baseline), during KE exercise and in the period 20 to 40 min after the end of the protocols. During baseline measurements, participants were lying for 20 minutes in the supine position on a stretcher in a quiet room, breathing with a respiratory rate of 0.2 Hz (12 breaths per min) (Figure 18). The respiratory control was carried out using the metronome provided by Paced Breathing 2.1 application for Android (Trex LLC, Canada).



*Figure 18. Cardiovascular assessment at rest*

Subsequently, after warming up, they were moved to the KE machine and were fixed to it by the belt positioned at the hip level (Figure 12). Cardiovascular measurements were recorded from the first to last repetition of the KE exercise. Several precautions were adopted to avoid data losses. As referred to above, the arm with the finger cuffs was positioned on an armrest to elevate it to the fourth intercostal space level to prevent movements in both the arm and the fingers. The other arm rested on the thigh to avoid grasping the machine. Participants were instructed to avoid hip flexion and encouraged to maintain normal breathing since a strong Valsalva manoeuvre may affect the BP recordings by photoplethysmography.

Nevertheless, the Valsalva manoeuvre was not forbidden. All data exceeded at least 80% of the total BP tracing for each protocol to ensure data quality. After performing the KE exercise, the electrocardiogram and the BP measured devices were removed, and participants continued with the following exercises. Once the session was completed, participants returned to the quiet room and the post-exercise measurements were conducted under the same conditions as the baseline for 40 minutes. No moving or speaking was allowed during all measurements.

### 4.3.2. Metabolic recording

Capillary blood lactate concentration (Lt) was obtained by using a portable blood lactate analyser with a sample analysis time of 15 s and a required blood sample of 0.5  $\mu$ L (Lactate Scout, SensLab GmbH, Germany). Lactate Scout uses an enzymatic-amperometric method for the detection of lactate in capillary blood. Data were obtained before and 1 and 3 min after each experimental session.

### 4.3.3. Mechanical recording

Mechanical performance of every repetition was recorded with a dynamic measure device (T-Force System, Ergotech, Murcia, Spain) for three exercises: KE, BPR, and SQ. This device involves a linear velocity transducer connected to a personal computer by means of a 14-bit resolution analogue to digital data acquisition board and custom software (T-Force Dynamic Measurement System, Version 2.35). Instantaneous velocity was sampled at a frequency of 1.000 Hz and subsequently smoothed with a fourth-order low-pass Butterworth filter with a cut-off frequency of 10Hz. The validity and reliability of this device have been previously reported (223).

## 4.4. Data analysis

### 4.4.1. Cardiovascular and autonomic parameters

#### 4.4.1.1. Effects during resistance exercise

For cardiovascular dynamics analysis during KE exercise, in addition to baseline values, HR and BP beat-to-beat (i.e., SBP, DBP and MAP) were obtained during the 40 repetitions performed in each session, excluding the recovery moments between sets. Moreover, the RPP was calculated as follows:  $RPP = HR \times SBP$  and reported in  $bpm \times mmHg \times 10^{-3}$ , and pulse pressure (PP) was considered as  $SBP - DBP$ .

The peak and mean values of each repetition was calculated for all the variables examined (i.e., the peak of HR [ $HR_{peak}$ ], SBP [ $SBP_{peak}$ ], DBP [ $DBP_{peak}$ ], MAP [ $MAP_{peak}$ ], RPP [ $RPP_{peak}$ ], and PP [ $PP_{peak}$ ]; and the mean of HR [ $HR_{mean}$ ], SBP [ $SBP_{mean}$ ], DBP [ $DBP_{mean}$ ], MAP [ $MAP_{mean}$ ], RPP [ $RPP_{mean}$ ], and PP [ $PP_{mean}$ ]) and the corresponding values for each group of repetitions were considered according to the respective comparison analysis: (a) the overall 40 repetitions, (b) the equal number of repetitions performed in the SSC in comparison with the sets of LSC (i.e., sets of 10 repetitions [1-10rep, 11-20rep, 21-30rep, and 31-40rep]), and (c) the epochs with equated work and accumulated resting time performed for both protocols (i.e., first five repetitions [5F] and last five repetitions [5L]).

Additionally, the behaviour of BP in relation to time throughout the KE exercise (in  $mmHg \times s$ ) was evaluated using the area under the curve with the trapezoidal method for mean values of SBP, DBP and MAP ( $AUC_{SBP}$ ,  $AUC_{DBP}$  and  $AUC_{MAP}$ , respectively)(278).

#### 4.4.1.2. Effects after resistance training session

HRV was used to assess the autonomic modulation of the heart. Analysis of the data consisted of time- and frequency-domain analysis. The time-domain analysis included the standard deviations of normal-to-normal intervals (SDNN), as a measure of global autonomic control, and the square root of the mean of the sum of the squares of differences between adjacent normal-to-normal intervals (RMSSD), as a measure of parasympathetic activity. For the spectral analysis of HRV, Fast Fourier Transformation method was employed. HF in absolute values and normalised units (HF<sub>n.u.</sub>) was calculated for estimating cardiac parasympathetic activity. The data analysis was performed for the last 5 min of the period of 10 min before the beginning of the session (baseline) and 5 min epochs during the 20–40 min period after the session since epochs of 5 min are recommended when taking short-term recordings (95). Automatic artefact correction (i.e., medium correction threshold level,  $\pm 0.25$  s) and calculation of HRV values were obtained using the Kubios HRV software v2.1 (The Biomedical Signal and Medical Imaging Analysis Group, Department of Applied Physics, University of Kuopio, Finland). The data were detrended with the smooth priors method. The Lambda value was fixed at 500. The mean artefact correction of the signal was  $1.04 \pm 2.53\%$ . In addition, HR values were recorded as a reflection of cardiac autonomic activity and as an independent predictor of sudden cardiac death risk (279).

On the other hand, BRS- quantified by the sequence method- was employed to estimate the effect of the sessions on the cardiac baroreflex control. Specifically, Lag 1 was used to detect the baroreceptor events (134,280). BRS analysis included the BRS<sub>count</sub>, BRS<sub>slope</sub>, and BEI. For BEI, due to the missing data in some recordings, only 24 participants were analysed. Additionally, BPV was used to estimate the sympathetic vasomotor tone. Our BPV analysis

consisted of spectral analysis of SBP variability. The autoregressive spectral method was used, and the low-frequency activity (0.04-0.15 Hz) in absolute values was calculated ( $LF_{SBP}$ ) (145).

Data recordings of BRS and BPV were performed for the last 10 min before the protocols (baseline) and the intervals 20-30 and 30-40 min after each session. Epochs of 10 min are usually used to analyse BRS after resistance exercise (188, 216). BRS and BPV data were obtained by using TFM software v2.3 (CNSystems, Graz, Austria)(277).

Regarding BP analysis, the beat-to-beat responses registered before (baseline) and after the sessions were analysed in epochs of 10 min. The percentage change of SBP, DBP, and MAP were calculated for all the participants. Percentages changes were calculated as follows:  $\Delta\%30\text{-Baseline} = (\text{value of the 20-30 epoch} - \text{value of baseline}) / \text{value of baseline}$ ;  $\Delta\%40\text{-Baseline} = (\text{value of the 30-40 epoch} - \text{value of baseline}) / \text{value of baseline}$ . Percentage changes were used to represent the differences in BP values. For measurements obtained with a photoplethysmography device, the responses to exercise in percentage changes have been previously validated and well correlated with simultaneous invasive procedures, being these non-invasive measurements a very sensitive method to follow rapid changes in arterial pressure (164).

Figure 19 illustrates an example of a cardiovascular recording. Specifically, this example is a recording of a post-exercise evaluation after a session with a long set configuration.



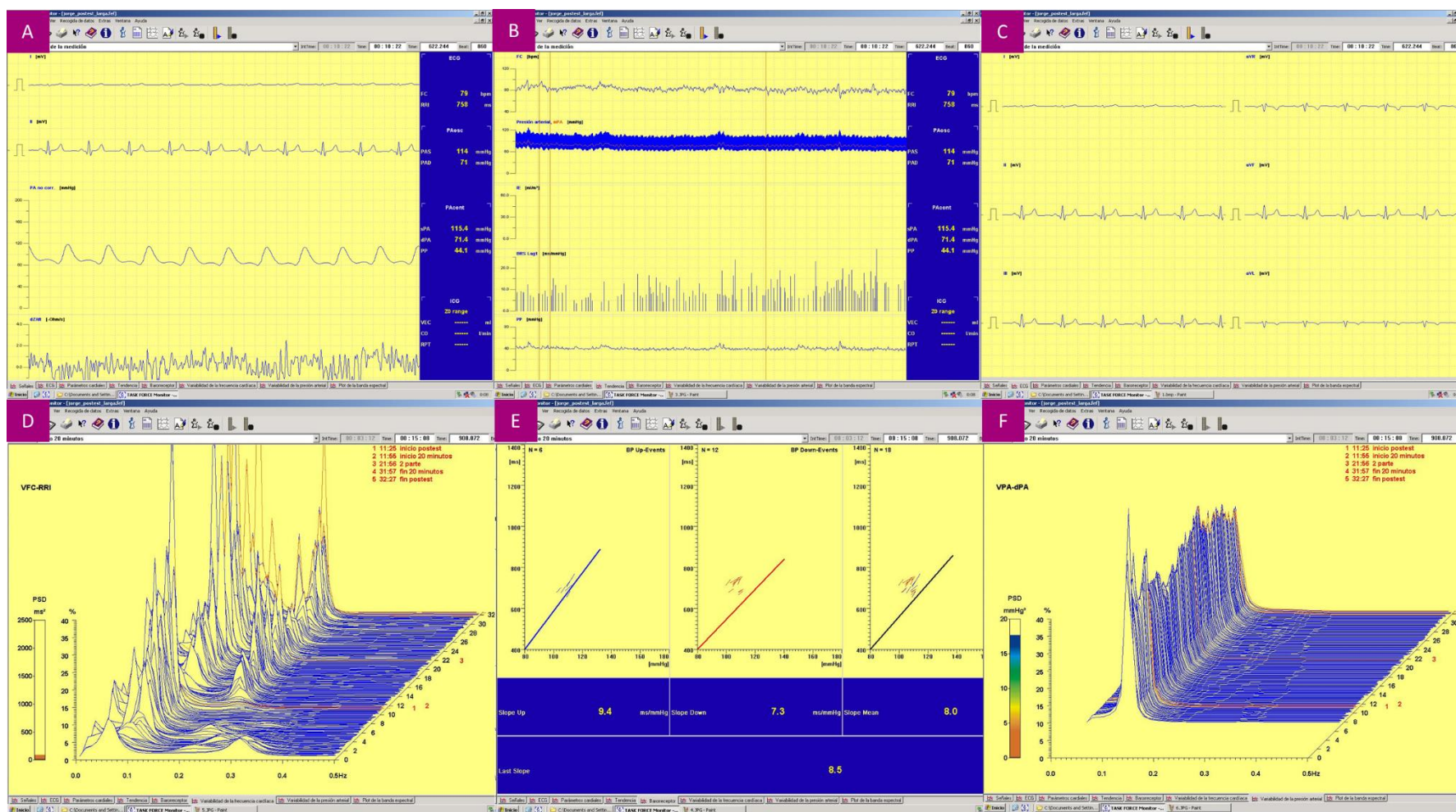


Figure 19. Cardiovascular assessment with the Task Force® Monitor via TFM software v2.3 (CNSystems, Graz, Austria). Panel A: Signs (i.e., ECG and finger beat-to-beat BP signals); Panel B: Trends (i.e., FC, BP, BRS and PP evolution throughout the recording); Panel C: ECG and leads; D: Heart rate variability; Panel E: BRS recording (i.e., BRS ramps -up, down and total); Panel F: Blood pressure variability.

#### 4.4.2. Metabolic parameters

Regarding lactate concentration, the maximum value of the two post-test measurements was selected, and the percentage change of lactatemia ( $\Delta\%Lt$ ) was calculated in both training sessions.

#### 4.4.1. Mechanical parameters

The total duration and the mean propulsive velocity (MPV) were collected. The total duration of each repetition was calculated as the sum of the concentric and eccentric phases and was managed to match the cardiac beats to the respective repetitions for the KE. In addition, it was used as an indicator of time under tension (TUT) for the KE.

The MPV consisted of the mean velocity during the propulsive phase of the exercise, that is, the portion of the concentric period in which the barbell acceleration is greater than the acceleration due to gravity and was used to estimate the neuromuscular fatigue of each session (223,281). The MPV of every repetition was calculated and averaged in both experimental sessions for KE, BPR, and SQ. Thereafter, other parameters were calculated for comparing the loss of mechanical performance between sessions. For the overall maintenance of velocity analysis, the mean to maximum MPV ratio of each session (MMR) was calculated as follows:  $([\text{average MPV}/\text{maximum MPV}] \times 100)$  (refs). Values near 100% imply less velocity loss. For quantifying the velocity loss throughout the sessions, the last five to the first five repetition ratio (5LFR) was obtained. For this calculation, the mean MPV of the last five repetitions and the first five ones were considered as follows:  $5LFR = ([(\text{average last five repetitions MPV}/\text{average first five repetitions MPV}) - 1] \times 100)$ . Lower values imply higher magnitudes of velocity loss and positive values was interpreted as velocity gains.

## 4.5. Statistical analysis

Descriptive parameters are shown as means  $\pm$  standard deviation. Normality was tested using Shapiro–Wilk test. The characteristics of participants were compared for sex using an independent sample t-test.

A three-way or two-way repeated measures analysis of variance (ANOVA), depending on the variable to be analysed, were employed in order to evaluate the main effect and interactions between sex, sessions, and times. Since sex did not interact with the rest of factors (i.e., time and session) for any variable, the following analyses were performed with pooled data from men and women

For the comparison of the cardiovascular parameters during the KE, the peak and mean values of HR, SBP, DBP, MAP, RPP, and PP were analysed performing three different two-way ANOVA. The first  $2 \times 2$  ANOVA was performed to evaluate the effect of the session (LSC vs. SSC) across time (baseline vs. overall exercise). Secondly, a  $2 \times 4$  ANOVA was performed to analyse the effect of the session (LSC vs. SSC) across the time, establishing this factor regarding the equal number of repetitions performed in the SSC in comparison with the sets of LSC (i.e., 1-10rep, 11-20rep, 21-30rep, and 31-40rep). Thirdly, a  $2 \times 2$  ANOVA was used to compare the epochs with equated work and accumulated resting time performed for both sessions (i.e., 5F and 5L).

Additionally, since the  $AUC_{SBP}$ ,  $AUC_{DBP}$  and  $AUC_{MAP}$ , were only measurements present during exercise, a paired t-test or Wilcoxon signed-rank (according to normality assumption) was used for comparing overall values between the experimental sessions. Also, a two-way ANOVA was conducted to analyse the effect of the session (LSC vs. SSC) across the time (i.e., 1-10rep, 11-20rep, 21-30rep, and 31-40rep).

For the comparison of the cardiovascular and autonomic variables before and after the sessions, a two-way ANOVA was performed in order to evaluate the main effect and interactions between sessions (LSC, SSC, and CON) and times (Baseline, 20-25, 25-30, 30-35, and 35-40 for HRV parameters; Baseline, 20-30 and 30-40 min for BRS and  $LF_{SBP}$ ; and %30-Baseline and  $\Delta\%$ 40-Baseline of SBP, DBP, and MAP).

For capillary lactate production, Wilcoxon signed-rank test was performed to analyse the  $\Delta\%$ Lt. Regarding mechanical parameters (i.e., the concentric, eccentric, and total TUT and MPV), a paired t-test or Wilcoxon signed-rank was used for comparing overall values between the experimental sessions and a two-way ANOVA was conducted to analyse the effect of the session (LSC vs. SSC) across the time (i.e., 1-10rep, 11-20rep, 21-30rep, and 31-40rep). Additionally, for MMR and 5LFR, a paired t tests or a Wilcoxon signed-rank test were used for analysing differences between sessions.

For parametric variables, the effect size for each ANOVA factor was reported using the partial eta squared ( $\eta^2$ ) and the pairwise comparisons were performed using Bonferroni correction. For variables that violated the assumption of normality, the alternative nonparametric ANOVA type test was employed using the nparLD R software package (282) for evaluating the main effects and interactions previously described. For main effects interpretation, relative treatment effect (RTE) was considered. RTE has a value between 0 and 1 and indicates the probability that a measurement in one factor level at a given time period is larger than a value of this variable in any other combination of group and time (283). If a significant interaction was detected, paired comparisons were performed using the Wilcoxon signed-rank test with Bonferroni correction. Furthermore, for the effect sizes for pairwise comparisons, the Hedge's  $g$  and the Matched Pair Rank Biserial Correlation were implemented for parametric and nonparametric contrasts, respectively. For Hedge's  $g$ , with its

corresponding 95% confidence interval, the lower thresholds to consider an effect size as small, medium, and large were 0.2, 0.5 and 0.8. Matched Pair Rank Biserial corresponds to the difference between the proportions of positive and negative ranks and score from 0 to 1 (284).

R software v3.6.1. (R Foundation, Vienna, Austria), GraphPad Prism v.9 (GraphPad Software, San Diego, CA, USA), Comprehensive Meta-Analysis v.2 (Biostat Inc., Englewood, NJ, USA), and IBM SPSS v.20.0. (IBM Corp, Armonk, NY, USA) were used for statistical analysis. The statistical significance level was set at 0.05.

Finally, a post hoc power analysis was calculated using the G Power software (version 3.1.9.2) For during analysis, statistical power ( $1 - \beta$ ) of a repeated measures ANOVA with 2 and 4 measurements for a sample size of 24, and a correlation among repeated measures of 0.5 and a medium effect size ( $f = 0.25$ ) is 0.65 and 0.82, respectively. For pre-post comparisons, the statistical power ( $1 - \beta$ ) of a repeated measures ANOVA with 3 and 5 measurements for a sample size of 32, and a correlation among repeated measures of 0.5 and a medium effect size ( $f = 0.25$ ) is 0.87 and 0.96, respectively.



## RESULTS

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The characteristics of participants are summarised in Table 4 and Table 5. Men and women present similar values for age and BMI; however, men showed higher weight, height, and 15RM values for all exercises than women. Concerning cardiovascular baseline measurements, no differences between sexes were found except for SBP and PP, as well as for BEI and  $LF_{SBP}$ , reporting lower values for women.

Table 4. Physical and functional characteristics of the participants

	Men (n = 24)	Women (n = 9)	Total (n = 33)	p-value
Age (yr)	23 ± 2	24 ± 3	23 ± 2	0.435 <sup>+</sup>
Weight (kg)	73.75 ± 8.80	62.11 ± 6.37	70.58 ± 9.67	<b>0.001*</b>
Height (cm)	1.76 ± 0.06	1.65 ± 0.06	1.73 ± 0.08	<b>&lt; 0.001*</b>
BMI (kg/m <sup>2</sup> )	23.80 ± 2.13	22.72 ± 1.93	23.50 ± 2.10	0.322 <sup>+</sup>
15RM in KE (kg)	79.21 ± 12.69	54.67 ± 9.50	72.52 ± 16.17	<b>&lt; 0.001*</b>
15RM in LC (kg)	54.98 ± 8.97	37.93 ± 9.10	50.33 ± 11.75	<b>&lt; 0.001*</b>
15RM in LP (kg)	49.00 ± 7.46	33.61 ± 4.86	44.80 ± 9.71	<b>&lt; 0.001*</b>
15RM in BPR (kg)	50.69 ± 11.68	29.18 ± 5.07	44.83 ± 14.11	<b>&lt; 0.001*</b>
15RM in SQ (kg)	79.88 ± 18.35	55.29 ± 10.32	73.18 ± 19.81	<b>&lt; 0.001*</b>

Values represent means ± SD. \* p values are derived from independent sample t-test and <sup>+</sup> p-values are derived from Mann-Whitney U test. Significant differences are highlighted in bold font.

BMI: body mass index; BPR: bench press; KE: knee extension; LC: leg curl; LP: lateral pull-down; SQ: parallel squat.

Table 5. Baseline cardiovascular characteristics of the participants

	Men (n = 24)	Women (n = 9)	Total (n = 33)	p-value
HR (bpm)	60 ± 9	60 ± 7	60 ± 8	0.489*
SBP (mmHg)	113 ± 9	106 ± 7	111 ± 9	<b>0.018*</b>
DBP (mmHg)	66 ± 7	63.98 ± 4	65 ± 7	0.268*
MAP (mmHg)	84 ± 8	81 ± 5	83 ± 7	0.163*
RPP (bpm x mmHg x 10 <sup>-3</sup> )	7 ± 1	6 ± 1	7 ± 1	0.147*
PP (mmHg)	47 ± 6	42 ± 4	46 ± 6	<b>0.007*</b>
SDNN (ms)	67 ± 24	59 ± 30	65 ± 26	0.235*
RMSSD (ms)	75 ± 33	69 ± 37	74 ± 33	0.463 <sup>+</sup>
HF (ms <sup>2</sup> )	3195 ± 2490	2953 ± 3398	3127 ± 2719	0.414 <sup>+</sup>
HFn.u.	66 ± 15	71 ± 12	67 ± 14	0.197*
BRS <sub>count</sub> (n)	63 ± 31	47 ± 16	59 ± 29	0.154 <sup>+</sup>
BRS <sub>slope</sub> (ms/mmHg)	27 ± 13	28 ± 15	27 ± 13.66	0.883 <sup>+</sup>
BEI (%)	88 ± 12	83 ± 9	86 ± 11	<b>0.022<sup>+</sup></b>
$LF_{SBP}$ (mmHg <sup>2</sup> )	7 ± 8	3 ± 4	6 ± 7	<b>0.022<sup>+</sup></b>

Values represent means ± SD. \* p-values are derived from independent sample t-test and <sup>+</sup> p values are derived from Mann-Whitney U test.

BEI: Baroreflex effectiveness index; BRS<sub>count</sub>: Number of baroreceptor sequences detected; BRS<sub>slope</sub>: magnitude of the baroreflex sensitivity; DBP: diastolic blood pressure; HF: high-frequency PI spectral power in absolute values; HFn.u.: high-frequency PI spectral power in normalised units; HR: heart rate; MAP: mean arterial pressure; PP: pulse pressure; RMSSD: root mean square of differences between adjacent PI; RPP: rate pulse product; SBP: systolic blood pressure; SDNN: standard deviations of pulse intervals.

The physiological and mechanical responses are described in the following sections separated into during and postexercise responses. For baseline physiological values, no significant differences between sessions for any variable were observed ( $p > 0.05$ ).

## 5.1. Set configuration effects during resistance exercise

### 5.1.1. Cardiovascular responses

#### 5.1.1.1. Overall responses

Regarding overall session HR, for the  $HR_{peak}$ , main effect of session ( $p < 0.001$ ;  $\eta^2 = 0.545$ ), time ( $p < 0.001$ ;  $\eta^2 = 0.957$ ), and a session by time interaction were detected ( $p < 0.001$ ;  $\eta^2 = 0.783$ ). For main effects of session, LSC showed higher values than SSC ( $p < 0.001$ ), whereas for main effects of time, values during exercise were greater than baseline ( $p < 0.001$ ). For pairwise comparison, both sessions showed higher values during exercise in comparison with baseline ( $p < 0.001$ ;  $g = 4.700$ ; 95% CI: [3.397, 6.004], and  $g = 2.732$ ; 95% CI: [1.956, 3.508] for LSC and SSC, respectively). Moreover, LSC results in higher  $HR_{peak}$  values than SSC during exercise ( $p < 0.001$ ;  $g = 1.252$ ; 95% CI: [0.838, 1.665]). Furthermore,  $HR_{peak}$  evolution from the baseline across the repetitions are presented in Figure 20.

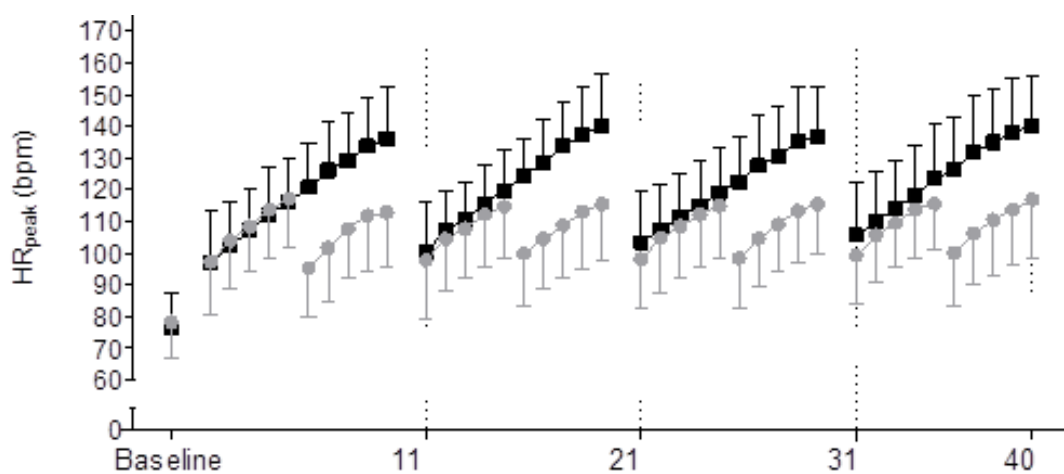


Figure 20. Peak heart rate ( $HR_{peak}$ ) values during baseline and the 40 repetitions for a long set configuration protocol (LSC, in black squares) and a short set configuration protocol (SSC, in grey circles). Data are displayed as means  $\pm$  SD.

For  $HR_{mean}$ , main effects of session ( $p < 0.001$ ;  $\eta^2 = 0.411$ ), time ( $p < 0.001$ ;  $\eta^2 = 0.964$ ), and a session by time interaction were detected ( $p < 0.001$ ;  $\eta^2 = 0.785$ ). For main effects of session, values in LSC were greater than SSC ( $p < 0.001$ ) whereas for main effects of time, during exercise period showed higher  $HR_{mean}$  than baseline ( $p < 0.001$ ). Post-hoc analyses revealed greater values during exercise in comparison with baseline in LSC ( $p < 0.001$ ;  $g = 5.070$ ; 95% CI: [3.662, 6.478]), and SSC ( $p < 0.001$ ;  $g = 3.292$ ; 95% CI: [2.416, 4.167]), reporting higher values during exercise for LSC in comparison with SSC ( $p < 0.001$ ;  $g = 0.942$ ; 95% CI: [0.611, 1.274]). Additionally,  $HR_{mean}$  evolution from the baseline across the 40 repetitions are presented in Figure 21.

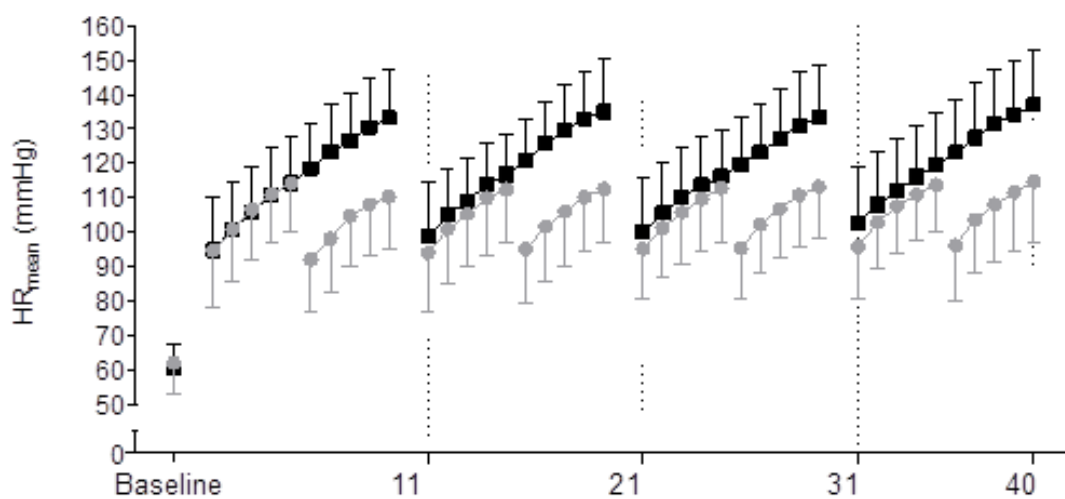


Figure 21. Mean heart rate ( $HR_{mean}$ ) values during baseline and the 40 repetitions for a long set configuration protocol (LSC, in black squares) and a short set configuration protocol (SSC, in grey circles). Data are displayed as means  $\pm$  SD.

Focusing on global BP responses, only main effects of time were detected for  $SBP_{peak}$  ( $p < 0.001$ ; RTE= 0.275 and 0.725 for baseline and exercise, respectively),  $DBP_{peak}$  ( $p < 0.001$ ; RTE= 0.251 and 0.749 for baseline and exercise, respectively), and  $MAP_{peak}$  ( $p < 0.001$ ;  $\eta^2 = 0.948$ ). Also, only main effects for time were observed for  $SBP_{mean}$  ( $p < 0.001$ ;  $\eta^2 = 0.831$ ),  $DBP_{mean}$  ( $p < 0.001$ ;  $\eta^2 = 0.883$ ), and  $MAP_{mean}$  ( $p < 0.001$ ;  $\eta^2 = 0.894$ ). Main effect of time in all BP parameters showed higher values during exercise versus baseline ( $p < 0.001$ ).

Moreover,  $SBP_{peak}$  and  $SBP_{mean}$  evolution from the baseline and across the repetitions are shown in Figure 22 and Figure 23, respectively.

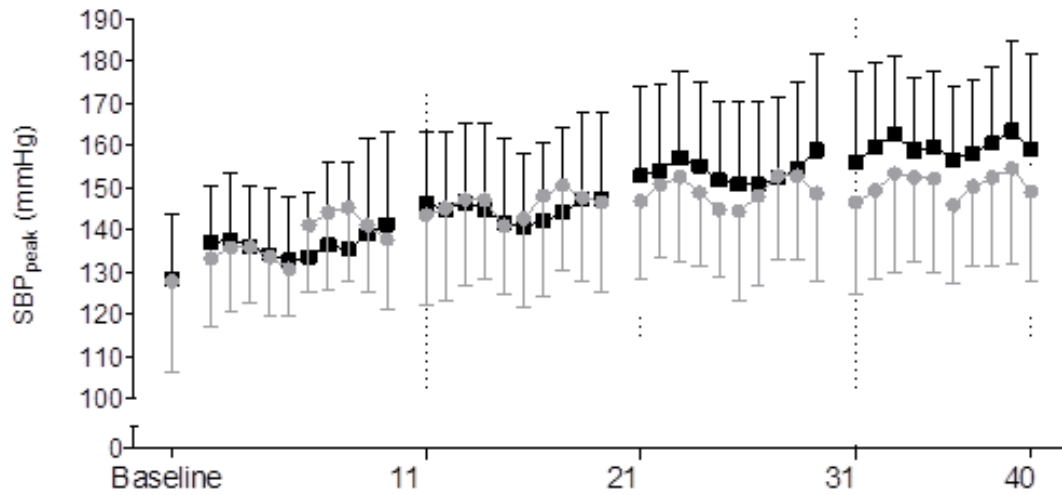


Figure 22. Peak systolic blood pressure ( $SBP_{peak}$ ) values during baseline and the 40 repetitions for a long set configuration protocol (LSC, in black squares) and a short set configuration protocol (SSC, in grey circles). Data are displayed as means  $\pm$  SD.

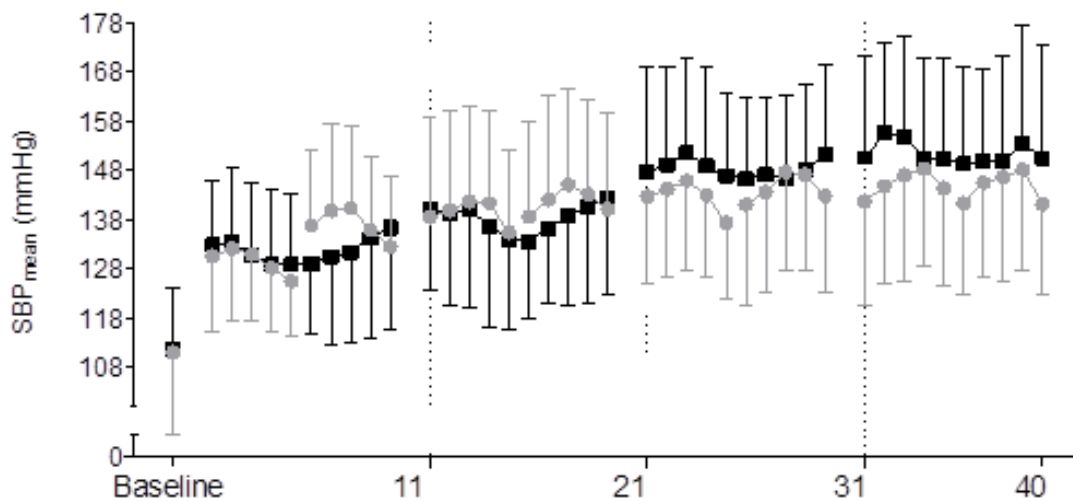


Figure 23. Mean systolic blood pressure ( $SBP_{mean}$ ) values during baseline and the 40 repetitions for a long set configuration protocol (LSC, in black squares) and a short set configuration protocol (SSC, in grey circles). Data are displayed as means  $\pm$  SD.

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Concerning session RPP, for  $RPP_{peak}$ , main effects of session ( $p = 0.005$ ; RTE= 0.531 and 0.469 for LSC and SSC, respectively), time ( $p < 0.001$ ; RTE= 0.251 and 0.749 for baseline and exercise, respectively), and a session by time interaction were detected ( $p = 0.002$ ). Whereas main effect of session reported higher values in LSC compared to SSC, main effect of time resulted in superior  $RPP_{peak}$  values during exercise than baseline. Post-hoc analyses showed higher values during exercise in both protocols versus baseline ( $p < 0.001$ ;  $r = 1.000$ ), being LSC values greater than SSC ( $p = 0.002$ ;  $r = 0.727$ ). For  $RPP_{mean}$ , main effects of session ( $p = 0.018$ ;  $\eta^2 = 0.220$ ), time ( $p < 0.001$ ;  $\eta^2 = 0.944$ ), and a session by time interaction were detected ( $p < 0.001$ ;  $\eta^2 = 0.428$ ). For main effect of session, LSC showed higher values than SSC ( $p = 0.018$ ) and for main effect of time, during exercise values were superior compared to baseline values ( $p < 0.001$ ). Pairwise comparisons showed higher values during exercise in LSC ( $p < 0.001$ ;  $g = 4.290$ ; 95% CI: [2.655, 5.926]) and SSC ( $p < 0.001$ ;  $g = 2.931$ ; 95% CI: [2.148, 3.714]) versus baseline, being LSC values greater than SSC ( $p = 0.003$ ;  $g = 0.682$ ; 95% CI: [0.239, 1.124]).

Regarding session PP, for  $PP_{peak}$ , main effects of session ( $p = 0.019$ ; RTE= 0.543 and 0.457 for LSC and SSC, respectively) and time ( $p < 0.001$ ; RTE = 0.370 and 0.630 for baseline and exercise, respectively) were observed, reporting higher values during exercise compared to baseline and for LSC compared to SSC. Nevertheless, a session by time interaction effect was not revealed ( $p = 0.427$ ). For  $PP_{mean}$ , neither main effect of session, nor time and nor session by time interaction were detected ( $p \geq 0.401$ ).

### 5.1.1.2. Responses across the sets

Peak values of cardiovascular data across the sets are presented in Figure 24. Analysis showed for  $HR_{peak}$  a main effect of session ( $p < 0.001$ ; RTE= 0.666 and 0.334 for LSC and SSC, respectively), reporting the LSC higher values compared to SSC. Additionally, a session by time interaction ( $p = 0.022$ ) was detected. Post hoc analysis did not detect differences between times within sessions ( $p \geq 0.072$ ). However, LSC showed higher values in comparison with SSC in all sets ( $p < 0.001$ ) (Figure 24A). Regarding peak BP values,  $SBP_{peak}$  (Figure 24B) showed a main effect of time ( $p < 0.001$ ;  $\eta^2 = 0.599$ ), with rises of peak values until 21-30rep ( $p \leq 0.003$ ). Moreover, a session by time interaction ( $p = 0.006$ ;  $\eta^2 = 0.163$ ). Pairwise comparison revealed that while  $SBP_{peak}$  increased until 21-30rep in LSC ( $p \leq 0.028$ ), SSC only revealed differences between sets in comparison with 1-10rep ( $p \leq 0.033$ ). Furthermore, only 31-40rep showed higher values in LSC in comparison with SSC ( $p = 0.041$ ). For  $DBP_{peak}$ , a main time effect ( $p < 0.001$ ; RTE= 0.368, 0.489, 0.558 and 0.585 for 1-10rep 11-20rep, 21-30rep and 31-40rep, respectively), achieving the 31-40rep the highest values. Moreover, a session by time interaction ( $p < 0.017$ ) were detected. In the LSC, higher values in 11-20rep, 21-30rep and 31-40rep in comparison with 1-10rep for LSC ( $p \leq 0.003$ ) and in 11-20 compared to 31-40 ( $p = 0.031$ ) were observed. In SSC, only differences were observed between 1-10rep and 21-30rep ( $p = 0.026$ ). As well, only differences were observed between protocols in 31-40rep, promoting the LSC the highest  $DBP_{peak}$  ( $p < 0.046$ ) (Figure 24C). For  $MAP_{peak}$ , main effects of time ( $p < 0.001$ ;  $\eta^2 = 0.466$ ), with augmentations until 11-20rep time period, and a tendency for the session by time interaction were detected ( $p = 0.051$ ;  $\eta^2 = 0.106$ ) (Figure 24D). Regarding the  $RPP_{peak}$ , analysis only reported main effects of session ( $p < 0.001$ ;  $\eta^2 = 0.466$ ) and time ( $p < 0.001$ ;  $\eta^2 = 0.387$ ). For the main effect of session,  $RPP_{peak}$  in LSC was higher than in SSC ( $p < 0.001$ ). For the main effect of time, 31-40rep was higher in comparison with the others time periods ( $p \leq 0.041$ ) (Figure 24E). For  $PP_{peak}$ , only main effect of time

( $p < 0.001$ ; RTE = 0.387, 0.478, 0.540, 0.591 and 0.595 for 1-10rep, 11-20rep, 21-30rep and 31-40rep, respectively) and a tendency for the main effect of session ( $p = 0.071$ ) was observed (Figure 24F). Effect sizes of the pairwise comparisons are shown in the Table 6 and Table 7.

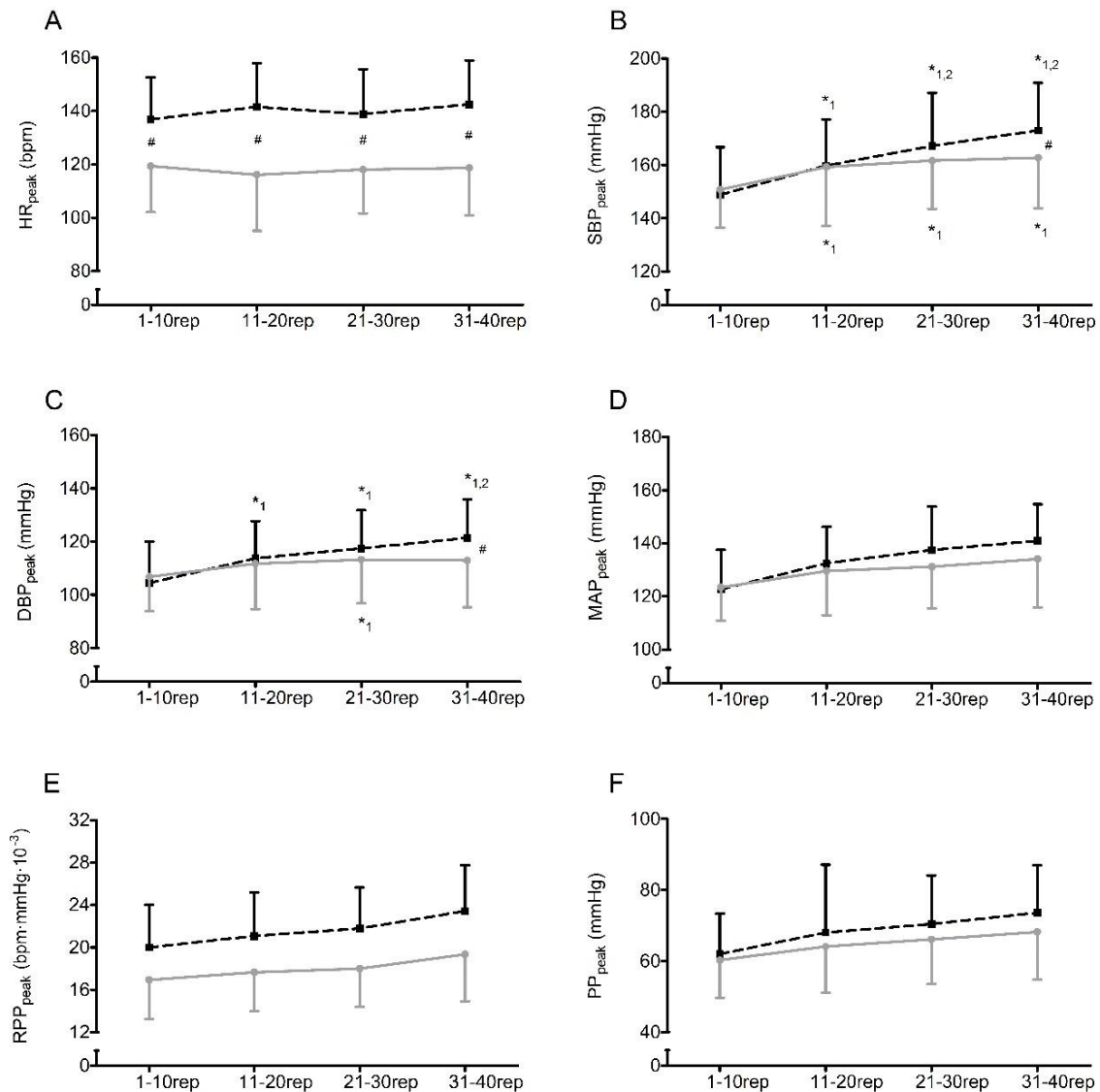


Figure 24. Peak cardiovascular response across a long set configuration protocol (LSC, in squares), and a short set configuration protocol (SSC, in circles). (A) Peak heart rate ( $HR_{peak}$ ); (B) peak systolic blood pressure ( $SBP_{peak}$ ); (C) peak diastolic blood pressure ( $DBP_{peak}$ ); (D) peak mean arterial pressure ( $MAP_{peak}$ ); (E) peak rate pressure product ( $RPP_{peak}$ ); (F) peak pulse pressure ( $PP_{peak}$ ). # differences between training sessions at a specific time-point and  $\S^{1,2,3,4}$  within-session differences from 1-10rep, 11-20rep, 21-30rep or 31-40rep, respectively. Data are displayed as means  $\pm$  SD.

The mean values of cardiovascular parameters throughout the sets are presented in Figure 25. For  $HR_{\text{mean}}$  (Figure 25A), only main effects of session ( $p < 0.001$ ;  $\eta^2 = 0.702$ ) and time ( $p = 0.007$ ;  $\eta^2 = 0.217$ ) were detected, showing higher values during the LSC compared to SSC ( $p < 0.001$ ) and for 31-40rep higher in comparison with 1-10rep ( $p = 0.023$ ) and 21-30rep ( $p < 0.001$ ). Regarding BP,  $SBP_{\text{mean}}$  showed main effect of time ( $p < 0.001$ ;  $\eta^2 = 0.618$ ) and a session by time interaction ( $p = 0.011$ ;  $\eta^2 = 0.175$ ). For main effect of time, analysis reported with a progressive increase until 21-30rep ( $p < 0.001$ ). Additionally, despite no differences between sessions were observed for any set ( $p \geq 0.104$ ), pairwise comparisons detected significant  $SBP_{\text{mean}}$  increments until 21-30rep ( $p \leq 0.007$ ) in LSC, but only until 11-20rep in SSC ( $p = 0.009$ ) (Figure 25B). For  $DBP_{\text{mean}}$  (Figure 25C), main effect of time ( $p < 0.001$ ;  $\eta^2 = 0.413$ ), with a progressive increase until 21-30rep ( $p \leq 0.022$ ), and a session by time interaction were detected ( $p = 0.008$ ;  $\eta^2 = 0.176$ ). Post-hoc analyses revealed significant  $DBP_{\text{mean}}$  increments until 21-30rep ( $p \leq 0.040$ ) in LSC, but in SSC only differences were observed between 1-10rep and 21-30rep ( $p = 0.030$ ). However, no differences between sessions were observed for any set ( $p \geq 0.143$ ). For  $MAP_{\text{mean}}$ , a main effect of time was observed ( $p < 0.001$ ; RTE= 0.358, 0.465, 0.573 and 0.604 for 1-10rep, 11-20rep, 21-30rep and 31-40rep, respectively), with higher values in 31-40rep, and a session by time interaction was detected ( $p = 0.022$ ). While LSC showed a tendency for the comparison between 1-10rep and 11-20rep ( $p = 0.051$ ) and a progressive increment of  $MAP_{\text{mean}}$  values until 21-30rep ( $p \leq 0.003$ ), SSC only revealed differences for all sets in comparison with 1-10rep ( $p \leq 0.028$ ). No differences between protocols were observed across the sets ( $p \geq 0.304$ ) (Figure 25D). Regarding  $RPP_{\text{mean}}$  (Figure 25E), main effects of session ( $p = 0.001$ ;  $\eta^2 = 0.399$ ), time ( $p < 0.001$ ;  $\eta^2 = 0.627$ ), and a session by time interaction were detected ( $p = 0.017$ ;  $\eta^2 = 0.169$ ). For the main effect of session higher values in LSC compared to SSC ( $p < 0.001$ ) was observed, whereas the main effect of time showed an incremental progression across the group of repetitions ( $p \leq 0.004$ ).



Post-hoc analyses showed significant increases across all the sets in LSC ( $p \leq 0.032$ ) but only differences between 1-10rep and the successive sets in SSC ( $p \leq 0.006$ ). Furthermore, LSC presented higher values than SSC ( $p \leq 0.012$ ) for all sets. For  $PP_{mean}$ , only main effect of time ( $p < 0.001$ ;  $\eta^2 = 0.550$ ) was detected, showing a progressive rise on  $PP_{mean}$  throughout the groups of repetitions ( $p < 0.001$ ) (Figure 25F). Effect sizes of the pairwise comparisons are shown in the Table 6 and Table 7.

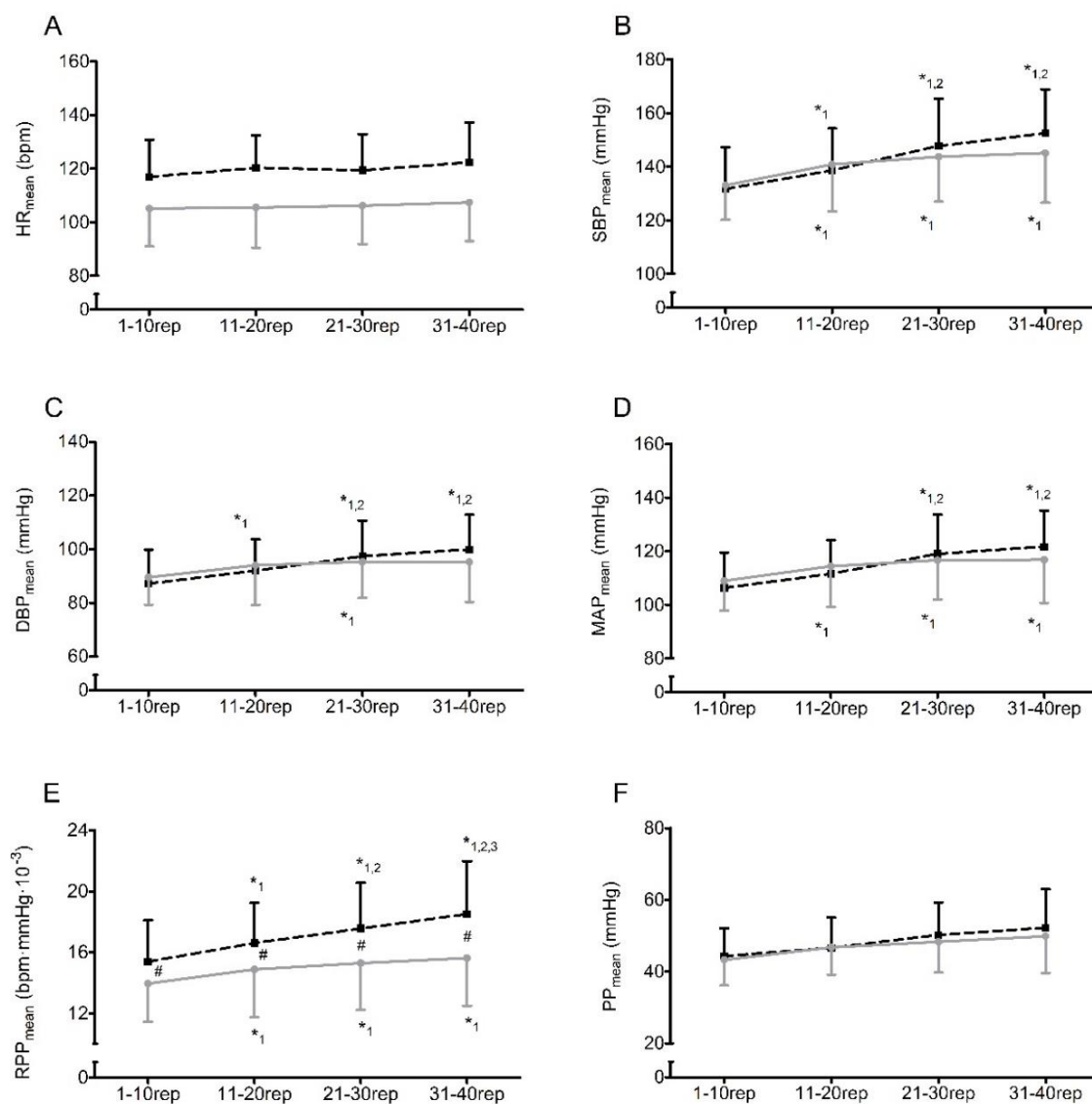


Figure 25. Mean cardiovascular response across a long set configuration protocol (LSC, in squares), and a short set configuration protocol (SSC, in circles). (A) Mean heart rate ( $HR_{mean}$ ); (B) mean systolic blood pressure ( $SBP_{mean}$ ); (C) mean diastolic blood pressure ( $DBP_{mean}$ ); (D) average mean arterial pressure ( $MAP_{mean}$ ); (E) mean rate pressure product ( $RPP_{mean}$ ); (F) mean pulse pressure ( $PP_{mean}$ ). # differences between training sessions at a specific time-point and \$^{1,2,3,4}\$ within-session differences from 1-10rep, 11-20rep, 21-30rep or 31-40rep, respectively. Data are displayed as means  $\pm$  SD.

RESULTS

Table 6. Effect sizes (Hedge's *G* with 95% CI or by the Rank Biserial Correlation, *r*) for cardiovascular values across protocols. Positive effect size values indicate higher values in column sets compared to row sets, while a negative effect size indicates decreases in values in column sets compared to row sets.

	11-20rep	21-30rep	31-40rep
<b>HR<sub>peak</sub> (mmHg)</b>			
<i>LSC</i>			
1-10rep	0.467	0.127	0.460
11-20rep		-0.275	0.127
21-30rep			0.587
<i>SSC</i>			
1-10rep	-0.087	-0.160	-0.101
11-20rep		-0.067	0.220
21-30rep			0.140
<b>SBP<sub>peak</sub> (mmHg)</b>			
<i>LSC</i>			
1-10rep	0.602 (0.310 – 0.893)	0.933 (0.518 – 1.348)	1.309 (0.859 – 1.759)
11-20rep		0.374 (0.132 – 0.616)	0.724 (0.451 – 0.998)
21-30rep			0.294 (0.009 – 0.580)
<i>SSC</i>			
1-10rep	0.377 (0.127 – 0.628)	0.590 (0.375 – 0.805)	0.648 (0.344 – 0.952)
11-20rep		0.103 (-0.055 – 0.261)	0.160 (-0.150 – 0.470)
21-30rep			0.057 (-0.15 – 0.264)
<b>DBP<sub>peak</sub>(mmHg)</b>			
<i>LSC</i>			
1-10rep	0.820	0.827	0.913
11-20rep		0.300	0.653
21-30rep			0.380
<i>SSC</i>			
1-10rep	0.493	0.667	0.540
11-20rep		0.227	0.160
21-30rep			0.145
<b>SBP<sub>mean</sub> (mmHg)</b>			
<i>LSC</i>			
1-10rep	0.432 (0.194 – 0.670)	0.929 (0.572 – 1.286)	1.253 (0.772 – 1.733)
11-20rep		0.519 (0.311 – 0.727)	0.833 (0.491 – 1.174)
21-30rep			0.264 (0.06 – 0.468)
<i>SSC</i>			
1-10rep	0.451 (0.192 – 0.710)	0.658 (0.331 – 0.986)	0.689 (0.330 – 1.049)
11-20rep		0.159 (-0.017 – 0.335)	0.227 (-0.006 – 0.461)
21-30rep			0.075 (-0.055 – 0.205)
<b>DBP<sub>mean</sub> (mmHg)</b>			
<i>LSC</i>			
1-10rep	0.379 (0.121 – 0.636)	0.761 (0.401 – 1.122)	0.960 (0.503 – 1.416)
11-20rep		0.407 (0.206 – 0.609)	0.613 (0.326 – 0.901)
21-30rep			0.183 (-0.003 – 0.369)
<i>SSC</i>			
1-10rep	0.31 (0.033 – 0.586)	0.447 (0.149 – 0.744)	0.400 (0.091 – 0.709)
11-20rep		0.089 (-0.083 – 0.262)	0.080 (-0.182 – 0.342)
21-30rep			-0.007 (-0.155 – 0.141)

(Continued)

<b>MAP<sub>mean</sub> (mmHg)</b>			
<i>LSC</i>			
1-10rep	0.613	0.860	0.927
11-20rep		0.813	0.980
21-30rep			0.387
<i>SSC</i>			
1-10rep	0.660	0.727	0.680
11-20rep		0.287	0.380
21-30rep			0.220
<b>RPP<sub>mean</sub>(mmHg)</b>			
<i>LSC</i>			
1-10rep	0.439 (0.23 – 0.648)	0.720 (0.489 – 0.95)	0.919 (0.611 – 1.227)
11-20rep		0.303 (0.168 – 0.438)	0.557 (0.287 – 0.828)
21-30rep			0.270 (0.095 – 0.446)
<i>SSC</i>			
1-10rep	0.275 (0.128 – 0.421)	0.433 (0.232 – 0.633)	0.545 (0.281 – 0.809)
11-20rep		0.128 (-0.005 – 0.262)	0.231 (0.043 – 0.418)
21-30rep			0.104 (0.006 – 0.203)

Table 7. Effect sizes (Hedge's *G* with 95% CI or by the Rank Biserial Correlation, *r*) for cardiovascular values across protocols. Positive effect size indicates higher values in long set configuration, whereas a negative effect size indicates higher for short set configuration.

<b>LSC vs. SSC</b>				
	<b>1-10rep</b>	<b>11-20rep</b>	<b>21-30rep</b>	<b>31-40rep</b>
<b>HR<sub>peak</sub> (mmHg)</b>	0.987	0.987	0.953	0.993
<b>SBP<sub>peak</sub> (mmHg)</b>	0.121 (-0.288 – 0.53)	-0.023 (-0.497 – 0.451)	-0.278 (-0.712 – 0.156)	-0.535 (-1.056 – 0.015)
<b>DBP<sub>peak</sub>(mmHg)</b>	-0.080	0.140	0.280	0.467
<b>SBP<sub>mean</sub> (mmHg)</b>	0.096 (-0.352 – 0.543)	0.129 (-0.243 – 0.5)	-0.231 (-0.764 – 0.302)	-0.406 (-0.897 – 0.085)
<b>DBP<sub>mean</sub> (mmHg)</b>	0.198 (-0.289 – 0.685)	0.147 (-0.363 – 0.656)	-0.149 (-0.586 – 0.288)	-0.321 (-0.748 – 0.106)
<b>MAP<sub>mean</sub> (mmHg)</b>	-0.153	-0.113	0.160	0.240
<b>RPP<sub>mean</sub>(mmHg)</b>	-0.530 (-0.939 – 0.121)	-0.574 (-1.00 – 0.139)	-0.721 (-1.092 – 0.35)	-0.839 (-1.29 – 0.389)

*LSC*: long set configuration; *SSC*: short set configuration; *HR<sub>peak</sub>*: Peak heart rate; *SBP<sub>peak</sub>*: peak systolic blood pressure; *DBP<sub>peak</sub>*: peak diastolic blood pressure; *SBP<sub>mean</sub>*: mean systolic blood pressure; *DBP<sub>mean</sub>*: mean diastolic blood pressure; *MAP<sub>mean</sub>*: average mean arterial pressure; *RPP<sub>mean</sub>*: mean rate pressure product.

### 5.1.1.3. Responses of repetition periods matched in accumulated work and rest time

Considering that both protocols are established with a similar work-to-rest ratio but differ in how the set is structured, the accumulated work and time were equalised at only two points: after the first five repetitions and after the last five repetitions. For the comparison between these repetitions epochs, both peak and mean values of the first five repetitions and the last five repetitions were contrasted. Descriptive and ANOVA results for these variables are shown in Table 8. In brief, no differences were found between protocols for any parameter during the 5F. Instead, for the 5L, all parameters were significantly higher in LSC compared to SSC, except for  $SBP_{mean}$ ,  $MAP_{mean}$ ,  $PP_{peak}$  and  $PP_{mean}$  ( $p > 0.05$ ).

### 5.1.1.4. Area under the curve of blood pressure

The overall analysis of  $AUC_{SBP}$ ,  $AUC_{DBP}$  and  $AUC_{MAP}$  did not detect significant differences between protocols ( $p = 0.080$ ,  $0.174$  and  $0.146$  for  $AUC_{SBP}$ ,  $AUC_{DBP}$  and  $AUC_{MAP}$ , respectively). However, when cluster of repetitions were considered, the  $AUC_{SBP}$  showed a main effect of time ( $p < 0.001$ ; RTE=  $0,430$ ,  $0,478$ ,  $0,529$  and  $0,563$  for 1-10rep, 11-20rep, 21-30rep and 40rep, respectively) and a session by time interaction ( $p = 0.009$ ), whereas a tendency for main effect of session ( $p = 0.079$ ; RTE=  $0.550$  and  $0.450$  for LSC and SSC, respectively) was detected. Pairwise comparisons showed that  $AUC_{SBP}$  was higher in 21-30rep ( $p = 0.036$ ,  $g = 0.465$ ; 95% CI:  $[0.210, 0.721]$ ) and 31-40rep ( $p = 0.003$ ,  $g = 0.784$ ; 95% CI:  $[0.413, 1.156]$ ) in comparison with 1-10rep in LSC, but without changes in SSC. Differences between protocols were only shown in 31-40rep ( $p = 0.011$ ,  $g = 0.665$ ; 95% CI:  $[0.139, 1.192]$ ), although a tendency was observed in 11-20rep ( $p = 0.078$ ) (Figure 26A). Regarding  $AUC_{DBP}$ , a main effect of time ( $p = 0.009$ ;  $\eta^2 = 0.183$ ) and a session by time interaction were detected ( $p = 0.006$ ;  $\eta^2 = 0.182$ ). Main effect of time analysis only reported higher  $AUC_{DBP}$  values in 21-30rep than

1-10rep ( $p = 0.030$ ). LSC showed higher values in 11-20rep ( $p = 0.041$ ,  $g = 0.359$ ; 95% CI: [0.114, 0.604]), in 21-30rep ( $p = 0.017$ ,  $g = 0.421$ ; 95% CI: [0.163, 0.680]), and in 31-40rep ( $p = 0.003$ ,  $g = 0.712$ ; 95% CI: [0.325, 1.099]) compared to 1-10rep, whereas SSC revealed no changes. Between-session differences were only found for 31-40rep ( $p = 0.014$ ,  $g = 0.656$ ; 95% CI: [0.123, 1.190]) (Figure 26B). Lastly, for  $AUC_{MAP}$ , a main effect of time ( $p = 0.002$ ;  $\eta^2 = 0.225$ ), with higher values and a session by time interaction were observed ( $p = 0.005$ ;  $\eta^2 = 0.170$ ). Post-hoc analyses showed a tendency for the differences between 1-10rep and 11-20rep ( $p = 0.052$ ) and higher values in 21-30rep ( $p = 0.009$ ,  $g = 0.450$ ; 95% CI: [0.192, 0.708]) and 31-40rep ( $p = 0.001$ ,  $g = 0.736$ ; 95% CI: [0.364, 1.109]) versus 1-10rep in LSC. In SSC, no changes were observed compared to the first set, being only lower than LSC for 31-40rep ( $p = 0.014$ ,  $g = 0.653$ ; 95% CI: [0.117, 1.189]) (Figure 26C).

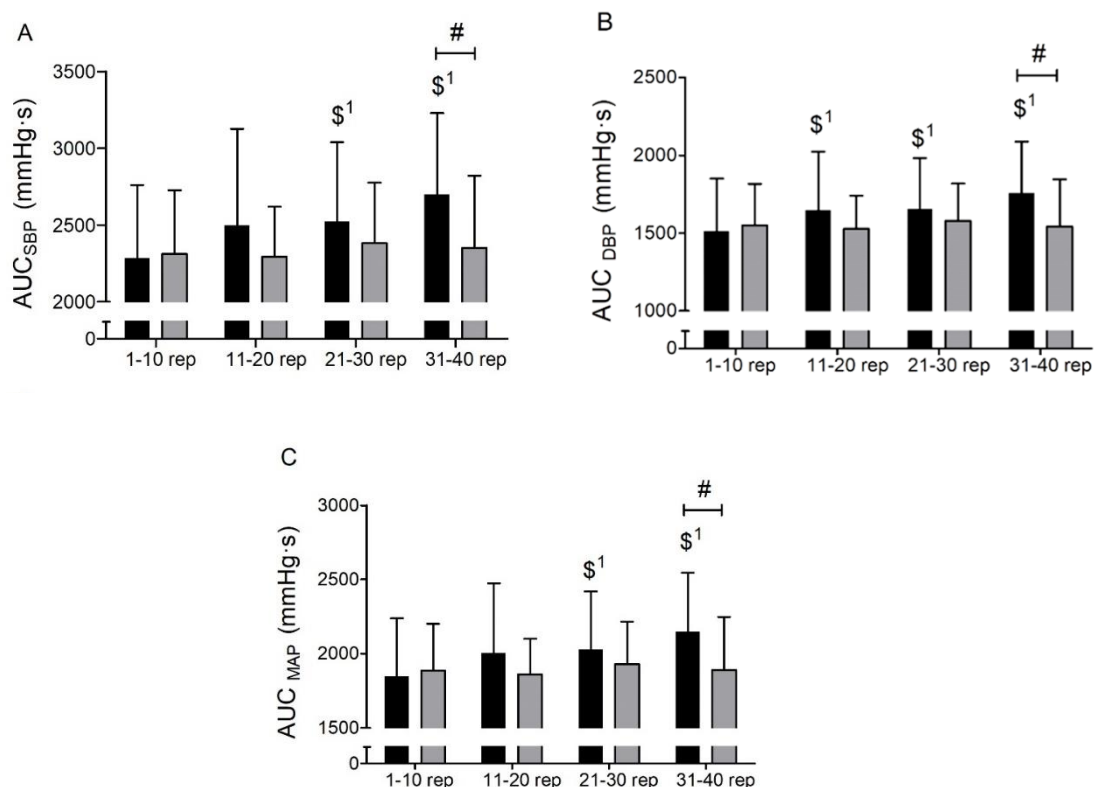


Figure 26. Analysis under the curve of (A) systolic blood pressure ( $AUC_{SBP}$ ), (B) diastolic blood pressure ( $AUC_{DBP}$ ), and (C) mean arterial pressure ( $AUC_{MAP}$ ) during a long set configuration session (LSC, black bars) and a short set configuration session (SSC, grey bars). # differences between training sessions at a specific time-point and \$<sup>1,2,3,4</sup> within-session differences from 1-10rep, 11-20rep, 21-30rep or 31-40rep, respectively. Data are displayed as means  $\pm$  SD.

## RESULTS

Table 8. Cardiovascular values in the first five repetitions (5F) and the last five repetitions (5L) of exercise during the long set (LSC) or short set configuration sessions (SSC). Effect size for 5L to 5F comparison and SSC to LSC comparison in 5L period is represented by Hedge's G with 95% CI or by the Rank Biserial Correlation (*r*). Positive effect size values indicate higher values for 5L (in 5L to 5F comparison) or for LSC (in SSC to LSC comparison in 5L period), while a negative effect size indicates higher values for 5F (in 5L to 5F comparison) or for SSC (in SSC to LSC comparison in 5L period) (*n* = 24).

Variable	5F vs. 5L		LSC vs. SSC		p-value ( $\eta^2$ or RTE)		
	5F (mean $\pm$ SD)	5L (mean $\pm$ SD)	Hedge's G (95% CI) or <i>r</i>	Hedge's G (95% CI) or <i>r</i>	session	time	s x t
<b>HR (bpm)</b>							
<i>Peak</i>							
LSC	119.02 $\pm$ 13.61	142.15 $\pm$ 16.45	0.987	0.993	<0.001 (LSC:0.603; SSC:0.397)	<0.001 (5F:0.415; 5L:0.585)	<0.001
SSC	117.51 $\pm$ 15.85	117.92 $\pm$ 18.49 *	0.000				
<i>Mean</i>							
LSC	106.94 $\pm$ 13.11	130.43 $\pm$ 15.99	1.523 (1.058 – 1.989)	1.353 (0.841 – 1.865)	<0.001 (0.600)	<0.001 (0.729)	<0.001 (0.824)
SSC	106.27 $\pm$ 14.53	107.99 $\pm$ 16.09 *	0.107 (-0.089 – 0.302)				
<b>SBP (mmHg)</b>							
<i>Peak</i>							
LSC	141.29 $\pm$ 14.33	170.58 $\pm$ 17.23	1.759 (1.238 – 2.281)	0.589 (0.113 – 1.065)	0.101 (0.113)	<0.001 (0.830)	0.017 (0.223)
SSC	140.92 $\pm$ 13.74	159.55 $\pm$ 18.9 *	1.063 (0.577 – 1.55)				
<i>Mean</i>							
LSC	131.03 $\pm$ 13.8	152.05 $\pm$ 16.87	1.304 (0.795 – 1.812)	0.385 (-0.102 – 0.872)	0.203 (0.069)	<0.001 (0.715)	0.212 (0.067)
SSC	129.47 $\pm$ 12.46	144.99 $\pm$ 18.54	0.920 (0.440 – 1.400)				
<b>DBP (mmHg)</b>							
<i>Peak</i>							
LSC	96.08 $\pm$ 12.25	119.19 $\pm$ 15.24	1.601 (0.97 – 2.231)	0.532 (0.013 – 1.052)	0.493 (0.021)	<0.001 (0.705)	0.001 (0.413)
SSC	100.68 $\pm$ 11.63	110.12 $\pm$ 17.56 *	0.566 (0.233 – 0.898)				
<i>Mean</i>							
LSC	85.64 $\pm$ 11.31	99.51 $\pm$ 13.42	1.075 (0.544 – 1.607)	0.254 (-0.186 – 0.694)	0.792 (0.030)	<0.001 (0.556)	0.041 (0.169)
SSC	88.04 $\pm$ 10.24	95.73 $\pm$ 15.27 *	0.537 (0.186 – 0.888)				

(Continued)

<b>MAP (mmHg)</b>							
<i>Peak</i>							
LSC	113.88 ± 11.36	139.66 ± 15.12	1.805 (1.253 – 2.357)		0.309	<0.001	0.003
SSC	117.11 ± 12.26	130.02 ± 18.06 *	0.762 (0.387 – 1.138)	0.559 (0.025 – 1.092)	(0.045)	(0.798)	(0.331)
<i>Mean</i>							
LSC	105.17 ± 11.53	121.47 ± 14.06	1.214 (0.698 – 1.73)		0.601	<0.001	0.094
SSC	106.55 ± 11.05	117.08 ± 16.21	0.706 (0.29 – 1.121)	0.279 (-0.177 – 0.735)	(0.012)	(0.637)	(0.117)
<b>RPP (bpm x mmHg x 10-3)</b>							
<i>Peak</i>							
LSC	16.51 ± 3.56	23.42 ± 4.33	0.993		<0.001	<0.001	<0.001
SSC	15.59 ± 2.91	18.22 ± 3.58 *	0.867	0.967	(LSC:0.583; SSC:0.417)	(5F:0.349; 5L:0.651)	<0.001
<i>Mean</i>							
LSC	14.02 ± 2.15	19.62 ± 3.88	1.459 (1.038 – 1.88)		0.001	<0.001	<0.001
SSC	13.70 ± 2.59	15.72 ± 3.34 *	0.624 (0.324 – 0.923)	1.038 (0.479 – 1.597)	(0.387)	(0.845)	(0.554)
<b>PP (mmHg)</b>							
<i>Peak</i>							
LSC	58.31 ± 10.47	71.27 ± 12.96	0.993		<0.001	0.003	0.742
SSC	52.33 ± 8.06	65.48 ± 12.33	0.987	0.407	(LSC:0.565; SSC:0.435)	(5F:0.357; 5L:0.643)	
<i>Mean</i>							
LSC	45.39 ± 8.47	52.09 ± 11.06	0.641 (0.263 – 1.018)		0.064	<0.001	0.607
SSC	41.18 ± 7.25	49.16 ± 9.84	0.861 (0.465 – 1.257)	0.271 (-0.234 – 0.775)	(0.142)	(0.572)	(0.012)

Values represent means ± SD. \*  $p < 0.05$ , differences between protocols for the values corresponding to the last five repetitions. Nonparametric effect size, expressed by  $r$ , was reported in absolute values without confident interval.

5F: first five repetitions; 5L: last five repetitions; DBP: diastolic blood pressure; HR: heart rate; MAP: mean arterial pressure; PP: pulse pressure;  $\eta^2$ : partial eta squared; RPP: rate pulse product; RTE: relative treatment effect; SBP: systolic blood pressure.

### 5.1.2. Mechanical responses

Concentric, eccentric, and total TUT of sessions were not significantly different between protocols ( $p = 0.250, 0.781, \text{ and } 0.367$  for concentric, eccentric, and total TUT, respectively). Focusing on TUT for equated number of repetitions, ANOVA revealed only a main effect of time for concentric ( $p < 0.001$ ;  $\eta^2 = 0.245$ ), with higher values in 1-10rep vs. 21-30rep ( $p = 0.003$ ) and vs. 31-40rep ( $p = 0.003$ ); and total ( $p = 0.001$ ;  $\eta^2 = 0.204$ ), and a tendency for this factor for the eccentric TUT ( $p < 0.052$ ;  $\eta^2 = 0.105$ ) (Figure 27).

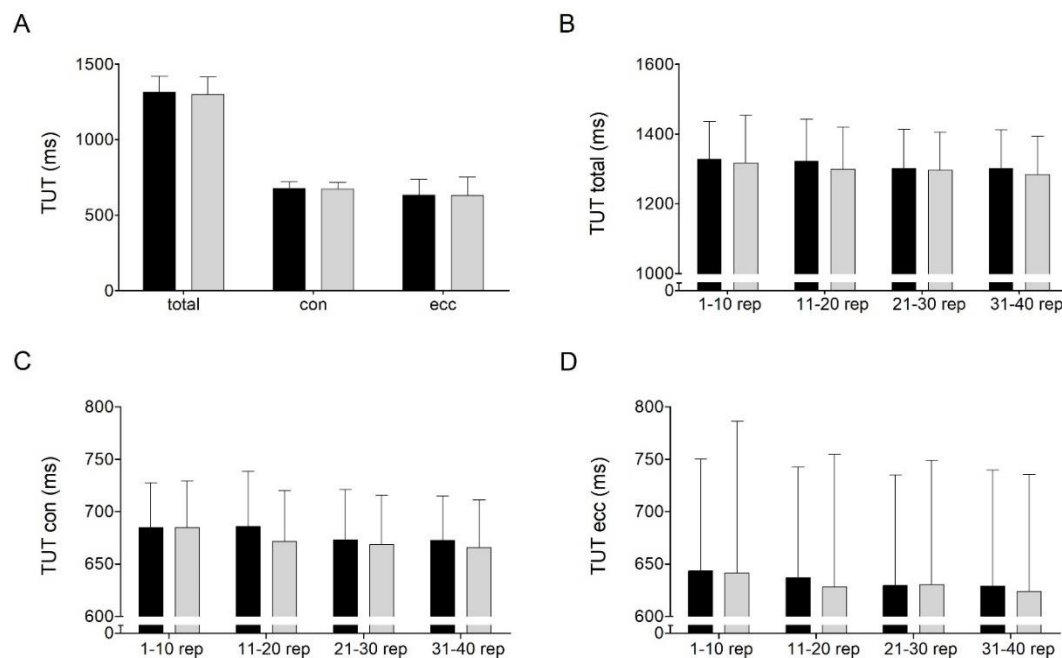


Figure 27. Time under tension (TUT). (A) Overall values of the total, concentric (con), and eccentric (ecc); (B) total, (C) concentric, and (D) eccentric TUT across the sets for long set configuration session (LSC, black bars) and a short set configuration session (SSC, grey bars). Data are displayed as means  $\pm$  SD.

Regarding the average MPV (Figure 28A), SSC reported higher values than LSC in KE ( $p = 0.020$ ;  $g = -0.515$ ; 95 % CI: -1.011, -0.019), BPR ( $p < 0.001$ ;  $g = -0.633$ ; 95 % CI: -1.133, -0.132) and SQ ( $p < 0.001$ ;  $g = -0.405$ ; 95 % CI: -0.898, 0.088). Concerning the analysis for equated number of repetitions for each individual exercise, for KE exercise (Figure 28B), the results showed main effect of session ( $p < 0.001$ ;  $\eta^2 = 0.372$ ); time ( $p = 0.010$ ;  $\eta^2 = 0.140$ ), and a session by time interaction ( $p = 0.029$ ;  $\eta^2 = 0.111$ ). For the main effect of session higher



values in SSC compared to LSC ( $p < 0.001$ ) was observed, whereas the main effect of time showed lower values in 31-40rep in comparison with 1-10rep ( $p = 0.010$ ). Post-hoc analyses showed significant lower values in 21-30rep ( $p = 0.034$ ,  $g = -0.202$ ; 95 % CI: -0.067, 0.471) and 31-40rep ( $p = 0.003$ ,  $g = 0.396$ ; 95 % CI: 0.181, 0.612) in comparison with 1-10rep in LSC. However, SSC remained stable across the groups of repetitions ( $p \geq 0.102$ ), reporting higher MPV compared to LSC for 11-20rep ( $p < 0.001$ ,  $g = 0.435$ ; 95 % CI: 0.133, 0.738), 21-30rep ( $p < 0.001$ ,  $g = 0.506$ ; 95 % CI: 0.214, 0.798), and 31-40rep LSC ( $p < 0.001$ ,  $g = 0.627$ ; 95 % CI: 0.297, 0.957). Regarding to BPR exercise (Figure 28C), only main effect of session ( $p < 0.001$ ;  $\eta^2 = 0.392$ ); time ( $p < 0.001$ ;  $\eta^2 = 0.763$ ). SSC results in a higher MPV than LSC ( $p < 0.001$ ) and a significant decrease was observed throughout the sets ( $p < 0.001$ ). Lastly, for SQ exercise (Figure 28D), the results revealed only main effect of session ( $p < 0.001$ ;  $\eta^2 = 0.405$ ), with higher MPV values for the SSC.

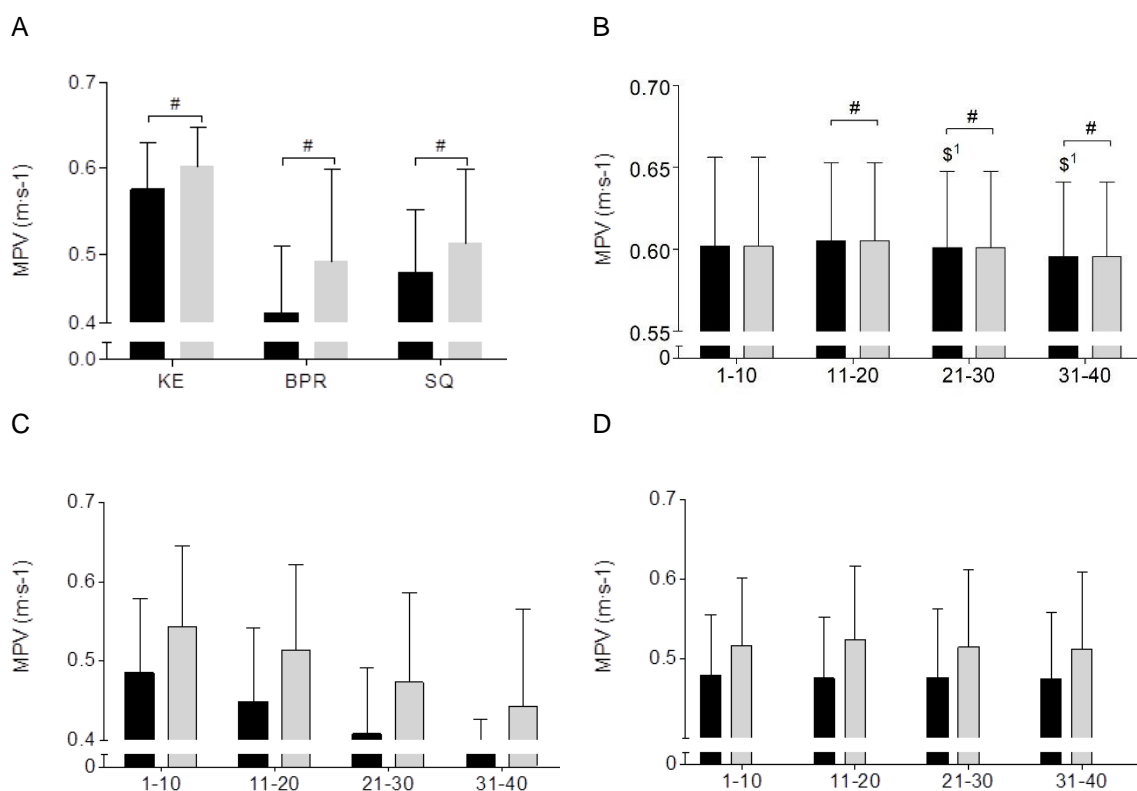


Figure 28. Average mean propulsive velocity (MPV). (A) Overall average MPV during a long set configuration session (LSC, grey bars) and a short set configuration session (SSC, black bars) for the knee extension (KE), bench press (BPR) and parallel squat (SQ) exercises; (B) Average MPV across the sets in KE exercise in LSC and SSC protocols; (C) Average MPV across the sets in BPR exercise in LSC and SSC protocols; (D) Average MPV across the sets in SQ exercise in LSC and SSC protocols. # differences between sessions. Data displayed as means  $\pm$  SD

Additionally, MMR and 5LFR were analysed (Figure 29). For MMR, SSC revealed higher values compared to LSC in KE ( $p < 0.001$ ;  $g = -0.909$ ; 95 % CI: 0.396, 1.422), BP ( $p < 0.001$ ;  $g = 0.920$ ; 95 % CI: 0.406, 1.433) and SQ ( $p = 0.001$ ;  $g = 0.564$ ; 95 % CI: 0.066, 1.061). Lastly, for 5LFR, the SSC showed higher (i.e., less negative) values in comparison with LSC in KE ( $p = 0.020$ ;  $g = 1.509$ ; 95 % CI: 0.931, 2.086), BP ( $p < 0.001$ ;  $g = 1.673$ ; 95 % CI: 1.091, 2.256) and SQ ( $p = 0.002$ ;  $g = 0.880$ ; 95 % CI: 0.351, 1.408).

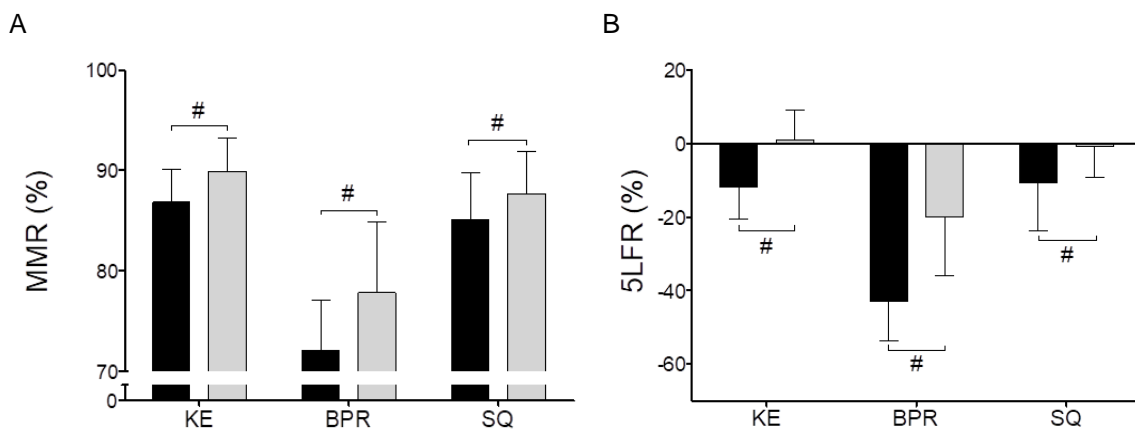


Figure 29. Maintenance of velocity calculated by the mean to the maximum ratio (MMR) (A) and velocity loss calculated as last five respect to the first five propulsive velocity ratio (5LFR) (B) during the long set configuration session (LSC, grey bars) and the short set configuration session (SSC, black bars) for the knee extension (KE), bench press (BPR) and parallel squat (SQ) exercises

## 5.2. Set configuration effects after resistance training session

### 5.2.1. Cardiovascular and autonomic response

For HR, main effect of session ( $p < 0.001$ ; RTE: 0.629, 0.598, and 0.273 for LSC, SSC, and CON, respectively), time ( $p < 0.001$ ; RTE: 0.378, 0.542, 0.540, 0.530 and 0.510 for Pre, 20-25, 25-30, 30-35, and 35-40, respectively), and a session by time interaction were detected ( $p < 0.001$ ). Post hoc analyses (Figure 30) showed higher values for all post-test epochs in LSC and SSC versus baseline ( $p < 0.001$ ) and versus CON ( $p < 0.001$ ). Furthermore, LSC data were higher in comparison with SSC during all the postexercise epochs ( $p < 0.001$  to 0.006).

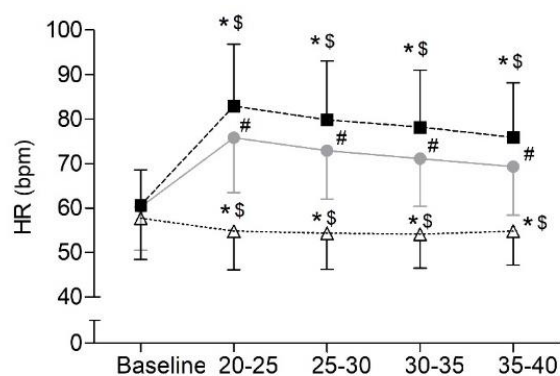


Figure 30. Heart rate (HR) before (baseline) and after a long set configuration session (LSC, in squares); a short set configuration session (SSC, in circles), and a control session (CON, in triangles). \* Within-session differences in comparison with baseline, # differences between training sessions at a specific time-period and \$ differences in comparison with CON at a specific time-period. For clarity, within session comparisons are only shown with respect to the baseline. Data are displayed as means  $\pm$  SD.

For SDNN, main effects for session ( $p = 0.004$ ; RTE: 0.416, 0.498, and 0.585 for LSC, SSC, and CON, respectively), time ( $p < 0.001$ ; RTE: 0.585, 0.451, 0.490, 0.476; and 0.498 for Baseline, 20-25, 25-30, 30-35, and 35-40, respectively), and an interaction of session by time were detected ( $p = 0.025$ ). Post hoc pairwise comparisons are shown in Figure 31A. Lower values were revealed after both experimental sessions in comparison with the CON ( $p < 0.001$ ). Nevertheless, lower values of SDNN at the 35-40 epoch were observed only after LSC with respect to the baseline ( $p < 0.001$ ). During all the postexercise measures, LSC showed lower SDNN values in comparison with SSC ( $p = 0.001$  to 0.024).

For RMSSD, neither a main effect of session ( $p = 0.238$ ; RTE: 0.457, 0.533, and 0.520 for LSC, SSC, and CON, respectively) or time ( $p = 0.070$ ; RTE: 0.578, 0.481, 0.474, 0.484, and 0.483 for baseline, 20-25, 25-30, 30-35, and 35-40, respectively) were detected, whereas a significant session by time interaction was observed ( $p = 0.013$ ). For LSC and SSC, RMSSD values after exercise were always lower in comparison with the baseline ( $p < 0.001$  to 0.002) and CON values ( $p < 0.001$ ). Furthermore, all post-training records were significantly lower in LSC when compared with SSC ( $p < 0.001$  to 0.004) (Figure 31B).

Regarding absolute HF values, neither a main effect of session ( $p=0.498$ ; RTE: 0.484, 0.496, and 0.520 for LSC, SSC, and CON, respectively) or time ( $p = 0.883$ ; RTE: 0.480, 0.486, 0.503, 0.510, and 0.520 for baseline, 20-25, 25-30, 30-35, and 35-40, respectively), nor session by time interaction were found ( $p = 0.687$ ) (Figure 31C).

Regarding HF<sub>n.u.</sub>, main effect of session ( $p < 0.001$ ; RTE: 0.364, 0.493, and 0.643 for LSC, SSC, and CON, respectively), time ( $p < 0.001$ ; RTE: 0.673, 0.495, 0.431, 0.441, and 0.460 for Pre, 20-25, 25-30, 30-35, and 35-40, respectively), and a session by time interaction were detected ( $p < 0.001$ ). Post hoc analyses (Figure 31D) showed lower values for all post-test epochs in LSC and SSC versus both the baseline and CON in all the epochs ( $p < 0.001$  to 0.031) except the 30-35 min period after SSC. Furthermore, LSC data were consistently lower in comparison with SSC during all the postexercise epochs ( $p < 0.001$  to 0.021).

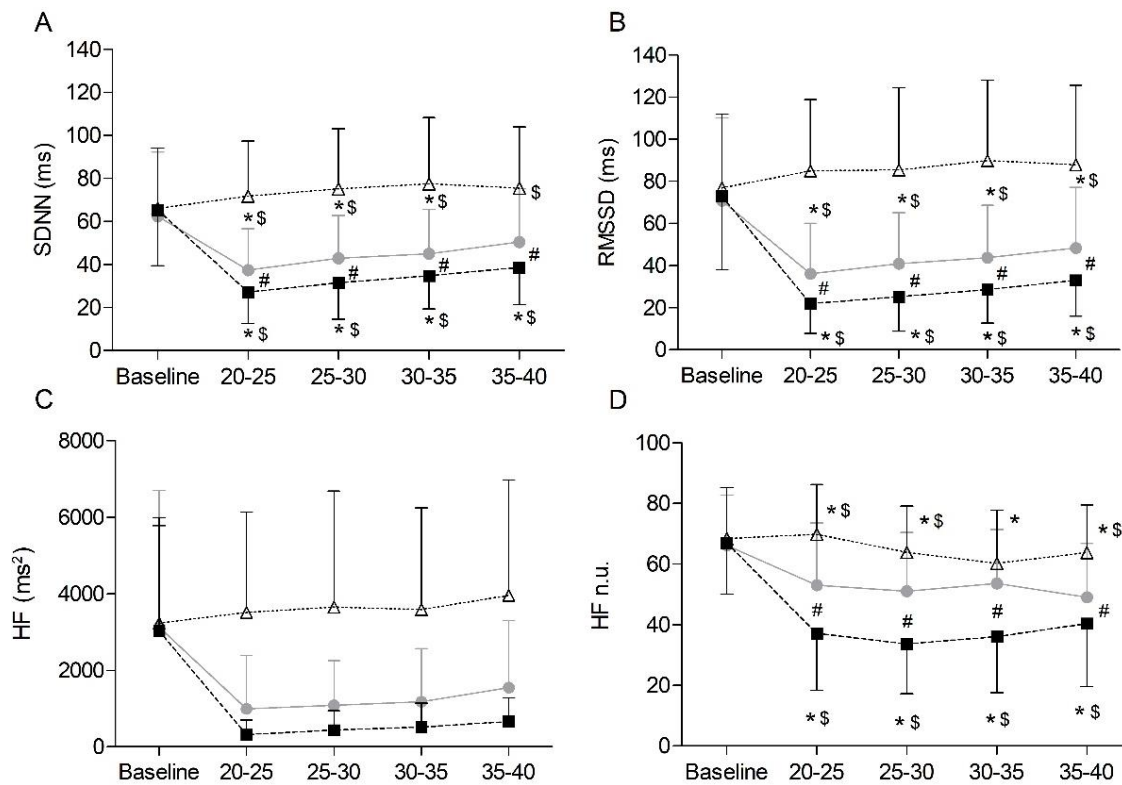


Figure 31. Cardiac autonomic control before (baseline) and after a long set configuration session (LSC, in squares); a short set configuration session (SSC, in circles), and a control session (CON, in triangles). (A) Standard deviations of pulse intervals (SDNN); (B) Root mean square of differences between adjacent PI (RMSSD); (C) High-frequency PI spectral power in absolute values (HF); (D) High-frequency PI spectral power in normalized units (HF n.u.). \* Within-session differences in comparison with baseline, # differences between training sessions at a specific time-period and \$ differences in comparison with CON at a specific time-period. For clarity, within session comparisons are only shown with respect to the baseline. Data are displayed as means  $\pm$  SD.

For  $BRS_{count}$ , a main effect for session ( $p < 0.001$ ; RTE: 0.567, 0.552, and 0.381 for LSC, SSC, and CON, respectively) and a session by time interaction were detected ( $p=0.011$ ). Nevertheless, a time effect was not observed ( $p = 0.212$ ; RTE: 0.468, 0.529, and 0.503 for baseline, 20-30, and 30-40, respectively). For all periods after training, LSC ( $p = 0.042$  and  $p=0.006$  for 20-30 and 30-40 epochs, respectively) and SSC ( $p = 0.002$  for both posttest epochs) showed higher values of  $BRS_{count}$  in comparison with CON. There were no differences between LSC and SSC at any postexercise time-period (Fig. 30A).

Regarding  $BRS_{slope}$ , neither a main effect for session ( $p = 0.230$ ; RTE: 0.461, 0.498, and 0.541 for SSC, LSC, and CON, respectively) or time ( $p = 0.387$ ; RTE: 0.472, 0.533, and 0.495 for Pre, 20-30, and 30-40, respectively) were observed. On the other hand, a significant session by time interaction was detected ( $p < 0.001$ ). In this sense, for all after training periods, lower values for  $BRS_{slope}$  were obtained after both LSC ( $p < 0.001$  in both periods) and SSC ( $p < 0.001$  and  $p=0.001$  for 20-30 and 30-40, respectively), in comparison with CON. In this regard, LSC presented lower values at each after training epoch in comparison with SSC ( $p < 0.001$  and  $p=0.002$  for 20-30 and 30-40 min, respectively). Additionally, both LSC and SSC presented lower values at the period 20-30 in comparison with the baseline ( $p < 0.001$  and  $p=0.001$ , respectively). However, at the period 30-40 min, the difference with respect to the baseline was still significant in LSC ( $p < 0.001$ ), but not in SSC ( $p = 0.053$ ) (Fig. 30B).

Regarding BEI, only 24 participants were analysed because of missing data. Neither main effect of session ( $p = 0.261$ ; RTE: 0.454, 0.531, and 0.514 for LSC, SSC, and CON, respectively) nor time ( $p = 0.254$ ; RTE: 0.540, 0.487, and 0.473 for baseline, 20-30, and 30-40 min, respectively) were detected. Nevertheless, a significant session by time interaction was observed ( $p = 0.029$ ) such that BEI decreased in LSC after the 20-30 min period time in comparison with baseline ( $p = 0.017$ ), but no significant differences were detected after SSC. However, recovery was only observed during SSC, where there were higher values during the 20-30 min period in comparison with the 30-40 min one ( $p = 0.006$ ) (Fig. 30C).

Regarding  $LF_{SBP}$ , our analysis did not detect neither main effect of session ( $p = 0.609$ ; RTE: 0.512, 0.514 and 0.473 for LSC, SSC, and CON, respectively), time ( $p = 0.141$ ; RTE: 0.461, 0.529, and 0.509 for baseline, 20-30, and 30-40, respectively), or session by time interaction ( $p = 0.104$ ) (Fig. 30D).

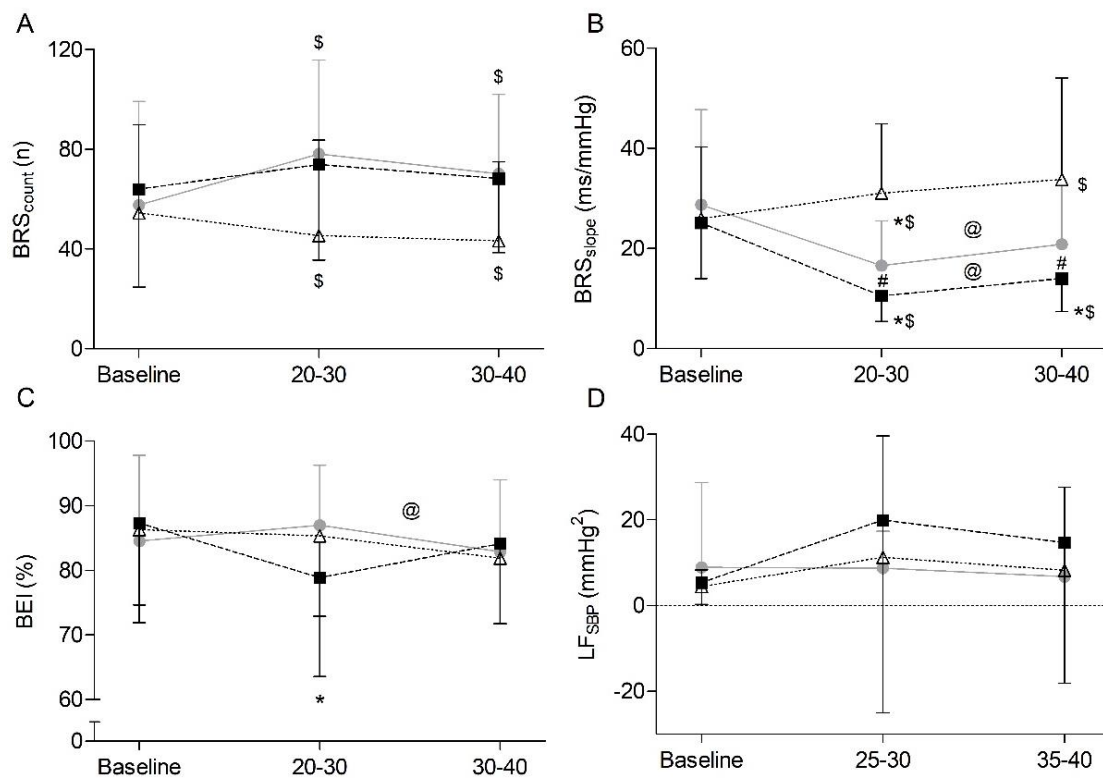


Figure 32. Cardiac baroreflex control and sympathetic vasomotor tone before (baseline) and after a long set configuration session (LSC, in squares), a short set configuration session (SSC, in circles), and a control session (CON, in triangles). (A) Number of baroreceptor sequences detected (ramps simultaneous in systolic blood pressure [SBP] and pulse intervals;  $BRS_{count}$ ); (B) Magnitude of the baroreflex sensitivity ( $BRS_{slope}$ ); (C) Baroreflex effectiveness index (BEI); (D) Low frequency of SBP ( $LF_{SBP}$ ). \* Within session differences in comparison with baseline, @ differences between epochs, # differences between training sessions at a specific time period and \$ differences in comparison with CON at a specific time period. Data are displayed as means  $\pm$  SD.

The effect size with respect to baseline values for the cardiac autonomic modulation and cardiac baroreflex response are reported in Table 7, whereas effect size of between experimental sessions are illustrated in Table 10.

## RESULTS

Table 9. Effect sizes (Matched Pair Rank Biserial Correlation,  $r$ ) for cardiac parasympathetic autonomic and baroreflex control with respect to the baseline across sessions. Positive values of effect size indicate higher values in comparison with the baseline, whereas a negative effect size indicates decreases in values in comparison with the baseline.

	20-25	25-30	30-35	35-40
<b>SDNN (ms)</b>				
LSC	-0.99	-0.95	-0.94	-0.96
SSC	-0.91	-0.81	-0.73	-0.52
CON	0.51	0.57	0.65	0.57
<b>RMSSD (ms)</b>				
LSC	-1.00	-0.99	-0.98	-0.98
SSC	-0.93	-0.89	-0.80	-0.76
CON	0.51	0.51	0.61	0.49
<b>HF<sub>n.u.</sub></b>				
LSC	-0.98	-1.00	-1.00	-0.98
SSC	-0.67	-0.70	-0.60	-0.80
CON	0.08	-0.41	-0.48	-0.33
	20-30	30-40		
<b>BRS<sub>count</sub> (n)</b>				
LSC	0.19	0.11		
SSC	0.45	0.36		
CON	-0.44	-0.49		
<b>BRS<sub>slope</sub> (ms/mmHg)</b>				
LSC	-0.99	-0.89		
SSC	-0.71	-0.48		
CON	0.57	0.41		
<b>BEI (%)</b>				
LSC	-0.61	-0.33		
SSC	0.12	-0.26		
CON	-0.11	-0.52		

LSC: long set configuration session, SSC: short set configuration session, CON: control session. SDNN: standard deviations of pulse intervals. RMSSD: root mean square of differences between adjacent PI. HF: high-frequency PI spectral power in absolute values. HF<sub>n.u.</sub>: high-frequency PI spectral power in normalized units. BRS<sub>count</sub>: Number of baroreceptor sequences detected. BRS<sub>slope</sub>: magnitude of the baroreflex sensitivity. BEI: Baroreflex effectiveness index.

Table 10. Effect sizes (Matched Pair Rank Biserial Correlation,  $r$ ) for cardiac parasympathetic autonomic and baroreflex control for between groups comparison. Positive values of effect size indicate higher values (i.e., lower reductions) for short set configuration, whereas a negative effect size indicates higher for long set configuration.

	LSC vs. SSC			
	20-25	25-30	30-35	35-40
<b>SDNN (ms)</b>	0.74	0.68	0.54	0.61
<b>RMSSD (ms)</b>	0.82	0.83	0.76	0.65
<b>HF<sub>n.u.</sub></b>	0.76	0.82	0.90	0.55
	20-30	30-40		
<b>BRS<sub>count</sub> (n)</b>	0.11	0.10		
<b>BRS<sub>slope</sub> (ms/mmHg)</b>	0.79	0.69		
<b>BEI (%)</b>	0.49	-0.06		

LSC: long set configuration session, SSC: short set configuration session, CON: control session. SDNN: standard deviations of pulse intervals. RMSSD: root mean square of differences between adjacent PI. HF: high-frequency PI spectral power in absolute values. HF<sub>n.u.</sub>: high-frequency PI spectral power in normalized units. BRS<sub>count</sub>: Number of baroreceptor sequences detected. BRS<sub>slope</sub>: magnitude of the baroreflex sensitivity. BEI: Baroreflex effectiveness index



For BP, no main effects or interactions were observed among factors ( $p > 0.05$ ) for any parameter. Absolute and percentage changes of SBP, DBP and MAP, and ANOVA results for these variables are shown in Table 11.

Table 11. Baseline and postexercise blood pressure values in the long set configuration (LSC), short set configuration (SSC) and control (CON) session.

session	Baseline (mean $\pm$ SD)	20-30 (mean $\pm$ SD)	30-40 (mean $\pm$ SD)	$\Delta\%$ 20-30/Baseline	$\Delta\%$ 30-40/Baseline	p-value		
						session	time	s x t
<b>SBP (mmHg)</b>								
LSC	108 $\pm$ 14	111 $\pm$ 9	111 $\pm$ 10	5.44 $\pm$ 23.52	4.46 $\pm$ 22.35	0.967	0.075	0.712
SSC	110 $\pm$ 13	110 $\pm$ 10	110 $\pm$ 10	0.25 $\pm$ 13.46	1.05 $\pm$ 16.15			
CON	111 $\pm$ 13	108 $\pm$ 8	109 $\pm$ 10	-1.62 $\pm$ 11.13	1.02 $\pm$ 4.35			
<b>DBP (mmHg)</b>								
LSC	67 $\pm$ 13	67 $\pm$ 5	66 $\pm$ 7	1.65 $\pm$ 14.34	-0.18 $\pm$ 15.23	0.512	0.861	0.972
SSC	65 $\pm$ 10	66 $\pm$ 9	66 $\pm$ 8	5.25 $\pm$ 22.03	5.97 $\pm$ 29.42			
CON	65 $\pm$ 9	65 $\pm$ 8	66 $\pm$ 9	1.10 $\pm$ 13.16	0.19 $\pm$ 3.80			
<b>MAP (mmHg)</b>								
LSC	82 $\pm$ 8	83 $\pm$ 6	82 $\pm$ 7	1.21 $\pm$ 10.03	0.57 $\pm$ 10.64	0.926	0.096	0.785
SSC	83 $\pm$ 11	83 $\pm$ 8	83 $\pm$ 8	1.63 $\pm$ 14.95	2.83 $\pm$ 19.25			
CON	83 $\pm$ 10	82 $\pm$ 8	83 $\pm$ 9	-0.17 $\pm$ 11.37	0.78 $\pm$ 3.51			

SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure;  $\Delta\%20-30$ /Baseline: Percentages changes between 20-30 epoch and baseline;  $\Delta\%30-40$ /Baseline: Percentages changes between 30-40 epoch and baseline

### 5.2.2. Metabolic response

Blood lactate concentration after resistance training was 6.13 mmol  $\cdot$  L<sup>-1</sup> for the SSC, whereas LSC achieved 11.34 mmol  $\cdot$  L<sup>-1</sup>. The Wilcoxon signed-rank test performed for  $\Delta\%Lt$ , showed higher lactatemia changes regarding to baseline ( $p < 0.001$ ;  $g = -1.079$ ;  $CI = -1.598 - -0.560$ ) after LSC ( $84.8 \pm 6.8\%$ ) in comparison with SSC ( $69.5 \pm 18.6\%$ ) (Figure 33).

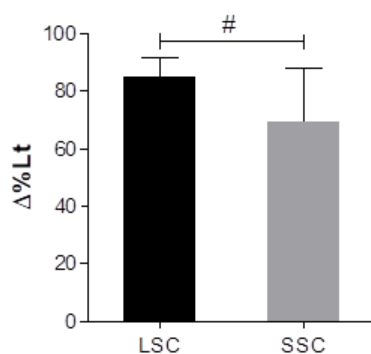


Figure 33. Percentage change of lactatemia ( $\Delta\%Lt$ ) in long set configuration session (LSC, black bars) and a short set configuration session (SSC, grey bars). # differences between training sessions.



## DISCUSSION

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The main findings of the present thesis were that: (i) despite the differences in the intensity of effort (SSC: 33% vs. LSC: 67%), both protocols resulted in a similar overall BP response during a RE, namely the KE exercise; (ii) the BP evolution across sets was different between protocols, reporting only the LSC a progressive evolution; (iii) the LSC reported higher peak values of SBP and DBP in the last repetitions; (iv) the set configuration affects to the chronotropic and an estimated myocardial oxygen demand, reporting lower HR and RPP responses during the SSC; (v) cardiac parasympathetic modulation after a whole-body RT session was affected by set configuration, since although both conditions produced a reduction of cardiac parasympathetic modulation, the LSC produced a greater drop in comparison with the SSC; (vi) neither protocol reported postexercise BP adjustments or sympathetic vasomotor tone changes after session; (vii) the set configuration affects to the glycolytic involvement and mechanical performance, entailing greater relative increase in lactate concentration after session and a prominent velocity loss in LSC compared to SSC.

## 6.1. Set configuration effects during resistance exercise

### 6.1.1. Cardiovascular response

The results revealed that when intensity, volume and resting time are equated, performing a bilateral KE exercise differing in the set configuration did not promote differences in the pressure response for the whole exercise. However, the BP evolution through the exercise was different between protocols despite overall values rose in a similar magnitude in both sessions (i.e., there are no differences for the overall peak and mean values of SBP, DBP and MAP, but there are differences in how these values rise over the sets).

The peak and mean values of SBP, DBP and MAP increased in LSC throughout the sets, being approximately stable after an accumulated volume of around 30 repetitions. In contrast, the values kept similar after the first 20 repetitions in SSC. Moreover, LSC achieved higher peak values of SBP and DBP in the last 10 repetitions (i.e., from 31st to 40th repetition) than SSC. Furthermore, differences were observed for overall peak and mean values of HR and RPP, revealing greater chronotropic response and a higher estimated myocardial oxygen demand during the LSC protocol. Particularly, the  $HR_{peak}$  was consistently higher in LSC than in SSC for all the sets. Besides, the  $RPP_{mean}$  increased until the last set in LSC, whereas in SSC it remained stable after the first 10 repetitions and remained consistently lower.

The literature shows dissimilar BP responses to different configurations of the set. Baum et al. (262) reported that introducing 3 s rest between repetitions (intermittent mode) lowered the BP response compared to continuous mode. These differences may be because of the rest disbalance between protocols, as the time between repetitions was added to the time between sets, implying a longer total resting time in the intermittent session (156). Nevertheless, a study by da Silva (264) reported no differences in SBP comparing a continuous design to two discontinuous structures with 5 or 15 s of rest in the middle of the sets. In this case, discontinuous protocols also showed longer total rest times with the inclusion of the respective intra-set rests. Conversely, other investigations have demonstrated that discontinuous KE protocols with short pauses between sets (2 to 10 s) (265,266) or an inter-repetition rest design (268) promoted higher BP response compared to a continuous one. In the first two studies, although the time between blocks of repetitions of the discontinuous structures was added to the total rest time (assuming more rest time), it was insufficient to reduce the pressure response and produced higher values during the repetitions after the intra-set rest (266) and after the completion of the set (265). Regarding the study by Mayo et al. (268), the authors reported that performing repetition-to-repetition leg presses with 18.5

seconds of rest resulted in a greater peak blood pressure response compared to a continuous design with the same work-to-rest ratio performing 5 sets of 8 repetitions with 3 minutes of rest between repetitions. This is in line with the findings of Paulo et al. (269). They reported that, even though protocols with an intensity of effort of 75% produced the highest peak of SBP and DBP changes during exercise compared to protocols with shorter structures (25% and 5%), performing the exercise repetition by repetition (5% intensity of effort) resulted in a higher pressor response than the 25% protocol. Lastly, a study by Iglesias-Soler et al. (267) revealed that two equated high-intensity protocols differing in the set configuration (i.e., traditional set reaching muscular failure session vs. inter-repetition rest session) achieved differences regarding overall SBP as only the traditional protocol increased the BP values across the sets. The differences in the load intensity, the type of set configuration used (basic cluster sets, inter-repetition rest sets, etc.), a dissimilar work-to-rest ratio, the insufficient resting time between repetitions or groups of repetitions, the total mass involved, the type of exercise (i.e., lower vs. upper limbs, or eccentric-concentric vs. concentric-eccentric fashion), and including or not Valsalva manoeuvres, and the higher differences in the intensity of effort managed (reaching or not the muscle failure), may be the reasons for the discrepancies between our findings and the literature as these factors can modulate the pressure response. Particularly, the latter reason is paramount as the management of the end of the set would provoke differences in physiological demand (224,225,234) and on peak BP values.

On the other hand, as explained above, when several repetitions were performed during a RE, a V-shape BP response is achieved (28). Mayo et al. (268) and Paulo et al. (269) have suggested that to benefit from V-shape BP response to resistance exercise some repetitions in a row must be performed. This is because extremely short set structures such as inter-repetition rest set configuration do not produce this shape in the BP responses and may even promote higher peak SBP values than longer or continuous structures. In our work, the results

corresponding to the epochs with equal work and rest time (i.e., 5F and 5L) confirmed this hypothesis since a similar response for the first five repetitions was revealed. In contrast, differences between protocols were observed in all the cardiovascular parameters for the 5L. Thus, our results suggest that more frequent sets would initially promote a slightly higher pressure response, whereas long set configurations would entail greater cardiovascular response as fatigue is accumulated. In this sense, the analysis of blood pressure under the curve analysis reinforces these results, as higher  $AUC_{SBP}$ ,  $AUC_{DBP}$  and  $AUC_{MAP}$  were observed in the LSC compared to SSC in the last 10 repetitions. In this regard, first repetitions of the SSC protocol require an extra effort due to the absence of the stretch-shortening cycle and demand stronger and more frequent Valsalva manoeuvre, affecting the initial average response as reported in previous studies (265,266). Furthermore, SSC entails repetitive central command activation that promotes several autonomic adjustments that trigger a sharp increase of BP (40,285,286). On the other hand, when fatigue is present after several repetitions, the LSC protocol would promote higher BP response due to the greater metabolic demand (29) and the subsequent metaboreflex activation (40,285,286). In addition, fatigue would also affect the extent and intensity of the Valsalva manoeuvre performed in the last repetitions of these sets (30). Therefore, our data suggest that a short set structure might mitigate the cardiovascular responses to RE when several repetitions and sets are completed.

Regarding HR and RPP responses, SSC attenuated both peak and mean HR and RPP responses compared to the LSC protocol. These findings agree with most previous studies that demonstrated that discontinuous structures reduced maximal (262,266,269) and mean HR values (264,268). However, other research has reported no differences in the HR response between long and short configurations (265–267), or even higher mean HR values in short sets (272). Particular protocol characteristics might account for the differences observed between studies. Iglesias-Soler et al. (267) showed similar global HR responses, but the traditional



structure promoted higher HR across the last two sets in comparison with the inter-repetition rest protocol. Besides, the small muscle mass involved in the unilateral KE exercise implemented by Polito et al. (265) produced small HR increases in both protocols, reducing the potential effects between protocols. Another study using deep back squat (272) reported lower peak HR but higher mean HR in a short set configuration compared to a traditional one. The differences in the type of contraction (i.e., first eccentric, then concentric) and the total amount of muscle mass involved) may be the reasons for the discrepancies with our findings. Regarding RPP response, several investigations agree with our peak (262,269) and mean RPP (264,267) findings. However, because RPP depends on HR and SBP, the fact that in some studies the short sets promoted higher SBP responses may explain that some authors found no difference (268) or higher RPP values (265) versus the long sets.

Moreover, the cardiovascular effects of set configuration on special populations have also been studied. Although in our case the participants were healthy and young individuals, the results obtained by Ribeiro-Torres et al. (270) agree with ours. They reported that an inter-repetition rest training protocol promotes lower cardiovascular stress during high intensity KE exercise in elderly coronary patients. Similar conclusions were reported by Paulo et al (272), as they observed smaller increases in cardiovascular load during a short set structure in medicated hypertensive individuals than during a longer protocol. Contrary, Dello Iacono et al. (287) reported that an inter-repetition rest and a double-repetition set structures induced higher HR than longer or traditional sessions in older men performing a back squat exercise. The impaired autonomic function observed in this population (288) and the reduced rest time between sets may explain the high cardiac impact of those designs.

### 6.1.2. Mechanical response

Mechanical measurements analysis showed a lower velocity loss during the short set configuration exercises performed versus the long set design. Specifically, average MPV values were higher for the SSC compared to the LSC in all exercises evaluated (i.e., KE, BPR and SQ). With respect to velocity maintenance, higher values were observed for the SSC throughout all exercises when comparing the mean velocity with the peak velocity achieved for each exercise. Finally, the analysis of velocity loss, as measured by the 5LFR, showed again lower velocity losses for the SSC compared to the LSC in all the exercises. In fact, for the KE exercise, it can be observed that in the SSC the 5LFR was higher than 0, meaning that in the last five repetitions the participants were able to mobilise the load much faster than in the first five repetitions.

These results are coincident with the findings of two recent meta-analysis (224,225) who concluded that short set configurations maximise the neuromuscular performance and attenuate the loss of velocity during an RT session. Likewise, other studies of acute effects also reported a greater loss of velocity during longer sets for different RE. In this sense, a study by Fariñas et al. (289) analysed the loss of velocity considering the values of the first and the last repetition of each session throughout an entire training programme. The authors reported higher percentages of velocity loss for long sets compared to short structures for the unilateral biceps curl exercise. In the same line, the recent work by Rial-Vázquez et al. (234) examined the velocity loss and the velocity maintenance in BPR and SQ by analysing six different variables. Three of these are the ones used in this study, but with the exception that the ratio between the last repetitions and the first repetitions was calculated by including only two repetitions, as in their cluster configuration participants performed sets of two repetitions. As in our study, they found greater velocity maintenance and lower velocity loss for the shorter sets during their interventions in both exercises. However, contrary to our results, authors only found differences in average MPV between configurations for the squat

## 6.2. Set configuration effects after resistance training session

### 6.2.1. Cardiovascular and autonomic response

Results from this study indicated that set configuration affects the postexercise cardiac parasympathetic modulation after a whole-body RT session including several exercises when load intensity (15RM), total volume (200 repetitions) and total rest time (360 s between sets for each exercise and 3 min between exercises) are equated. Specifically, our data demonstrate that the long set configuration produces a significantly greater reduction of cardiac parasympathetic modulation in comparison with the short set configuration during the 40 min postexercise. These results are a novelty since, as far as we know, this is the first study investigating the set configuration effect after a whole-body RT session composed of a series of exercises that match a more traditional style of RT. Some studies have explored the set configuration effect using a single-exercise model (233,267,273,274) limiting the applicability to typical training protocols routines including several exercises. Iglesias-Soler et al. (267) showed no differences in cardiac parasympathetic modulation recovery while comparing an inter-repetition rest set versus a set to failure during the first postexercise minutes. On the contrary, and in line with our results, Mayo et al. (233) showed that a long set configuration with a high intensity of effort (8/10, i.e., 80%) and a short set (4/10, 40% intensity of effort) elicited higher reductions of cardiac parasympathetic modulation than a session with a very short set (1/10, i.e., 10%). Moreover, Mayo et al. (273) also revealed that longer sets to failure caused a higher loss of cardiac vagal control, while an inter-repetition protocol was scarcely affected when a squat or bench press exercise session is performed. Lastly, the recent study by Kassiano et al. (274) corroborated that, despite their four squat exercise protocols reducing the parasympathetic cardiac control, the inter-repetition rest session produced the least withdrawal. These findings, along with those of the present study, indicate that the type of set

configuration used determines the magnitude reductions of the cardiac parasympathetic modulation when the rest of loading parameters are maintained equated.

Previous investigations have reported that HR is, by itself, a surrogate of autonomic activity (290) both at rest (279) and during recovery (291). Therefore, both HRV and HR are good indices of increased risk of a cardiac event. In our study, the results of both parameters showed a similar trend. In fact, HR values were higher even after 20 minutes of the long set configuration. This suggests a slower HR recovery (i.e., slower parasympathetic reactivation) in this configuration, reinforcing the findings of the effect of game configuration on autonomic response.

The length of the cardiac parasympathetic modulation reduction lasted up to 40 min after both experimental sessions. Our results partially agreed with Kingsley et al. (292), who indicated that parasympathetic activity might not be fully recovered up to 30 min after an RT session composed of upper- and lower-body exercises. However, Mayo et al. (233) reported a shorter time of reduced cardiac parasympathetic modulation for short set configurations. These discrepancies may be due to several reasons. On the one hand, the whole-body multi-exercise nature of our design, which included both single and multi-joint exercise, in comparison with the one-exercise model employed by Mayo et al. (233), might partially explain the differences observed. On the other hand, the differences in the intensity of effort magnitude and total volume performed in each study might also determine the recovery of cardiac parasympathetic modulation. Whereas previous studies used fewer repetitions per session (e.g., the 40 repetitions used by Mayo et al. or the 90 repetitions by Kingsley et al., our sessions had each participant complete a total of 200 repetitions. In this sense, a previous study (195) showed that an RT session with a greater volume promotes longer reductions in

parasympathetic activity compared to sessions with a lower volume, which is in agreement with our findings.

Additionally, even though in our study the time differences only were observed until 40 min postexercise, the magnitude of the reductions suggests that the recovery length in the long set configuration could be longer in comparison with the short structure, but this is speculation.

The recovery time differences between protocols may be due to the incapacity of the baroreflex to synchronise the BP responses with changes in HR. Despite that both RT protocols promoted a reduction in BRS during recovery, the long set configuration caused a higher reduction and a slower recovery to the baseline values than the short one, suggesting that this incapacity might be particularly important in more strenuous protocols (212,292–294). These results are partially in agreement with the results obtained by Mayo et al. (233) since they only reported BRS reductions after both long and short intra-set rest configurations. Nevertheless, in that study, the reductions in comparison with baseline were significant up to 40 min for both set configurations. Discrepancies may be due to the differences between studies in the intensity of effort used. This, therefore, points to the suitability of managing the set configuration to attenuate the impact on cardiac parasympathetic modulation after RT and promote faster recovery while keeping all other loading parameters equal. Hence, short sets should be recommended when attenuating the effects of RT on cardiac parasympathetic modulation is required.

The reductions in cardiac baroreflex activity may also be produced by an increase in arterial stiffness triggered by the higher sympathetic tone of central arteries (214). Our analysis did not detect significant changes in sympathetic vascular tone, which is coincident with Queiroz et al. (215) who did not find differences in LFSBP after an RT protocol in healthy

men. Conversely, other studies showed increments of LFSBP after RT sessions (38,187,212–214). Thus, when different loading intensities were compared (187), only the heavy RE session produced significant increases in LFSBP. In turn, the studies that showed increases in vasomotor tone after the session compared to a control employed high intensity protocols (212,214), or, alternatively, moderate-low intensity protocols in hypertensive subjects (38,213), with the consequent alterations in sympathetic vasomotor activity characteristic of the pathology (295,296). These findings suggest that intensity may be a factor affecting the sympathetic vasomotor tone, and thus modulating arterial stiffness. Further studies are needed to elucidate the effect of the RT variables on vascular sympathetic tone and how the set configuration might modulate this response in high-intensity protocols.

A possible explanation for the differences in the magnitude of the reduction of the cardiac parasympathetic modulation between sessions may be the different glycolytic involvement of both protocols since the parasympathetic activity is negatively related to lactatemia (216,217). In this sense, as can be read in the Metabolic response section, the long set configuration produced higher lactatemia in comparison with the shorter one.

Regarding the BP analysis, negligible changes were observed after both RT sessions. However, a meta-analysis by Casonatto et al. (39). demonstrated that a single bout of RT decreases the BP from 60 min up to 24 hours after the session. Furthermore, Mayo et al. (273) only reported BP reductions after session when an RT protocol leading to failure was performed. Therefore, muscular failure may be a key factor in promoting BP reductions and may be a plausible reason why it was not found in our study. Possibly and according to some works by Figueiredo et al. (192,195), other loading parameters in our study were not suitable to induce the postexercise hypotension observed in other studies, such as the total volume performed, or the intensity selected. On the other hand, it has been suggested that the

hypotensive effect is mostly observed in hypertensive people (33,39,215) or, for normotensive people, individuals with a high-normal blood pressure level (184). Thus, the profile of our sample might not be suitable for inducing a hypotensive effect after an acute RT session. Moreover, as previously reported (184), not all individuals experience the PEH (only approximately 65%) and sometimes even post-exercise values increase. This may be the reason that no overall significant results were detected (i.e., at the sample level), even though some participants did exhibit reductions in BP after the resistance sessions.

Finally, sex by time by session interaction was not observed for any cardiovascular and autonomic parameters, suggesting that men and women present a comparable response to both long and short set configurations. Similar to our findings, no significant sex by time by session interactions were observed after performing a multi-exercise whole-body RT protocol on several indicators of cardiac and baroreflex control (212,297). However, as these authors point out, women have certain particularities in cardiovascular response after their protocol. Several works have also demonstrated that healthy, young and sedentary women have higher vagal modulation and sympathovagal balance at rest compared with men (298–301) but evidence in physically active and/or athletic women is scarce. More research is therefore needed, with larger female samples and monitoring the different women-specific physiological variables, in order to determine whether or not there are differences in the cardiovascular response to resistance exercise between the sexes.

### 6.2.2. Metabolic response

In agreement with previous studies (228,236,242) and the recent meta-analysis (225), blood lactate concentration was higher after the long set configuration compared with the shorter structure. This suggests that even when performing the same number of repetitions, with the same load and the same total rest time, performing the session with short sets

reduces glycolytic involvement compared to the longer ones. Specifically, our LSC produced almost twice the blood lactate concentration compared to the SSC (6.13 mmol ·L<sup>-1</sup> for the SSC and 11.34 mmol ·L<sup>-1</sup> for LSC), in line with previous investigations (234,240).

As previously mentioned, the glycolytic involvement may explain the reductions in parasympathetic activity after exercise. In this sense, although lactate values have only been measured minutes after the session, as stated by other authors, structures with equal work-rest ratio but shorter sets produce lower lactate concentrations (238), and a slower recovery to the baseline values (239) than sets with a longer set configuration. Hence, we can suggest that the lactate production achieved in each session may be one of the factors influencing the differences in the magnitude of the cardiac parasympathetic withdrawal after session and his evolution during recovery.



## CONCLUSIONS

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The conclusions of this thesis are described in the following.

- Both set configuration protocols benefit from the V-shape BP response advantage and entail similar overall BP responses during moderate-intensity KE exercise.
- Long set configuration with an intensity of effort of 67% produces a progressive and incremental BP response throughout the sets, whereas the short set configuration with an intensity of effort of 33% maintains a stable BP pattern from its first sets during a moderate-intensity KE exercise.
- Long set configuration with an intensity of effort of 67% achieve higher peak values of SBP and DBP in the last repetitions in comparison with the short set configuration with an intensity of effort of 33% during a moderate-intensity KE exercise.
- Greater overall chronotropic response and a higher estimated myocardial oxygen demand are exhibited by the long set configuration with an intensity of effort of 67% compared to short sets with an intensity of effort of 33% during a moderate-intensity KE exercise.
- Lower peak heart rate and mean rate pressure product values are achieved throughout sets in the short set configuration with an intensity of effort of 33% than the long set with an intensity of effort of 67% during a moderate-intensity KE exercise.
- Both long (intensity of effort of 67%) and short (intensity of effort of 33%) set configuration reduce the cardiac parasympathetic activity after a moderate-intensity high-volume resistance training session composed by several whole-body exercises.
- A short set configuration with an intensity of effort of 33% attenuates the cardiac parasympathetic activity withdrawal after a whole-body moderate-intensity RT session in comparison with the long set configuration with an intensity of effort of 67%.

- Neither the long set configuration with an intensity of effort of 67% nor the short set configuration with an intensity of effort of 33% reduce post-exercise blood pressure values after RT session compared to previous baseline.
- None of the RT protocols produce changes in sympathetic vasomotor modulation after a moderate-intensity whole-body RT session composed of several exercises, regardless of the set configuration.
- A multi-exercise RT session with a short set configuration with an intensity of effort of 33% reduces the glycolytic involvement due to the lower percentage change in lactate concentration compared to a long set configuration with an intensity of effort of 67%.
- The short set configuration with an intensity of effort of 33% promotes lower loss of mechanical performance than the long set configuration with an intensity of effort of 67% in both lower body and upper body exercises, i.e., less velocity loss and higher maintenance of velocity and mean propulsive velocity during exercise and across sets.

## LIMITATIONS OF THE STUDY

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The study of this thesis has some limitations that should be considered. Firstly, the range of intensity of effort managed in our protocols (i.e., 33% versus 67%) is small, potentially limiting the differences between protocols during exercise. Furthermore, a moderate-load intensity was used, showing more humble responses in comparison with higher intensities (19). Secondly, our data during exercise report the cardiovascular response of a single-exercise model session, which does not accurately reflect the conventional RT session composed of several exercises. Thirdly, all women were using oral contraceptive pills and performed the protocols during the mid-follicular to the late luteal phase of their menstrual cycle. In this regard, previous studies suggested that the use of oral contraceptive pills does not affect HRV during the menstrual cycle in healthy women (302). However, the effects of the menstrual cycle on cardiac autonomic modulation have not been clarified completely (303). Fourthly, some photoplethysmographic devices have reported certain limitations, as underestimating the DBP values (164). However, as previous studies have demonstrated, the photoplethysmographic method is a valid non-invasive alternative to the intra-arterial method (304,305). Moreover, despite the evidence on the validity and reliability of the cardiovascular device used in this study (277), it only provides an indirect assessment of cardiac autonomic modulation. There is extensive debate regarding the relationship between changes in cardiac variability and the activity of a particular branch of the autonomic nervous system (121). To improve the physiological interpretation of autonomic data, the study design was developed controlling the possible confounding variables such as participants conditions, respiratory rate and environmental conditions. In this sense, we controlled breathing frequency in order to avoid the effect of the increased respiratory rate after exercise on HRV measures (306). This is because the respiratory activity is involved in the change in power spectral density distribution, particularly the measures of parasympathetic modulation (HF and HF<sub>n.u.</sub>) (307,308). While breath control might have removed some experimental effects (309), the

changes are presumed to be similar between protocols based on data that paced breathing and spontaneous breathing may result in similar effects (310), however more research on this topic is pertinent. Furthermore, due to the technical limitations regarding the time spent to apply the instrumentation and calibrate the device, from the end of the session to 20 min, HR and BP were not evaluated. Further investigations with measurements during and immediately after the exercise must be carried out to assess the effect of set configuration on HR and BP kinetics. Lastly, our participants were healthy and active young adults, limiting the extrapolation of our results to other population profiles.



## FUTURE LINES OF RESEARCH

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This doctoral thesis has focused on analysing the effects of the set configuration on cardiovascular and autonomic parameters during and after resistance exercise. Considering the results obtained, it is of further interest to extend the knowledge in this line of research as well as the emergence of new related ones.

### **Load parameters, protocols, and exercises**

Future studies need to compare protocols with more widely differences in the intensity of effort or with different loads to identify which structures are suitable for reducing cardiovascular demand in relation to the other load parameters while maintaining the benefits of RE. Moreover, given the similar BP responses in both protocols and in view of the rest period being a BP modulating factor (156,158), it is plausible to hypothesise that if the SSC session had longer recovery times, the pressor response would be attenuated. Future research should investigate how combining these two factors that modulate the cardiovascular responses, shorter sets and longer rests, may attenuate the pressure response during exercise.

### **Sex-related cardiovascular and autonomic response**

Research on the physiological differences between men and women is constantly increasing. However, it has not yet been fully clarified how sex differences, as well as the female menstrual cycle itself or the use of hormone-controlling drugs, may affect different physiological responses, whether in performance, fatigue, or cardiovascular parameters.

In this sense, future research projects should include designs with a larger experimental sample of women and studies with analysis of cardiovascular, metabolic, and mechanical variables during the different phases of the menstrual cycle over several cycles and their response to RE. Other aspects to investigate would be the modification of the different acute responses throughout the female life cycle (i.e., menarche, fertility, pre-menopause,

menopause), or the effect of the use of hormonal contraceptive methods on acute responses to exercise.

### Pathological population and elderly

Several pathologies are associated with autonomic impairment, such as CVDs, diabetes mellitus, Parkinson's disease, spinal cord injury, and others. In addition, the ageing process itself produces an autonomic derailment, which increases cardiovascular degeneration in this population. At the same time, as mentioned previously in this thesis, the risk of suffering a cardiac event during and immediately after physical exercise increases in these population groups. Therefore, it is interesting to develop similar studies in these populations to determine safer RT protocols.

### Performance athlete

Recently, due to technological advances, devices have become available that allow athletes to be monitored throughout seasons and training sessions, with HRV being one of the most important variables. Therefore, it is essential to investigate which strategies will minimise these parameters in performance athletes in order to prescribe individual RT using HRV.

### Cardiovascular chronic adaptations

Successive RT sessions over time may produce different physiological adaptations, which are related to the acute responses induced by each session. In this respect, the cardiovascular and autonomic effects of set configuration need to be investigated to establish whether the acute benefits of a short set structure maintain the long-term effects of RT. These adaptations could be analysed for healthy and pathological populations as well as elderly people and performance athletes.

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# Appendix A

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Abstract of at least 3000 words in an official language





## INTRODUCCIÓN

El entrenamiento de fuerza es actualmente uno de los pilares dentro del estilo de vida saludable, convirtiéndose en una herramienta dentro de los programas de prevención y rehabilitación para diferentes patologías, dentro de las que se incluyen las enfermedades cardiovasculares (5–9). De hecho, las nuevas directrices para 2021 de la Sociedad Europea de Cardiología ya incluyen el entrenamiento de fuerza entre sus recomendaciones de actividad física (10).

Sin embargo, aunque los beneficios para la salud superan el riesgo (13), el entrenamiento de fuerza desencadena una serie de respuestas cardiovasculares y autonómicas que aumentan el riesgo de sufrir un evento cardiovascular agudo tanto durante como después de la sesión en individuos aparentemente sanos (14), y especialmente en personas con patologías que concurren con disfunción autonómica (15–18), tales como las enfermedades cardiovasculares, la diabetes mellitus o lesión medular. Los eventos cardiovasculares de riesgo ante la práctica de entrenamiento de fuerza, son entre otros, una hemorragia subaracnoidea, una disección arterial, muerte súbita cardíaca o el infarto de miocardio (17,18). Estos eventos pueden ser ocasionados por diferentes respuestas fisiológicas adversas, tales como los aumentos abruptos de presión arterial (PA) durante la realización del ejercicio de fuerza (19), y las reducciones de la modulación autonómica cardíaca tras una sesión de entrenamiento de fuerza, las cuales se mantienen hasta 30 minutos del cese del ejercicio (20).

A mayores, en los últimos años, la evaluación cardiovascular y autonómica ha comenzado a ser usada para la monitorización de los entrenamientos en sujetos sanos y deportistas (21), permitiendo evaluar el estado del deportista, así como la fatiga y

recuperación de las sesiones de entrenamiento, o los efectos a largo plazo de los diferentes mesociclos (22,23).

Por todo esto, se hace necesario desarrollar y evaluar protocolos de entrenamiento de fuerza que puedan disminuir el impacto cardiovascular y autonómico durante y después del ejercicio, manteniendo todos los beneficios asociados al mismo. Esto podría ayudar a identificar que estructuras o protocolos son más seguros y/o menos fatigantes para los diferentes grupos poblacionales que se puedan beneficiar de este tipo de ejercicio.

## **MARCO TEÓRICO**

Durante un ejercicio de fuerza se producen aumentos concomitantes de la frecuencia cardiaca (FC) y de la PA (19,28). A su vez, tras una sesión de entrenamiento de fuerza se ha observado una pérdida de control autonómico parasimpático cardíaco (204), así como un efecto hipotensor (39), i.e., la reducción transitoria pero sostenida de la PA sistólica (PAS) y/o diastólica (PAD) por debajo de los niveles de control después de un período de ejercicio.

Ambas respuestas agudas al entrenamiento están influenciadas, y por tanto pueden ser moduladas, por los diferentes parámetros de la carga (intensidad, volumen, descanso, tipo de contracción, etc.), así como por otros factores como las características de la persona o la posición durante el periodo de recuperación. Otro parámetro de la carga con el que se ha comprobado que se pueden modular tanto las repuestas como las adaptaciones al entrenamiento es la configuración de la serie. Esta se establece en función de la relación entre el número de repeticiones realizadas y el máximo número de repeticiones que es posible realizar hasta el fallo muscular en cada serie de trabajo, lo cual permite modificar la intensidad de esfuerzo de cada protocolo de entrenamiento. Bajo este parámetro se establecen dos grandes grupos. En primer lugar, un modelo de configuración de la serie tradicional, también

denominado configuración de la serie larga, la cual consiste en la realización de las series de forma continua. Frente a este diseño, se establece un modelo alternativo consistente en la modificación de los periodos de trabajo y pausa, fraccionando la serie en pequeños grupos de repeticiones. Este tipo de entrenamiento se denomina entrenamiento clúster o configuración de la serie corta (220). Investigaciones previas han revelado que de forma aguda las configuraciones de la serie cortas permiten mantener el rendimiento mecánico en términos de velocidad y potencia, reportando menores pérdidas de velocidad a lo largo de la sesión y mayores mantenimientos de la misma (224,225). A su vez, este tipo de estructuras permiten reducir la percepción del esfuerzo, así como la implicación glucolítica. Por último, con respecto a las repuestas cardiovasculares, las últimas investigaciones concluyen que durante el entrenamiento de fuerza realizar series cortas permite atenuar la respuesta de la FC y, a pesar de divergencias entre los resultados existentes, reducir la respuesta de la PA. Asimismo, tras la realización de una sesión de fuerza, la configuración de la serie corta permite atenuar la pérdida del control autonómico parasimpático cardiaco en comparación con una sesión con una estructura de la serie larga. Con respecto al efecto hipotensor del ejercicio, la evidencia muestra que son las estructuras largas, próximas o hasta el fallo muscular, las que producirán un efecto hipotensor mayor en comparación con las series cortas, las cuales podrían no llegar a producir reducciones significativas de la PA tras ejercicio. Sin embargo, hasta la fecha los estudios que analizan las repuestas cardiovasculares y autonómicas tras el entrenamiento de fuerza son realizados en diseños de un solo ejercicio, lo que limita su aplicación práctica a las sesiones convencionales de entrenamiento. Por tanto, se propone examinar que las diferentes repuestas durante y después del entrenamiento de fuerza y así poder identificar que estructuras de la serie son más seguras, permitiendo a su vez la optimización del rendimiento mecánico.

## OBJETIVOS E HIPÓTESIS

Esta tesis explorará el impacto del entrenamiento de fuerza sobre el sistema cardiovascular y su control, y cómo manipulando los diferentes parámetros de la carga (específicamente la configuración de la serie) se pueden modular las respuestas al mismo. Así, se analizarán las respuestas cardiovasculares, autonómicas, mecánicas y metabólicas de dos protocolos de entrenamiento de fuerza equiparados en intensidad, volumen y descanso total, pero con diferente configuración de la serie, es decir, con intensidades de esfuerzo diferentes.

Se hipotetiza que la configuración de la serie corta promoverá una menor respuesta hemodinámica durante el ejercicio y atenuarán la reducción de la modulación parasimpática cardíaca después de la sesión, junto con una menor pérdida de rendimiento mecánico e implicación glucolítica. Además, a pesar de prever que ningún protocolo producirá cambios en la modulación simpática vascular, la configuración de la serie larga producirá un efecto hipotensor post-ejercicio mayor en comparación con la configuración de la serie corta.

## MÉTODO

Se llevó a cabo un estudio con un diseño de medidas repetidas con 33 participantes (24 hombres y 9 mujeres), todos ellos jóvenes mayores de edad, sanos y físicamente activos, estudiantes del grado en CCAFYD y sin ninguna contraindicación médica para la realización de ejercicio con sobrecargas. Los participantes firmaron previamente un consentimiento informado para participar en el estudio aprobado por el Comité de Ética de la UDC y realizado de acuerdo con la Declaración de Helsinki.

Todos los participantes acudieron al laboratorio un total de 6 sesiones separadas en el tiempo por al menos 48 horas. Las primeras dos sesiones fueron sesiones de familiarización, a lo largo de las cuales se les explicó a los sujetos como debían realizar los ejercicios, se tomaron

mediciones para estandarizar la ejecución en todas sesiones, y se realizaron mediciones antropométricas para la posterior caracterización de la muestra. En la tercera sesión, los participantes realizaron una evaluación de la fuerza mediante un test de 15RM de cada uno de los ejercicios. Finalmente, las últimas tres sesiones se corresponden a las sesiones experimentales y la sesión control, las cuales fueron realizadas en orden aleatorio por cada sujeto. Las sesiones experimentales, compuestas por los ejercicios de extensión de rodilla, curl de bíceps, jalón al pecho, press de banca y sentadilla paralela, fueron igualadas en torno a los parámetros de la carga intensidad, volumen y descanso total. En ambas sesiones los participantes realizaron un total de 40 repeticiones con la carga del 15RM y con un tiempo de descanso total de 360 segundos para cada uno de los ejercicios, descansando 3 minutos entre ellos. Las diferencias entre protocolos fueron establecidas en base a la configuración de la serie. La sesión tradicional o también denominada configuración de la serie larga (LSC), consistió en la ejecución de 4 series de 10 repeticiones con 2 minutos de recuperación entre series. La otra sesión, la cual se denominó sesión clúster o configuración de la serie corta (SSC), se compuso de 8 series de 5 repeticiones con 51 segundos de recuperación entre series. Por último, la sesión control (CON) consistió en 80 minutos (el tiempo estimado de duración de las sesiones experimentales), donde los participantes permanecían en el laboratorio sin la realización de actividad física de ningún tipo.

En todas las sesiones se realizaron evaluaciones cardiovasculares, metabólicas y mecánicas. Para ello, una vez llegado el participante al laboratorio un dispositivo de medición cardiovascular, compuesto por un electrocardiograma y un módulo de evaluación de la presión arterial latido a latido, le era colocado. En los primeros 20 minutos de cada sesión (i.e., tanto las sesiones experimentales como la sesión control), el participante se disponía sobre una camilla en posición supina en una habitación a oscuras y en silencio (periodo de baseline). Durante la evaluación el participante debía respirar bajo un control respiratorio marcado por

un metrónomo, evitando moverse y sin hablar. En las sesiones experimentales, tras el registro cardiovascular baseline se realizaba una medición de la concentración de lactato capilar en la oreja mediante un analizador de lactato portátil. Una vez finalizados ambos pretest, los participantes realizaban un calentamiento previamente estandarizado y eran movidos a la máquina de extensión de rodilla para comenzar el protocolo que les correspondiese en esa sesión. Durante el ejercicio de extensión de rodilla, la evaluación cardiovascular (i.e., FC y PA) fue registrada desde la primera a la última repetición así como los descansos entre series. Una vez finalizado el ejercicio de extensión de rodilla los dispositivos de evaluación cardiovascular eran quitados y los participantes continuaban con la realización del resto de ejercicios que componían la sesión. Una vez completada la última repetición del último ejercicio (sentadilla paralela), se realizaba dos nuevas mediciones de concentración de lactato al primer y tercer minuto post-ejercicio. Tras estas valoraciones, los participantes volvían a la sala de valoración cardiovascular, donde se realizaron las dichas evaluaciones post-ejercicio durante 40 minutos en las mismas condiciones que durante el baseline. A mayores, durante el ejercicio de extensión de rodilla, press banca y sentadilla paralela el rendimiento mecánico fue registrado mediante un encoder.

Para el análisis cardiovascular durante ejercicio (en concreto, el ejercicio de extensión de rodilla), a mayores de los valores de baseline, se obtuvieron los valores pico y medios de FC y PA (i.e., PAS, PAD y PAM), así como el doble producto (DP) y la presión de pulso (PP). Dichos parámetros fueron obtenidos tanto para una evaluación global de todo el ejercicio (i.e., las 40 repeticiones), para la evaluación a igualdad de número de repeticiones realizadas en ambos protocolos (i.e., grupos de 10 repeticiones) y para la evaluación de periodos de repeticiones con el mismo trabajo y descanso acumulado (i.e., las cinco primeras repeticiones y las cinco últimas). A mayores, se evaluó del comportamiento de la PA en relación con el tiempo a lo

largo del ejercicio mediante el análisis del área bajo la curva de los valores medios de PAS, PAD y PAM.

Con respecto al análisis cardiovascular y autonómico pre-post ejercicio, a mayores de los valores de FC y PA se obtuvieron diferentes índices autonómicos y de la sensibilidad barorrefleja. Para la variabilidad de la frecuencia cardiaca, se emplearon registro de 5 minutos del SDNN, RMSDD, HF y HFn.u., como indicadores del control autonómico cardiaco parasimpático. Para el análisis de la sensibilidad barorrefleja, así como para la valoración de la modulación simpática vasomotora, se emplearon periodos de 10 minutos.

Para el análisis metabólico, se seleccionó el valor máximo de las dos mediciones post-ejercicio y se calculó el cambio porcentual de la lactacidemia en ambas sesiones de entrenamiento. Por último, con respecto a las variables mecánicas, la duración total de cada repetición en el ejercicio de extensión de rodilla (calculado como la suma entre la fase concéntrica y la fase excéntrica) fue tomado para realizar la correspondencia de los latidos cardíacos con las respectivas repeticiones y empleado como indicador del tiempo bajo tensión para dicho ejercicio. A mayores la velocidad media propulsiva de todos los ejercicios evaluados fue calculada, así como parámetros de mantenimiento de la velocidad o pérdidas de velocidad.

## **RESULTADOS Y DISCUSIÓN**

Los principales hallazgos de esta tesis fueron que: (i) a pesar de las diferencias en la intensidad del esfuerzo (SSC: 33% vs. LSC: 67%), ambos protocolos produjeron una respuesta global de la PA similar durante un ejercicio de fuerza, en concreto para la extensión de rodilla bilateral; (ii) la evolución de la PA a lo largo de las series fue diferente entre los protocolos, informando una evolución progresiva sólo durante la LSC; (iii) además la LSC registró valores pico más altos de PAS y PAD en las últimas repeticiones; (iv) la configuración de las series

afecta a la demanda cronotrópica y de oxígeno miocárdica estimada, alcanzando valores más bajos de FC y DP durante la SSC; (v) la modulación parasimpática cardíaca después de una sesión de entrenamiento de fuerza compuesta por varios ejercicios donde intervienen los grandes grupos musculares se vio afectada por la configuración de la serie, ya que aunque ambas condiciones causaron una reducción de la modulación parasimpática cardíaca, la LSC produjo una mayor caída en comparación con la SSC; (vi) ninguna de las sesiones informó de alteraciones de la PA después del ejercicio o cambios en la modulación vasomotora simpática; (vii) la configuración de la serie afecta a la implicación glucolítica y al rendimiento mecánico, lo que implica un mayor aumento relativo de la concentración de lactato después de la sesión y una pérdida de la velocidad en el LSC superior en comparación con el SSC.

#### *Efectos de la configuración de la serie durante del ejercicio de fuerza*

Los resultados de este estudio muestran que cuando se igualan la intensidad de la carga, el volumen y el tiempo total de descanso, la configuración de la serie no determina la respuesta presora durante ejercicio, si bien, establece diferencias en la evolución de la PA a lo largo del ejercicio. Estos hallazgos concuerdan con los obtenidos por un estudio previo (264). Sin embargo existen estudios que reportan mayores valores de PA para la sesión con una estructura larga (262) (267), o incluso para las cortas (265,266) (268). Estas conclusiones contradictorias entre estudios pueden deberse a los reducidos tiempos de recuperación entre series establecidos en ciertos protocolos, dado que es un factor principal para la respuesta presora (158). Asimismo, no todos los diseños equipararon el tiempo de trabajo y de descanso y las estructuras de la serie comparadas en algunas investigaciones incluían intensidades del esfuerzo muy dispares. Por último, y en línea con nuestros resultados, un estudio reciente mostró que a pesar de que configuraciones de la serie largas son las producen los mayores cambios en la repuesta pico de la PAS y PAD, protocolos realizados repetición a repetición



pueden promover repuestas presoras más altas en comparación a series cortas con mayor número de repeticiones (269).

Para los valores de FC y DP, nuestro estudio demostró que la configuración de la serie corta atenuaba la respuesta en comparación a las series largas. Estos hallazgos son similares con la mayoría de los estudios previos que demostraron que las estructuras discontinuas reducían tanto los valores de FC pico (262,266,269) como los promedios (264,268), a pesar de que otros estudios no han reportado diferencias (265–267), o incluso valores medios de FC más altos en las estructuras cortas (272). Estas discrepancias pueden deberse a las características específicas de dichos diseños (distintos ejercicios, con tipos de contracción diferentes, con mayor o menos masa muscular implicada, etc.). En relación al DP, la mayoría de la investigaciones coinciden con nuestros resultados, tanto para los valores pico (262,269) con los medios (264,267). Sin embargo, teniendo en cuenta que el DP depende de la FC y la PAS, esto puede explicar por qué algunos autores no encontraron diferencias entre protocolos (268) o incluso encontraron DP más altos en las sesiones con configuraciones cortas en comparación con las largas (265).

Con respecto a las variables de rendimiento mecánico, los resultados mostraron una mayor velocidad media propulsiva en todos los ejercicios durante el protocolo de configuración corta, así como un mejor mantenimiento de la velocidad y menor pérdida de la misma a lo largo de los ejercicios, tal y como han reportado estudios previos (224).

#### *Efectos de la configuración de la serie después del entrenamiento de fuerza*

Con respecto a las repuestas tras el entrenamiento de fuerza, los resultados confirman que la configuración de la serie es un parámetro modulador del control autonómico parasimpático cardíaco. Estos hallazgos son novedosos, ya que las investigaciones previas que

evaluaron el efecto de configuración de la serie sobre el control autonómico cardíaco utilizaban modelos de un solo ejercicio (233,267,273). Específicamente nuestro estudio establece que a pesar de que tanto la LSC como la SSC produjeron pérdidas de control autonómico parasimpático cardíaco, la LSC provocó una mayor pérdida de control autonómico parasimpático cardíaco tras la sesión en comparación a la SSC. En cuanto a la duración de las reducciones, nuestros resultados mostraron que la retirada parasimpática se mantuvo en ambos protocolos experimentales hasta los 40 minutos después de la sesión, si bien, las diferencias en la magnitud a los 40 minutos sugieren que la duración de recuperación en el LSC podría mayor en comparación con la estructura corta. Otros estudios han confirmado que configuraciones de la serie larga, con una alta intensidad de esfuerzo o incluso alcanzando el fallo muscular, provocaron mayores pérdidas de control autonómico parasimpático cardíaco que estructuras cortas (233,273). No obstante, el estudio realizado por Mayo et al. (233) informó que el período de reducción del control autonómico parasimpático cardíaco fue más breve para configuraciones cortas. Estas discrepancias pueden deberse al mayor volumen realizado o la mayor masa muscular implicada (195). Con respecto a la sensibilidad barorrefleja, este se vio afectado de la misma manera por la configuración de la serie. Ambas sesiones presentaron reducciones (212,292–294), aunque el LSC provocó una mayor pérdida y una recuperación más lenta a los valores basales que el SSC.

Por otro lado, al igual que en investigaciones previas (215), nuestros datos no demostraron cambios significativos en la  $LF_{SBP}$ , sugiriendo que la intensidad de la carga puede ser un factor que podría afectar a los cambios en la modulación vasomotora simpática tras ejercicio (187,212,214).

En cuanto al análisis de la PA, al contrario de lo reportado en la literatura Casonatto et al. (39), no se encontraron reducciones significativas tras ejercicio. Una posible razón es que

ningún protocolo implicaba el fallo muscular Mayo et al. (273). Por otro lado, las características de nuestros participantes (jóvenes, sanos y normotensos) podría no ser adecuado para inducir un efecto hipotensor después de una sesión aguda de fuerza (33,215).

Con respecto a la implicación glucolítica, la LSC mostró valores de lactato más altos en comparación con la SSC (238–240). Esta mayor lactacidemia, es a su vez una posible explicación de las diferencias en la magnitud de la pérdida del control autonómico parasimpático cardíaco entre protocolos (216,217).

En resumen, nuestros hallazgos sugieren que cuando personas normotensas realizan un ejercicio de fuerza, tanto una configuración de la serie corta con una intensidad del esfuerzo del 33% como una configuración de la serie larga con una intensidad del esfuerzo del 67% producen aumentos global similares en la PA. Sin embargo, la evolución de la PA a lo largo de las series es diferente en cada protocolo, con incrementos progresivos únicamente en la configuración de la serie larga, la cual alcanza valores pico superiores a la configuración corta en las últimas repeticiones. A mayores, durante la configuración corta se observa una menor respuesta cronotrópica y un menor trabajo del miocardio. Por otro lado, los resultados demuestran que tras la realización de una sesión de entrenamiento de fuerza compuesta por varios ejercicios que implican los grandes grupos musculares, a pesar de que ambos protocolos produzcan pérdidas de control parasimpático cardíaco, la configuración de la serie corta atenúa esta pérdida. Ninguna de las sesiones promovió reducciones de la PA con respecto a los valores previos al ejercicio ni cambios en el tono vasomotor simpático. Por último, la configuración de la serie corta promovió menores pérdidas de velocidad así como una implicación glucolítica menor en comparación a la configuración larga.

En conclusión, los resultados de esta tesis, junto con la evidencia científica existente, permite señalar la idoneidad de gestionar la configuración de la serie para modular tanto las

repuestas hemodinámicas durante el ejercicio de fuerza, así como para atenuar la pérdida de control parasimpático cardíaco después de una sesión, reduciendo al mismo tiempo la implicación glucolítica y permitiendo mantener el rendimiento mecánico.

## LIMITACIONES

El estudio de esta tesis no está exento de limitaciones. En primer lugar, el rango de intensidad de esfuerzo gestionado en nuestros protocolos (i.e., 33% vs. 67%) es pequeño, lo que podría limitar las diferencias entre protocolos. Además, en este estudio se utilizó una intensidad de carga moderada, mostrando respuestas más humildes de PA en comparación con intensidades más bajas (19). En segundo lugar, nuestros datos durante el ejercicio informan de la respuesta cardiovascular de una sesión de un solo ejercicio, que no refleja con exactitud la sesión de RT convencional compuesta por varios ejercicios. En tercer lugar, las mujeres incluidas en este estudio usaban píldoras anticonceptivas orales y realizaron los protocolos durante la fase folicular media a la fase lútea tardía de su ciclo menstrual. En este sentido, estudios previos sugirieron que el uso de píldoras anticonceptivas orales no afecta la variabilidad de la frecuencia cardíaca durante el ciclo menstrual en mujeres sanas (302). Sin embargo, los efectos del ciclo menstrual sobre el control autónomo cardíaco no están confirmados (303). En cuarto lugar, algunos dispositivos fotopletoográficos han reportado ciertas limitaciones, como subestimar los valores de DBP (164). Sin embargo, como han demostrado estudios previos, el método fotopletoográfico es una alternativa no invasiva válida al método intraarterial (304,305). Al mismo tiempo, a pesar de las pruebas sobre la validez y fiabilidad del dispositivo cardiovascular utilizado en este estudio (278), este sólo proporciona una evaluación indirecta de la modulación autonómica cardíaca. Existe un amplio debate sobre la relación entre los cambios en la variabilidad cardíaca y la actividad de una rama concreta del sistema nervioso autónomo (121). Para mejorar la interpretación fisiológica de los datos

autónomos, el diseño del estudio se desarrolló controlando las posibles variables extrañas como las condiciones de los participantes, la frecuencia respiratoria y las condiciones ambientales. Además, debido a las limitaciones técnicas en cuanto al tiempo empleado para colocar el instrumental y calibrar el dispositivo tras la sesión, desde el final de la misma hasta los 20 minutos posteriores, no se evaluaron ni la FC y la PA. Deben realizarse más investigaciones con mediciones durante e inmediatamente después del ejercicio para evaluar el efecto de la configuración del conjunto en la cinética de la FC y la PA. Por último, nuestros participantes eran adultos jóvenes sanos y activos, lo que limita la extrapolación de nuestros resultados a otros perfiles poblacionales, tales como personas con riesgo cardiovascular.



# Appendix B

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Informed consent





**- Hoja de información****HOJA DE INFORMACIÓN AL PARTICIPANTE**

**TÍTULO:** *Efectos agudos de la configuración de la serie del entrenamiento de fuerza en variables cardiovasculares y hemodinámicas*

**INVESTIGADOR PRINCIPAL:** Eliseo Iglesias Soler

Este documento tiene por objeto ofrecerle información sobre un **estudio de investigación** en el que se le invita a participar. Este estudio se está realizando desde la Facultad de Ciencias do Deporte y la Educación Física, Universidade da Coruña.

Si decide participar en el mismo, debe recibir información personalizada del investigador, **leer antes este documento** y hacer todas las preguntas que necesite para comprender los detalles sobre el mismo. Si así lo desea, puede llevar el documento, consultarlo con otras personas, y tomarse el tiempo necesario para decidir si participar o no.

La participación en este estudio es completamente **voluntaria**. Vd. puede decidir no participar o, si acepta hacerlo, cambiar de opinión retirando el consentimiento en cualquier momento sin obligación de dar explicaciones.

**¿Cuál es el propósito del estudio?**

El principal objetivo de este proyecto es estudiar el efecto que la configuración de la serie puede ejercer en las respuestas hemodinámicas agudas y en los cambios del control neural cardíaco.

**¿Por qué me ofrecen participar a mí?**

La selección de las personas invitadas a participar depende de unos criterios que están descritos en el protocolo de la investigación. Estos criterios sirven para seleccionar a la población en la que se responderá el interrogante de la investigación. Vd. es invitado a participar porque potencialmente cumple esos criterios, al ser una persona sana, mayor de edad y físicamente activa.

### **¿En qué consiste mi participación?**

El estudio consistirá en 2 sesiones de familiarización, 1 sesión de evaluación inicial y tres sesiones experimentales (de valoración). Salvo en una de las sesiones experimentales (sesión control: ver más abajo) usted tendrá que realizar 5 tipo de ejercicios de musculación: Leg Extension (extensión de rodilla), Leg Curl (ejercicio de isquiotibiales), Lat Pull (ejercicio de dorsal), Bench Press (press banca) y Parallel Squat (sentadilla paralela). En las sesiones de familiarización usted será formado en la correcta ejecución de los ejercicios; en la sesión de evaluación se determinará para cada ejercicio la carga con la que usted puede hacer un máximo de 15 repeticiones (15RM); las sesiones experimentales serán de tres tipos: C1, C2 y C3. La sesión C1 consistirá en la ejecución para cada ejercicio de 4 series de 10 repeticiones con la carga 15RM correspondiente; la sesión C2 implicará la realización de 8 series de 5 repeticiones de cada ejercicio; la sesión C3 o sesión control no implicará ningún tipo de trabajo físico. Antes y después de cada sesión experimental se realizarán mediciones no invasivas de variables cardiovasculares. Asimismo, antes y después de cada sesión experimental, serán realizadas punciones en el lóbulo de su oreja para obtener muestras de 0.5 microlitros (una gota) con el fin de determinar los niveles de lactato en sangre.

Para garantizar unas condiciones experimentales adecuadas se deberá:

- Realizar todas las pruebas en la misma franja horaria según la disponibilidad individual
- No ingerir alimentos, alcohol, productos con cafeína ni tabaco en las 3 horas previas a cada intervención
- No modificar de manera significativa la alimentación de los días de valoración.
- No haber realizado un esfuerzo alto o inusual 24 horas antes
- Llevar ropa y calzado adecuado y cómodo.

Es necesario que si Vd. decide participar en este estudio, se comprometa a asistir a las sesiones de toma de datos. En el momento en que la falta de asistencia sea repetida y provoque que no se cumplan los periodos de tiempo fijados, se decidirá a apartarle del estudio.

### **¿Qué riesgos o inconvenientes tiene?**

La realización de las cargas de trabajo diseñadas puede generar fatiga y dolor muscular de aparición tardía (“agujetas”). Para reducir cualquier riesgo de lesión, todas las valoraciones irán precedidas por un calentamiento específico diseñado y dirigido por un especialista. Las ejecuciones de los ejercicios serán supervisadas por al menos un investigador experimentado

Si durante el transcurso del estudio se conociera información relevante que afecte a la relación entre el riesgo y el beneficio de la participación, se le transmitirá para que pueda decidir abandonar o continuar.

**¿Obtendré algún beneficio por participar?**

No se espera que Vd. obtenga beneficio directo por participar en el estudio. El único beneficio es valorar qué tipo de metodología de entrenamiento de fuerza genera un menos estrés cardiovascular y/o una menor desestabilización del control cardiaco autónomo y reflejo.

**¿Recibiré la información que se obtenga del estudio?**

Si Vd. lo desea, se le facilitará un resumen de los resultados del estudio.

También podrá recibir los resultados de las pruebas que se le practiquen si así lo solicita. Estos resultados pueden no tener aplicación clínica ni una interpretación clara, por lo que, si quiere disponer de ellos, deberían ser comentados con el investigador principal del estudio.

**¿Se publicarán los resultados de este estudio?**

Los resultados de este estudio serán difundidos en publicaciones científicas, pero no se transmitirá ningún dato que pueda llevar a la identificación de los participantes.

**¿Cómo se protegerá la confidencialidad de mis datos?**

El tratamiento, comunicación y cesión de sus datos se hará conforme a lo dispuesto por la Ley Orgánica 15/1999, de 13 de diciembre, de protección de datos de carácter personal. En todo momento, Vd. podrá acceder a sus datos, corregirlos o cancelarlos.

Sólo el equipo investigador tendrá acceso a todos los datos recogidos por el estudio. Se podrá transmitir a terceros información que no pueda ser identificada. En el caso de que alguna información sea transmitida a otros países, se realizará con un nivel de protección de los datos equivalente, como mínimo, al exigido por la normativa de nuestro país. La transmisión de datos a terceros tiene por finalidad el realizar un análisis más exhaustivo de algunos parámetros registrados que por razones técnicas no podrían ser analizados en nuestro laboratorio.

**¿Existen intereses económicos en este estudio?**

Vd. no será retribuido por participar.

Es posible que de los resultados del estudio se deriven productos comerciales o patentes. En este caso, Vd. no participará de los beneficios económicos originados.

Todas las mediciones se llevarán a cabo en las instalaciones de la Facultad de Ciencias del Deporte y la Educación Física de la Universidade da Coruña, por lo que en ningún caso se contempla el alquiler o arrendamiento de instalaciones.

**¿Quién me puede dar más información?**

Puede contactar con Dr. Eliseo Iglesias Soler *en el teléfono 981167000 (ext.4061)* o en la dirección *de correo* [eliseo@udc.es](mailto:eliseo@udc.es) para más información.

**Muchas gracias por su colaboración.**

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**- Hoja de consentimiento informado**

**DOCUMENTO DE CONSENTIMIENTO INFORMADO**

**TÍTULO: Efectos agudos de la configuración de la serie del entrenamiento de fuerza en variables cardiovasculares y hemodinámicas**

Yo, \_\_\_\_\_

- He leído la hoja de información al participante del estudio arriba mencionado que se me entregó, he podido hablar con el investigador principal del proyecto y hacerle todas las preguntas sobre el estudio necesarias para comprender sus condiciones y considero que he recibido suficiente información sobre el estudio.
- Comprendo que mi participación es voluntaria, y que puedo retirarme del estudio cuando quiera, sin tener que dar explicaciones.
- Accedo a que se utilicen mis datos en las condiciones detalladas en la hoja de información al participante.
- Presto libremente mi conformidad para participar en el estudio.

Respeto a la conservación y utilización futura de los datos y/o muestras detallada en la hoja de información al participante,

- NO accedo a que mis datos sean conservados una vez terminado el presente estudio
- Accedo a que mis datos se conserven una vez terminado el estudio, siempre y cuando sea imposible, incluso para los investigadores, identificarlos por ningún medio
- Accedo a que los datos y/o muestras se conserven para usos posteriores en líneas de investigación relacionadas con la presente, y en las condiciones mencionadas.

En cuanto a los resultados de las pruebas realizadas,

DESEO conocer los resultados de mis pruebas

NO DESEO conocer los resultados de mis pruebas

El/la participante,

**Fdo.:**

**Fecha:**

El/la investigador/a,

**Fdo.: *investigador principal***

**Fecha:**

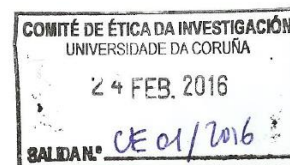
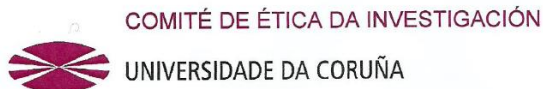
# Appendix C

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Ethical committee approval







CE 01/2016

**INFORME  
DEL COMITÉ DE ÉTICA DE LA UNIVERSIDAD DE A CORUÑA**

El Comité de Ética de la Universidad de A Coruña (CE-UDC), reunido en sesión ordinaria de 24 de febrero de 2016 y una vez estudiada la documentación presentada por D. Eliseo Iglesias Soler, Investigador Principal del Proyecto de Investigación titulado “*Efectos agudos de la configuración de la serie del entrenamiento de fuerza en variables cardiovasculares y hemodinámicas*”, estima que el mencionado Proyecto respeta las exigencias y los principios éticos y la normativa jurídica aplicables.



Por todo lo anterior, acordó por unanimidad, en el ámbito de sus competencias,

**INFORMAR FAVORABLEMENTE**

La viabilidad del Proyecto de Investigación presentado por el investigador D. Eliseo Iglesias Soler.

El Comité de Ética de la Universidad de A Coruña velará por el respeto de las exigencias y los principios éticos y la normativa jurídica aplicables durante el desarrollo del correspondiente Proyecto.

Y para que conste a los efectos oportunos, firma el presente informe en A Coruña, a 24 de febrero de 2016.



Comité de Ética  
UNIVERSIDADE DA CORUÑA

Fdo.: Rafael Colina Garea  
Presidente del CE-UDC



# Appendix D

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Scientific contributions during the pre-doctoral period



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## Papers published

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### Scientific publications derived from the present Doctoral Thesis

- **Rúa-Alonso, M.**, Mayo X., Mota, J., Kingsley, J.D., Iglesias-Soler, E. A short set configuration attenuates the cardiac parasympathetic withdrawal after a whole-body resistance training session. *Eur J Appl Physiol*. 2020 Aug; 120(8):1905-1919. doi: 10.1007/s00421-020-04424-3.
- **Rúa-Alonso, M.**, Mayo X., Rial-Vázquez J., Fariñas J., Aracama, A., Iglesias-Soler, E. Hemodynamic response during different set configurations of a moderate-intensity resistance exercise (*Under review*).

### Other scientific publications

- Rial-Vázquez J, Mayo X, Tufano JJ, Fariñas J, **Rúa-Alonso M**, Iglesias-Soler E. Cluster vs. traditional training programmes: changes in the force-velocity relationship. *Sports Biomech*. 2020 Mar 21:1-19. doi: 10.1080/14763141.2020.1718197.
- Iglesias-Soler E, Rial-Vázquez J, Boullosa D, Mayo X, Fariñas J, **Rúa-Alonso M**, Santos L. Load-velocity Profiles Change after Training Programs with Different Set Configurations. *Int J Sports Med*. 2020 Dec 22. doi: 10.1055/a-1323-3456.
- Iglesias-Soler E, **Rúa-Alonso M**, Rial-Vázquez J, Lete-Lasa JR, Clavel I, Giráldez-García MA, Rico-Díaz J, Corral MR-D, Carballeira-Fernández E and Dopico-Calvo X (2021) Percentiles and Principal Component Analysis of Physical Fitness from a Big Sample of Children and Adolescents Aged 6-18 Years: The DAFIS Project. *Front. Psychol*. 12:627834. doi: 10.3389/fpsyg.2021.627834
- Rial-Vázquez J, **Rúa-Alonso M**, Fariñas J, Aracama, A, Tufano JJ and Iglesias-Soler E. Heart rate responses and cardiovascular adaptations to resistance training programs differing in set configuration. *Res Q Exerc Sport*. 2021 doi: 10.1080/02701367.2021.2008293

### International stays

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- International stay in the Centro de Investigação em Actividade Física, Saúde e Lazer at Sports Faculty of University of Porto (FADEUP) from the 1st of March to the 31 th of May 2019.
- International stay in the Centro de Investigação em Actividade Física, Saúde e Lazer at Sports Faculty of University of Porto (FADEUP) from the 15th of March to the 16 th of May 2019.

Stays supervisor: Jorge Mota

### Grants, awards, and scholarships

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#### Grants and scholarships

- Inditex-UDC 2019 stay abroad grants for pre-doctoral students
- IACOBUS Programme—Research stays from the European Association of International Cooperation Galicia-North of Portugal.

#### Awards

- Communication award in exercise physiology and biomechanics area (X International Congress of the Spanish Association of Sports Sciences- A Coruña 2018).
- IACOBUS Programme— Scientific publications (papers) award from the European Association of International Cooperation Galicia-North of Portugal.
- Communication award in physical activity and health area (XI International Congress of the Spanish Association of Sports Sciences- Murcia 2021).

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### Conference proceedings

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- **Rúa Alonso, M.**, Iglesias-Soler, E. & Mayo, X. *Acute cardiovascular effects of set configuration of resistance training*. X International Congress of the Spanish sport science association, A Coruña (Nov 2018). Poster.
- **Rúa-Alonso, M.**; Rial-Vázquez, J; Fariñas, J. *Hemodynamic assessment by beat-by-beat blood pressure recording*. X International Congress of the Spanish sport science association, A Coruña (Nov 2018). Practical workshop
- Rial-Vázquez, J; Iglesias-Soler, E; Fariñas, J; **Rúa-Alonso, M**; Rodríguez Quintana, S. *Changes in Force-Velocity Profile performing different resistance training programmes differing in set configuration for parallel squat exercise*. X International Congress of the Spanish sport science association, A Coruña (Nov 2018). Poster.
- Rial-Vázquez, J; Iglesias-Soler, E; Fariñas, J; **Rúa-Alonso, M**; Rodríguez Quintana, S. *Changes in Force-Velocity Profile performing different resistance training programmes differing in set configuration for bench press exercise*. X International Congress of the Spanish sport science association, A Coruña (Nov 2018). Poster.
- **Rúa-Alonso, M.**, Iglesias-Soler, E., Mayo, X., Rial-Vázquez, J., Fariñas, J. *Acute changes in heart rate variability after resistance training sessions differing in set configuration*. 24th Annual Congress of the ECSS in Prague, Czech Republic (Jul 2019). Oral Communication.
- Rial-Vázquez, J., Iglesias-Soler, E., Fariñas-Rodríguez, J., **Rúa-Alonso, M.** *Changes in the location on force-velocity relationship of force and velocity performed with the 1RM load after two resistance training programs differing in set configuration*. 24th Annual Congress of the ECSS in Prague, Czech Republic (Jul 2019). Oral Communication.
- **Rúa-Alonso, M.**, Iglesias-Soler, E., Mayo, X., Rial-Vázquez, J., Farinas, J. *Acute effect on glycolytic involvement after resistance training sessions differing in set configuration*. XI Symposium on Metabolism - Ageing & Metabolism, O Porto. (Oct 2019). Poster.

- **Rúa-Alonso, M.**, Iglesias-Soler, E., Mayo, X., Rial-Vázquez, J., Farinas, J. *Similar velocity loss between men and women during resistance training sessions differing in set configuration.* International Sport Forum Congress in Madrid, Spain (Nov 2019) Oral communication.
- Rial-Vázquez, J; Iglesias-Soler, E; Fariñas, J; **Rúa-Alonso, M.** *Evolution of the velocity loss and the glycolytic involvement throughout two resistance training programmes differing in set configuration.* International Sport Forum Congress, Madrid (Nov 2019). Poster
- Carballeira-Fernández, E., Clavel-SanEmeterio, I., Rial-Vázquez, J., **Rúa-Alonso, M.**, Iglesias-Soler, E. *Estudio de la condición física relacionada con la salud en escolares de Galicia a través de la herramienta DAFIS.* Congreso Internacional CAPAS-Ciudad (Nov 2019). Poster.
- **Rúa-Alonso, M.** *Variabilidad de la frecuencia cardiaca. Conceptualización y métodos de evaluación.* Congreso Internacional de entrenamiento y rendimiento deportivo in Chile (Mar 2021). Ponencia invitada.
- Aracama, A., Iglesias Soler, E., Tufano, J.J., Rial Vázquez, J., Fariñas, J., **Rúa Alonso, M.** *Lighter versus heavier-load training with equal power outputs: effects on the force velocity profile of squat and bench press.* 26th Annual Congress of the ECSS - ECSS Virtual Congress (Sep 2021). Poster.
- **Rúa-Alonso M**, Clavel I, Giráldez-García MA, Rico-Díaz J, Dopico-Calvo X; Iglesias-Soler, E. *DAFIS project: Principal component analysis of physical fitness in children and adolescents.* XI International Congress of the Spanish sport science association, Murcia (Oct 2021). Oral communication.
- **Rúa Alonso, M** *Replicability of the force-velocity profile in the Squat Jump in young female basketball players.* XI International Congress of the Spanish sport science association, Murcia (Oct 2021). Poster.
- Martínez, A.; Fariñas, J.; Rial-Vázquez, J.; **Rúa-Alonso, M.**; Giráldez-García MA; Álvarez E. *Efecto de los hábitos de actividad física y sedentarismo durante el embarazo sobre la función vascular útero-placentaria* XVIII Congreso Internacional de la Sociedad Española de Medicina del Deporte, Murcia (Nov 2021). Comunicación Oral



## Research projects

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- **Cátedra SXD Galicia Activa** de la Secretaría Xeral para o Deporte a través de la Fundación Deporte Galego y Universidade da Coruña.  
Contratada como ayudante de investigación en diferentes periodos entre 2018 y 2021.
- **Proyecto de asesoramiento en realización de estudio de validación de una adaptación submáxima de la prueba de valoración cardiovascular FitQuest**, entre la Fundación Universidade da Coruña e INGESPORT, Health & Spa Consultin S.L.  
Contratada como ayudante de investigación en el 2019
- **Proyecto de evaluación de la condición física y de variables biomecánicas y la planificación y supervisión del entrenamiento de sus clientes**, entre la Fundación Universidade da Coruña y EFISAUDE S.L.  
Contratada como ayudante de investigación en el 2021
- **Contratos de asistencia técnica:**
  - Contrato de asistencia técnica para asesoramiento en evaluación cardiovascular y de la composición corporal de usuarios del servicio de deportes del Ayuntamiento de Cambre (2018).
  - Contrato de asistencia técnica para el asesoramiento e implementación de las pruebas de selección de bomberos correspondientes a la bolsa de empleo del CIS Provincial de Ourense (2019).
  - Contrato de asistencia técnica para la para la evaluación de la condición física y de variables biomecánicas y la planificación y supervisión del entrenamiento de los clientes (2019-2021).
  - Contrato de asistencia técnica para la para evaluación y asesoramiento sobre nutrición, suplementación, composición corporal y rendimiento deportivo de los remeros (2018-2019)



# Appendix E

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Scientific publications derived from the present Doctoral Thesis





## A short set configuration attenuates the cardiac parasympathetic withdrawal after a whole-body resistance training session

María Rúa-Alonso<sup>1</sup> · Xian Mayo<sup>1,2</sup> · Jorge Mota<sup>3</sup> · J. Derek Kingsley<sup>4</sup> · Eliseo Iglesias-Soler<sup>1</sup>Received: 4 January 2020 / Accepted: 19 June 2020  
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### Abstract

**Purpose** We aimed to analyse the acute effects of set configuration on cardiac parasympathetic modulation and blood pressure (BP) after a whole-body resistance training (RT) session.

**Methods** Thirty-two participants (23 men and 9 women) performed one control (CON) and two RT sessions differing in the set configuration but with the same intensity (15RM load), volume (200 repetitions) and total resting time (360 s between sets for each exercise and 3 min between exercises): a long set configuration (LSC: 4 sets of 10 repetitions with 2 resting minutes) and a short set configuration session (SSC, 8 sets of 5 repetitions with 51 resting seconds). Heart rate variability, baroreflex sensitivity, the low frequency of systolic blood pressure oscillations (LFSBP), BP and lactatemia were evaluated before and after the sessions and mechanical performance was evaluated during exercise.

**Results** LSC induced greater reductions on cardiac parasympathetic modulation versus SSC after the session and the CON ( $p < 0.001$  to  $p = 0.024$ ). However, no LFSBP and BP significant changes were observed. Furthermore, LSC caused a higher lactate production ( $p < 0.001$ ) and velocity loss ( $p \leq 0.001$ ) in comparison with SSC.

**Conclusion** These findings suggest that SSC attenuates the reduction of cardiac parasympathetic modulation after a whole-body RT, improving the mechanical performance and decreasing the glycolytic involvement, without alterations regarding vascular tone and BP.

**Keywords** Cardiac autonomic control · Baroreflex sensitivity · Set configuration · Resistance exercise

### Abbreviations

15RM	15-Repetition maximum load
5LFR	Last five to the first five repetition velocity ratio
BEI	Baroreflex effectiveness index
BP	Blood pressure
BPV	Blood pressure variability

BPR	Bench press
BRS	Baroreflex sensitivity
CON	Control session
DBP	Diastolic blood pressure
HF	High frequency in absolute values
HF <sub>n.u.</sub>	High frequency in normalised units
HR	Heart rate
HRV	Heart rate variability
KE	Knee extension
LFSBP	Low frequency of systolic blood pressure
LSC	Long set configuration session
Lt	Capillary blood lactate concentration
MAP	Mean arterial pressure
MMR	Average mean propulsive velocity to maximum velocity ratio
MPV	Mean propulsive velocity
PI	Pulse interval
RMSSD	Root mean square of differences between adjacent pulse interval
RT	Resistance training
RTE	Relative treatment effect

Communicated by Guido Ferretti.

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<sup>3</sup> Research Centre in Physical Activity, Health and Leisure, Faculty of Sports, University of Porto, Porto, Portugal

<sup>4</sup> Cardiovascular Dynamics Laboratory, Exercise Physiology, Kent State University, Kent, USA

SBP	Systolic blood pressure
SDNN	Standard deviations of normal-to-normal pulse intervals
SQ	Parallel squat
SSC	Short set configuration session

## Introduction

The autonomic nervous system, through the “paired antagonistic innervation”, i.e. sympathetic and parasympathetic activity (Hess 2014), is responsible for the cardiovascular response to ensure the physiological demands and maintain the cardiovascular homeostasis. Several feedback and feed-forward mechanisms, moderated by central and peripheral neural structures, are involved to induce these responses (Fisher et al. 2015). Despite the contradictory viewpoints regarding the markers of autonomic regulation (Eckberg 1997; Billman 2011; Parati et al. 2006), currently some non-invasive methods allow evaluating them. Heart rate variability (HRV) and baroreflex sensitivity (BRS) are indicators of cardiac parasympathetic activity (Malik 1996; Ogoh et al. 2005). HRV provides information about the integrated activity of the parasympathetic nervous system over time (Rosenwinkel et al. 2001), whereas BRS indicates how efficiently the cardiac baroreflex is able to adapt the following heartbeats in response to changes in systolic blood pressure (SBP) (Stuckey et al. 2012), evaluating the ability of the parasympathetic system to respond reflexively to a discrete stimulus. Additional information regarding sympathetic vasomotor tone can be estimated assessing the low frequency of systolic blood pressure oscillations (LFSBP), which is closely associated with arterial stiffness (Bruno et al. 2012) and may reveal the activity of sympathetic outflow (Pagani et al. 1986; Malliani et al. 1991).

Resistance training (RT) is currently recommended as a significant component of a healthy fitness lifestyle and as a means of prevention for several diseases (Pollock et al. 2000). However, paradoxically after an RT session, the risk of suffering a cardiac event increases in apparently healthy individuals (Goodman et al. 2016) and especially in people with elevated cardiac risk (Albert et al. 2000), due to the reductions in cardiac autonomic modulation (Rosenwinkel et al. 2001). Several investigations have studied the acute effect of RT on cardiac autonomic modulation (Rezk et al. 2006; Heffernan et al. 2008; Kingsley et al. 2014), cardiac baroreflex (Heffernan et al. 2007, 2008; Niemelä et al. 2008) and vascular tone (Queiroz et al. 2015; Kingsley et al. 2019). Whilst the acute effects of RT on vascular tone remain unclear, the review by Kingsley and Figueroa (2014) summarised that RT induces a parasympathetic withdrawal after exercise, with the consequent increased risk of suffering a cardiac event as previously mentioned. To reduce

this elevated risk of suffering a cardiac event, the loading parameters of the RT session should be properly selected to minimise the cardiac parasympathetic withdrawal. In this regard, a limited load intensity (Niemelä et al. 2008; Lima et al. 2011), a small volume (Figueiredo et al. 2015a) or an adequate rest interval length (Figueiredo et al. 2016) may reduce this loss. In addition, the set configuration is another loading parameter that may attenuate the reductions of cardiac parasympathetic modulation after a session of RT (Mayo et al. 2015, 2016). Set configuration refers to the number of repetitions performed in each set in relation to the maximum number of feasible repetitions of such set (Iglesias-Soler et al. 2014b). Short set configurations, with a low intensity of effort (Steele 2014), produce smaller reductions on the cardiac autonomic modulation (Iglesias-Soler et al. 2014a) and cardiac baroreflex (Mayo et al. 2015, 2016) in comparison with long set configurations, close to, or leading to muscular failure, which may result in a higher reduction in mechanical performance (Latella et al. 2019). Moreover, short sets produce a non-significant, or slight glycolytic involvement, in comparison with long sets (Iglesias-Soler et al. 2012; Rial-Vázquez et al. 2020), whilst allowing comparable or greater gains in strength (Oliver et al. 2013; Iglesias-Soler et al. 2015). Since the relationship between the glycolytic involvement and the parasympathetic withdrawal was observed previously both during exercise (Buchheit et al. 2007) and when it is injected intravenously at rest (George et al. 1989; Yeragani et al. 1994, 1996), short sets may be a unique strategy to promote health benefits whilst reducing the possible adverse effects of the transient reductions in cardiac parasympathetic modulation (Albert et al. 2000). Nevertheless, previous studies analysing the set configuration on cardiac autonomic modulation and cardiac baroreflex have used a one-exercise model (Iglesias-Soler et al. 2014a; Mayo et al. 2015, 2016). This one-exercise model does not accurately reflect the conventional and suitable RT session, performing several upper- and lower-body RT exercises (American College of Sports Medicine 2009). Thus, it is important to expand on the current body of literature using more than one resistance exercise.

On the other hand, concomitant with the transient reduction in cardiac parasympathetic modulation there may be an acute decrease in blood pressure (BP) after an RT session. For this reduction to occur, the session needs to meet some characteristics, such as an medium intensity of load (Rezk et al. 2006; Figueiredo et al. 2015b; Neto et al. 2016), enough volume within session (Simão et al. 2005; Figueiredo et al. 2015a), the onset of muscular failure (De Souza et al. 2013), or exercises that involve enough muscle mass (Polito and Farinatti 2009; Mohebbi et al. 2016). Nevertheless, it remains unclear if the magnitude of this effect can be modulated by the interaction of different loading parameters (Casonatto et al. 2016). In this regard, studies analysing the



effects of set configuration on the postexercise BP are scarce, showing mixed results regarding the hypotensive effect of different configurations (Mayo et al. 2015, 2016). In this sense, to the best of our knowledge, the postexercise BP after different set configuration sessions has only been studied by a single-exercise model (Mayo et al. 2015, 2016) but not for routines composed by several RT exercises involving major muscle groups.

Therefore, we aimed to compare the effect of two different whole-body RT set configuration protocols (long versus short set configuration) on the cardiac parasympathetic modulation, vascular tone and postexercise BP response. We hypothesised that a short set configuration session would attenuate the reduction on cardiac parasympathetic activity in comparison with a long set configuration, showing lower neuromuscular fatigue and a reduced glycolytic involvement. Our second hypothesis was that there would not be differences between set configurations regarding the vascular tone and BP response after whole-body RT sessions.

## Methods

### Participants

Thirty-two apparently healthy individuals (23 men and nine women) with self-reported previous experience of at least 6 months with RT participated in this cross-sectional study. The participants were screened and excluded if they had a prior history of cardiovascular disease, any medical contraindications for lifting weights, or were using any controlled medication. This study was approved by the local Institutional Ethics Committee, and the participants read and signed an informed consent form.

### Study design

The participants visited the laboratory a total of six times separated at least by 72 h. The first and second sessions were conducted to familiarise the participants with the resistance exercises. In the third session, 15-repetition maximum load (15RM) was determined for all exercises. After assigning the participants into different experimental sequences, following a randomised block design in order to warrant an equivalent regarding the sex distribution, the final three sessions consisted of two experimental [long (LSC) and short (SSC) set configuration] and one control (CON) protocols. Participants were assessed before and after each session for cardiovascular and metabolic variables. In addition, mechanical performance was collected during some exercises. A schematic representation of the study is presented in Fig. 1.

The experimental sessions were composed of five resistance exercises performed in the same order: knee extension

(KE), leg curl, lateral pull-down, bench press (BPR), and parallel squat (SQ). Guided machines were used for performing the KE (Technogym, Gambettola, Italy), leg curl, and lateral pull-down (Biotech Fitness Solutions, Brazil) exercises, whereas BPR and SQ were performed on a Smith Machine (Telju Fitness, Toledo, Spain). Participants were encouraged to produce the maximal intended velocity during the concentric phase of the exercises and to complete the full range of movement for each repetition of each exercise.

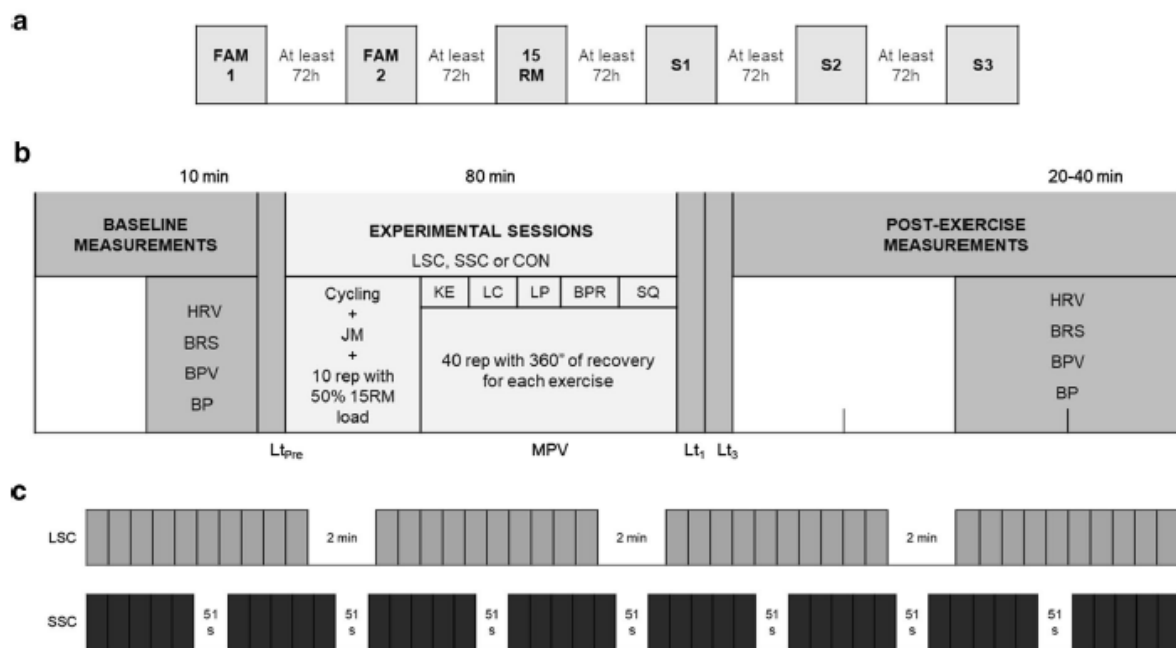
### Familiarisation sessions

In the familiarisation sessions, the participants were instructed on how to perform each resistance exercise. In this regard, the individual position references for each exercise were registered to standardise the execution conditions across the study. The full range of each exercise was objectively determined by the investigator for all exercises, excepted for SQ, which was controlled by placing an adjustable bench at the height required to achieve a parallel squat.

The first session started with a 5-min warm-up in a cycle ergometer at 60–80 revolutions per min (Monark 828E; Monark Exercise AB, Vansbro, Sweden) as well as joint mobilisation, followed by 2 sets of 15 repetitions with approximately 50% of perceived maximum load and 2 min of recovery between sets and exercises. In addition, height was measured by a stadiometer (Seca 202; Seca Ltd., Hamburg, Germany), body mass measured with an electronic scale (Omron BF-508, Omron Healthcare Co., Kyoto, Japan) and body mass index was calculated. In the second session, participants were instructed to perform the same warm-up, joint mobilisation and 2 sets at 75% of perceived maximum load. In the last set of each exercise, participants were encouraged to perform the maximal number of repetitions, to get more experience reaching muscular failure.

### 15RM test

In the third session, the 15RM test was conducted to assess the maximum load that each participant could lift no more than 15 times for each exercise using correct form and technique. The session started with the general warm-up previously described, followed by 10 repetitions of each exercise performed at 50% of the load from the last set of the familiarisation session. Then, after 5 min of rest, participants performed a set with approximately 110% of the load from the last set of the familiarisation session. If participants performed 16 repetitions, the load was increased, whereas if they could not complete 15 repetitions, the load was reduced. The first load which they performed no more than 15 repetitions was considered the 15RM. The test comprised a maximum of 2 attempts interspersed with at least 5 min rest. Participants were instructed to perform the concentric portion



**Fig. 1** **a** Schematic representation of the study. *FAM* familiarisation session, *S* experimental session. **b** Graphical simplification assessment. *LSC* long set configuration session, *SSC* short set configuration session, *CON* control session, *HRV* heart rate variability, *BRS* baroreflex sensitivity, *BPV* blood pressure variability, *BP* blood pressure, *Lt* Capillary blood lactate concentration, *MPV* mean propulsive velocity, *JM* joint mobilisation, *KE* knee extension, *LC* leg curl, *LP* lateral

pull-down, *BPR* bench press, *SQ* parallel squat. **c** Representation of the experimental sessions. All sessions consisted of 40 repetitions and 360 s of total rest with the 15RM load for each exercise and with 3 min of rest between exercises. *LSC*: 4 sets of 10 repetitions with 2 min of rest between sets. *SSC*: 8 sets of 5 repetitions with 51 s of rest between sets

of each repetition as fast and explosive as possible. Muscle failure was defined when the participants could not complete the full range of movement of the exercise or the load could not be moved. The order of the resistance exercises was the same as we previously described.

### Experimental sessions

Each participant completed the two experimental sessions (*LSC* and *SSC*) and the *CON* in random order. In all sessions, the participants were instructed to refrain from alcohol, and caffeine for 3 h and exercise for 24 h prior to the testing sessions, and keep hydration and feeding habits stable. Participants were tested in the postprandial state (3 h) upon arrival to the laboratory. Sessions were separated by at least 72 h and were performed at the same time of the day ( $\pm 1.5$  h) in a temperature and humidity-controlled room (23 °C and 50% respectively). Both experimental sessions entailed performing a total of 200 repetitions (40 per exercise) with the 15RM load and with a total rest of 42 min (360 s between sets for each exercise and 3 min between exercises) but differing in the set configuration. *LSC* consisted on 4 sets of 10 repetitions (i.e. an intensity of effort

of 66%, 10 out of 15RM) with 2 min of rest between sets and 3 min between exercises. *SSC* consisted of 8 sets of 5 repetitions (i.e. an intensity of effort of 33%, 5 out of 15RM) with a rest of 51 s between sets and 3 min between resistance exercises. After a baseline assessment, and before both *LSC* and *SSC*, the general warm-up previously described was performed. In addition, before each exercise, a specific warm-up consisting of 10 repetitions with 50% of 15RM was carried out. In *CON*, before and after the measurements, the participants remained seated in the laboratory for 80 min without performing any resistance exercise.

### Procedures

#### Physiological recording

Cardiovascular parameters were registered using the Task Force® Monitor (CNSystems, Graz, Austria). A three-lead electrocardiogram obtained a continuous heart rate (HR) with a sampling frequency of 1000 Hz. Beat-by-beat monitoring of SBP, diastolic blood pressure (DBP), and mean arterial pressure (MAP) were obtained by photoplethysmography. The finger cuffs were placed on the proximal phalange



of the index and the middle fingers of the right hand, sited on the fourth intercostal space. The absolute values of the finger pressure were automatically and continuously transformed into values of brachial artery by an oscillometric device. It consisted of an arm cuff tightly attached to the left arm with the compressed air outlet on the brachial artery and the lower edge of the cuff approximately 2.5 cm from the elbow crease. Considering the delay caused by the cardiovascular device colocation and calibration procedures, and to allow the comparability with previous resistance exercise studies using similar epochs, cardiovascular data were obtained 10 min before the sessions and 20 min after the end of the protocols (i.e. in the period 20–40 min). During this time, participants were lying in the supine position on a stretcher in a quiet room, breathing with a respiratory rate of 0.2 Hz (12 breaths per min) to avoid the effect of respiratory rate on HRV measures (Penttilä et al. 2001). Participants were asked not to move or speak during the measurements. (Laborde et al. 2017).

Capillary blood lactate concentration (Lt) was obtained using a portable blood lactate analyser with a sample analysis time of 15 s and a required blood sample of 0.5 µL (Lactate Scout, SensLab GmbH, Germany). Lactate Scout uses an enzymatic-amperometric method for the detection of lactate in capillary blood and his reliability has been previously evaluated (Tanner et al. 2010). Data were obtained immediately before, and 1 and 3 min after each experimental session.

### Mechanical recording

The mean propulsive velocity (MPV) of every repetition was recorded with a linear velocity transducer (T-Force System, Ergotech, Murcia, Spain). Validity and reliability of this device have been previously reported (Sánchez-Medina and González-Badillo 2011). MPV consisted of the mean velocity during the propulsive phase of the exercise, that is, the portion of the concentric period in which the barbell acceleration is greater than the acceleration due to gravity (Sánchez-Medina et al. 2010). MPV was registered for three exercises: KE, BPR, and SQ.

### Data analysis

HRV was used to assess the autonomic modulation of the heart. Analysis of the data consisted of time- and frequency-domain analysis. The time-domain analysis included the standard deviations of normal-to-normal pulse intervals (PI) of the HR (SDNN), a measure of global autonomic control, and the root mean square of differences between adjacent PI (RMSSD), a measure of parasympathetic activity. For the spectral analysis of HRV, Fast Fourier Transformation method was employed.

High-frequency power (0.15–0.4 Hz) in absolute values (HF) and normalised units (HF<sub>n.u.</sub>) was calculated for estimating cardiac parasympathetic activity. The data analysis was performed for the last 5 min of the period of 10 min before the beginning of the session (baseline) and 5 min epochs during the 20–40 min period after the session, since epochs of 5 min are recommended when taking short-term recordings (Malik 1996). Automatic artefact correction (i.e. medium correction threshold level,  $\pm 0.25$  s) and calculation of HRV values were obtained using the Kubios HRV software v2.1 (The Biomedical Signal and Medical Imaging Analysis Group, Department of Applied Physics, University of Kuopio, Finland). The data were detrended with the smooth priors method. The Lambda value was fixed at 500. The mean artefact correction of the signal was  $1.04 \pm 2.53\%$ . In addition, HR values were recorded as a reflection of cardiac autonomic activity and as an independent predictor of sudden cardiac death risk (Hjalmarson 2007).

BRS, quantified by the sequence method, was employed to estimate the effect of the sessions on the cardiac baroreflex. This method is based on the identification of sequences of three or more consecutive beats in which SBP and the PI increase progressively (+PI/+SBP) or fall (−PI/−SBP) in a linear fashion (Bertinieri et al. 1988). In specific, the sequences of three or more beats for which SBP and PI of the next beat (Lag 1) changed in the same direction (Blaber et al. 1995) were analysed. The threshold change was defined as 1 mmHg for BP and 6 ms for PI. BRS analysis included the total number of detected sequences (BRS<sub>count</sub>), the mean slope of such sequences (BRS<sub>slope</sub>), and the ratio between the number of SBP ramps followed by the respective reflex PI ramps and the total number of SBP ramps observed in a given time window, known as the baroreflex effectiveness index (BEI) (Rienzo et al. 2001). BEI reflects the number of times the baroreflex is active in controlling the HR in response to BP oscillations, which is indicative of the severity and duration of several diseases, such as renal failure (Johansson et al. 2007). For BEI, only 24 participants were analysed.

Blood pressure variability (BPV) was used to estimate the sympathetic vasomotor tone. Our BPV analysis consisted of spectral analysis of SBP variability. The autoregressive spectral method was used, and the low-frequency activity (0.04–0.15 Hz) in absolute values was calculated (LFSBP) (Pagani et al. 1997).

Data recordings of BRS and BPV were performed for the last 10 min before the protocols (baseline) and for the intervals 20–30 and 30–40 min after each session. Epochs of 10 min are usually used to analyse BRS after resistance exercise (Niemelä et al. 2008; Queiroz et al. 2015). BRS and BPV data were obtained using TFM software v2.3 (CNSsystems, Graz, Austria) (Fortin et al. 2001).

For BP analysis, the beat-to-beat responses registered before (baseline) and after the sessions were analysed in epochs of 10 min. The percentage change of SBP, DBP, and MAP was calculated for all the participants. Percentages changes were calculated as follows:  $\Delta\%30\text{-Baseline} = (\text{value of the 20–30 epoch} - \text{value of baseline}) / \text{value of baseline}$ ;  $\Delta\%40\text{-Baseline} = (\text{value of the 30–40 epoch} - \text{value of baseline}) / \text{value of baseline}$ . Percentage changes were used to represent the differences in BP values. For measurements obtained with a photoplethysmography device, the responses to exercise in percentage changes have been previously validated and well correlated with simultaneous invasive procedures, being these non-invasive measurements a very sensitive method to follow rapid changes in arterial pressure (Gomides et al. 2010).

Regarding Lt, the maximum value of the two post-test measurements was selected, and the percentage change of lactatemia ( $\Delta\%Lt$ ) was calculated in both training sessions.

MPV was used to estimate the neuromuscular fatigue of each session. The MPV of every repetition was calculated and averaged in both experimental sessions for KE, BPR, and SQ. Thereafter, other parameters were calculated for comparing the loss of mechanical performance between sessions. For the overall maintenance of velocity analysis, the mean to maximum MPV ratio of each session (MMR) was calculated as follows:  $([\text{average MPV}/\text{maximum MPV}] \times 100)$  (refs). Values near 100% imply less velocity loss. For quantifying the velocity loss throughout the sessions, the last five to the first five repetition ratio (5LFR) was obtained. For this calculation, the mean MPV of the last five repetitions and the first five ones were considered as follows:  $5LFR = ((\text{average last five repetitions MPV}/\text{average first five repetitions MPV}) - 1) \times 100$ . Lower values imply higher magnitudes of velocity loss and positive values was interpreted as velocity gains.

### Statistical analysis

Descriptive parameters are shown as means  $\pm$  standard deviation. Normality was tested using the Shapiro–Wilk test. The characteristics of participants were compared between sexes using independent sample *t* test or Mann Whitney *U* test, respectively. As all physiological variables violated the assumption of normality and a logarithmic transformation was not possible, a nonparametric ANOVA type test was employed using the nparLD R software package (Noguchi et al. 2012) for evaluating the main effects and interactions between sex (men, women), sessions (LSC, SSC, and CON) and times (Baseline, 20–25, 25–30, 30–35, and 35–40 for HRV and HR parameters; Baseline, 20–30 and 30–40 min for BRS and LFSBP; and  $\%30\text{-Baseline}$  and  $\Delta\%40\text{-Baseline}$  of SBP, DBP, and MAP). Since gender did not interact with the rest of factors (i.e. time and session), a two-way

nonparametric ANOVA type test was performed with pooled data from men and women. If a significant interaction was detected, paired comparisons were performed using the Wilcoxon signed-rank test with Bonferroni correction. For main effects' interpretation, relative treatment effect (RTE) was considered. RTE has a value between 0 and 1 and indicates the probability that a measurement in one group at a given time-period is larger than a value of this variable in any other combination of group and time (Schild et al. 2016).

For capillary lactate production, Wilcoxon signed-rank test was performed to analyse the delta differences between experimental sessions ( $\Delta\%Lt$ ). For mechanical responses, paired *t* tests and Wilcoxon signed-rank test were used for analysing differences between sessions. Furthermore, training effect size was reported using Hedge's *g* (*g*) and Matched Pair Rank Biserial Correlation (*r*) for parametric and non-parametric contrasts, respectively. Matched Pair Rank Biserial corresponds to the difference between the proportions of positive and negative ranks (Kerby 2014).

R software v3.6.1. (R Foundation, Vienna, Austria), GraphPad Prism 5.01 (GraphPad Software, San Diego, CA, USA), Comprehensive Meta-Analysis v.2 (Biostat Inc., Englewood, NJ, USA), and IBM SPSS v.20.0. (IBM Corp, Armonk, NY, USA) were used for statistical analysis. Statistical significance level was set at 0.05.

Finally, a post-hoc power analysis was calculated using the G Power software (version 3.1.9.2). The statistical power ( $1 - \beta$ ) of a repeated measures ANOVA with 3 and 5 measurements for a sample size of 32, and a correlation among repeated measures of 0.5 and a medium effect size ( $f = 0.25$ ) are 0.87 and 0.96, respectively.

### Results

The characteristics of participants are summarised in Table 1. Men and women were matched for age and body mass index; however, men showed higher weight, height, and 15RM values for all exercises than women.

For HR, main effect of session ( $p < 0.001$ ; RTE: 0.629, 0.598, and 0.273 for LSC, SSC, and CON, respectively), time ( $p < 0.001$ ; RTE: 0.378, 0.542, 0.540, 0.530 and 0.510 for Pre, 20–25, 25–30, 30–35, and 35–40, respectively), and a session by time interaction were detected ( $p < 0.001$ ). Post-hoc analyses (Fig. 2a) showed higher values for all post-test epochs in LSC and SSC versus baseline ( $p < 0.001$ ) and versus CON ( $p < 0.001$ ). Furthermore, LSC data were higher in comparison with SSC during all the postexercise epochs ( $p < 0.001$  to 0.006).

For SDNN, main effects for session ( $p = 0.004$ ; RTE: 0.416, 0.498, and 0.585 for LSC, SSC, and CON, respectively), time ( $p < 0.001$ ; RTE: 0.585, 0.451, 0.490, 0.476; and 0.498 for Baseline, 20–25, 25–30, 30–35, and 35–40,



**Table 1** Physical and functional characteristics of the participants ( $n=32$ )

	Men ( $n=23$ )	Women ( $n=9$ )	Total ( $n=32$ )	$p$ value
Age (years)	23±2	24±3	23±2	0.456 <sup>+</sup>
Weight (kg)	73.14±8.45	62.11±6.37	70.04±9.30	<0.001*
Height (cm)	1.76±0.06	1.65±0.06	1.73±0.08	<0.001*
BMI (kg/m <sup>2</sup> )	23.64±2.03	22.72±1.93	23.38±2.01	0.402 <sup>+</sup>
15RM in KE (kg)	79±13	55±10	72±16	<0.001*
15RM in LC (kg)	54±9	38±9	50±11	<0.001*
15RM in LP (kg)	49±8	34±5	45±10	<0.001*
15RM in BPR (kg)	51±12	29±5	45±14	<0.001*
15RM in SQ (kg)	80±19	55±10	73±20	0.001*

Values represent means ± SD

BMI body mass index, KE knee extension, LC leg curl, LP lateral pull-down, BPR bench press, SQ parallel squat

\* $p$  values are derived from independent sample  $t$  test and <sup>+</sup> $p$  values are derived from Mann–Whitney  $U$  test

respectively), and an interaction of session by time were detected ( $p=0.025$ ). Post-hoc pairwise comparisons are shown in Fig. 2b. Lower values were revealed after both experimental sessions in comparison with the CON ( $p<0.001$ ). Nevertheless, lower values of SDNN at the 35–40 epoch were observed only after LSC with respect to the baseline ( $p<0.001$ ). During all the postexercise measures, LSC showed lower SDNN values in comparison with SSC ( $p=0.001$ – $0.024$ ).

For RMSSD, neither a main effect of session ( $p=0.238$ ; RTE: 0.457, 0.533, and 0.520 for LSC, SSC, and CON, respectively) nor time ( $p=0.070$ ; RTE: 0.578, 0.481, 0.474, 0.484, and 0.483 for baseline, 20–25, 25–30, 30–35, and 35–40, respectively) was detected, whereas a significant session by time interaction was observed ( $p=0.013$ ). For LSC and SSC, RMSSD values after exercise were always lower in comparison with the baseline ( $p<0.001$ – $0.002$ ) and CON values ( $p<0.001$ ). Furthermore, all post-training records were significantly lower in LSC when compared with SSC ( $p<0.001$ – $0.004$ ) (Fig. 2c).

Regarding absolute HF values, neither a main effect of session ( $p=0.498$ ; RTE: 0.484, 0.496, and 0.520 for LSC, SSC, and CON, respectively) or time ( $p=0.883$ ; RTE: 0.480, 0.486, 0.503, 0.510, and 0.520 for baseline, 20–25, 25–30, 30–35, and 35–40, respectively), nor session by time interaction was found ( $p=0.687$ ) (Fig. 2d).

Regarding HF<sub>n.u.</sub>, main effect of session ( $p<0.001$ ; RTE: 0.364, 0.493, and 0.643 for LSC, SSC, and CON, respectively), time ( $p<0.001$ ; RTE: 0.673, 0.495, 0.431, 0.441, and 0.460 for Pre, 20–25, 25–30, 30–35, and 35–40, respectively), and a session by time interaction was detected ( $p<0.001$ ). Post-hoc analyses (Fig. 2e) showed lower values for all post-test epochs in LSC and SSC versus both the baseline and CON in all the epochs ( $p<0.001$ – $0.031$ ) except the 30–35 min period after SSC. Furthermore, LSC data were consistently lower in comparison with SSC during all

the postexercise epochs ( $p<0.001$ – $0.021$ ). The effect size with respect to baseline values for the cardiac autonomic modulation is reported in Table 2.

For BRS<sub>count</sub>, a main effect for session ( $p<0.001$ ; RTE: 0.567, 0.552, and 0.381 for LSC, SSC, and CON, respectively) and a session by time interaction was detected ( $p=0.011$ ). Nevertheless, a time effect was not observed ( $p=0.212$ ; RTE: 0.468, 0.529, and 0.503 for baseline, 20–30, and 30–40, respectively). For all periods after training, LSC ( $p=0.042$  and  $p=0.006$  for 20–30 and 30–40 epochs, respectively) and SSC ( $p=0.002$  for both post-test epochs) showed higher values of BRS<sub>count</sub> in comparison with CON. There were no differences between LSC and SSC at any postexercise time-period (Fig. 3a).

Regarding BRS<sub>slope</sub>, neither a main effect for session ( $p=0.230$ ; RTE: 0.461, 0.498, and 0.541 for SSC, LSC, and CON, respectively) or time ( $p=0.387$ ; RTE: 0.472, 0.533, and 0.495 for Pre, 20–30, and 30–40, respectively) was observed. On the other hand, a significant session by time interaction was detected ( $p<0.001$ ). In this sense, for all after training periods, lower values for BRS<sub>slope</sub> were obtained after both LSC ( $p<0.001$  in both periods) and SSC ( $p<0.001$  and  $p=0.001$  for 20–30 and 30–40, respectively), in comparison with CON. In this regard, LSC presented lower values at each after training epoch in comparison with SSC ( $p<0.001$  and  $p=0.002$  for 20–30 and 30–40 min, respectively). In addition, both LSC and SSC presented lower values at the period 20–30 in comparison with the baseline ( $p<0.001$  and  $p=0.001$ , respectively). However, at the period 30–40 min, the difference with respect to the baseline was still significant in LSC ( $p<0.001$ ), but not in SSC ( $p=0.053$ ) (Fig. 3b).

Regarding BEI, only 24 participants were analysed because of missing data. Neither main effect of session ( $p=0.261$ ; RTE: 0.454, 0.531, and 0.514 for LSC, SSC, and CON, respectively) nor time ( $p=0.254$ ; RTE: 0.540, 0.487,

**Fig. 2** Cardiac autonomic control before (baseline) and after a long set configuration session (LSC, in squares); a short set configuration session (SSC, in circles), and a control session (CON, in triangles). HR: heart rate (a), SDNN: standard deviations of pulse intervals (b), RMSSD: root mean square of differences between adjacent pulse intervals (c), HF: high-frequency power in absolute values (d), HFn.u.: high-frequency power spectral power in normalised units (e). \*Within-session differences in comparison with baseline, #differences between training sessions at a specific time-period and \$differences in comparison with CON at a specific time-period. For clarity, within session comparisons are only shown with respect to the baseline. Data are displayed as means  $\pm$  SD ( $n = 32$ )

and 0.473 for baseline, 20–30, and 30–40 min, respectively) was detected. Nevertheless, a significant session by time interaction was observed ( $p = 0.029$ ) such that BEI decreased in LSC after the 20–30 min period time in comparison with baseline ( $p = 0.017$ ), but no significant differences were detected after SSC. However, recovery was only observed during SSC, where there were higher values during the 20–30 min period in comparison with the 30–40 min one ( $p = 0.006$ ) (Fig. 3c). Effect sizes versus the baseline for the cardiac baroreflex response is reported in Table 2.

Regarding LFSBP, our analysis did not detect neither main effect of session ( $p = 0.609$ ; RTE: 0.512, 0.514 and 0.473 for LSC, SSC, and CON, respectively), time ( $p = 0.141$ ; RTE: 0.461, 0.529, and 0.509 for baseline, 20–30, and 30–40, respectively), nor session by time interaction ( $p = 0.104$ ) (Fig. 3d).

For SBP, DBP, and MAP, no interactions or main effects were observed amongst protocols ( $p > 0.05$ ).

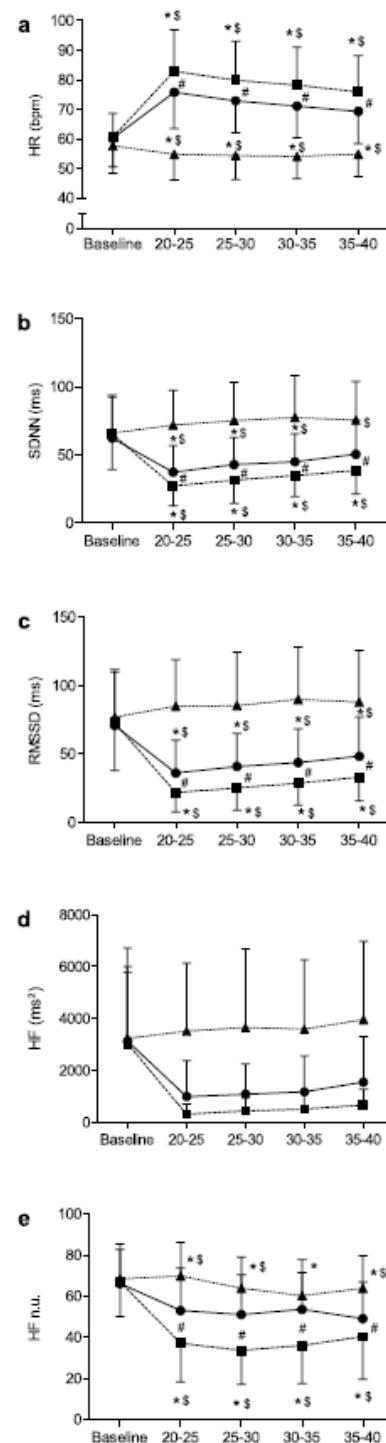
Glycolytic metabolism implication analysis ( $\Delta\%L$ ) showed higher values of lactatemia ( $p < 0.001$ ;  $g = -1.079$ ; CI  $-1.598$  to  $-0.560$ ) after LSC ( $84.8 \pm 6.8\%$ ) in comparison with SSC ( $69.5 \pm 18.6\%$ ).

Regarding mechanical measurements (Fig. 4), LSC produced a higher loss of velocity in comparison with SSC for all exercises ( $p < 0.001$ – $0.020$ ) as showed by MPV, MMR, and 5LFR analyses.

## Discussion

The main findings of this study are that whilst (a) both long and short set configurations produced a reduction of cardiac parasympathetic modulation after a whole-body RT session, (b) the long sets produced a greater drop in comparison with the short sets; (c) there was a higher glycolytic involvement during the long set configuration session concomitant with a prominent loss in mechanical performance versus the short set design. In parallel, there were no alterations regarding the BP or the vascular tone after any session.

Our results indicate that when the intensity of load (15RM), total volume (200 repetitions), and total resting time (360 s between sets for each exercise and 3 min



between exercises) are equated, a whole-body RT session including several exercises but differing in the set configuration affects the postexercise cardiac parasympathetic

**Table 2** Effect sizes (matched pair rank Biserial correlation,  $r$ ) for heart rate, cardiac autonomic and baroreflex control with respect to the baseline across sessions

	20–25	25–30	30–35	35–40
<b>HR (bpm)</b>				
LSC	1.00	1.00	1.00	0.97
SSC	1.00	1.00	0.98	0.90
CON	-0.72	-0.78	-0.74	-0.56
<b>SDNN (ms)</b>				
LSC	-0.99	-0.95	-0.94	-0.96
SSC	-0.91	-0.81	-0.73	-0.52
CON	0.51	0.57	0.65	0.57
<b>RMSSD (ms)</b>				
LSC	-1.00	-0.99	-0.98	-0.98
SSC	-0.93	-0.89	-0.80	-0.76
CON	0.51	0.51	0.61	0.49
<b>HF<sub>n.u.</sub></b>				
LSC	-0.98	-1.00	-1.00	-0.98
SSC	-0.67	-0.70	-0.60	-0.80
CON	0.08	-0.41	-0.48	-0.33
		20–30		30–40
<b>BRScout (<math>n</math>)</b>				
LSC		0.19		0.11
SSC		0.45		0.36
CON		-0.44		-0.49
<b>BR<sub>slope</sub> (ms/mmHg)</b>				
LSC		-0.99		-0.89
SSC		-0.71		-0.48
CON		0.57		0.41
<b>BEI (%)</b>				
LSC		-0.61		-0.33
SSC		0.12		-0.26
CON		-0.11		-0.52

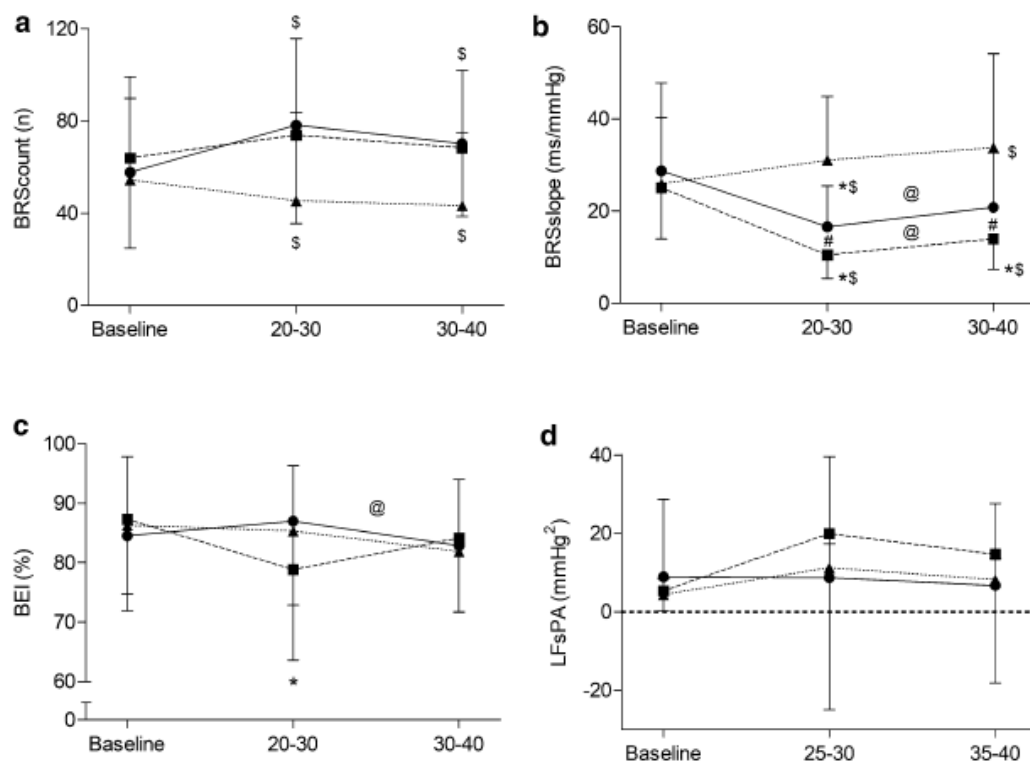
Positive values of effect size indicate higher values in comparison with the baseline, whereas a negative effect size indicates decreases in values in comparison with the baseline ( $n=32$  excepted for BEI,  $n=24$ )

LSC long set configuration session, SSC short set configuration session, CON control session, HR heart rate, SDNN standard deviations of pulse intervals, RMSSD root mean square of differences between adjacent PI, HF high-frequency PI spectral power in absolute values, HF<sub>n.u.</sub> high-frequency PI spectral power in normalised units, BRScout number of baroreceptor sequences detected, BR<sub>slope</sub> magnitude of the baroreflex sensitivity, BEI baroreflex effectiveness index

modulation. In specific, our data demonstrate that the long set configuration produces a significantly greater reduction of cardiac parasympathetic modulation in comparison with the short set configuration during the 40 min postexercise. These results are a novelty since, as far as we know, this is the first study investigating the set configuration effect after a whole-body RT session composed of a series of exercises that match a more traditional style of RT. Previous studies have explored the set configuration effect using a single-exercise model (Iglesias-Soler et al. 2014a; Mayo et al. 2015, 2016), limiting the applicability to typical training protocols routines including several exercises. A previous study by

Iglesias-Soler et al. (2014a) showed no differences in cardiac parasympathetic modulation recovery whilst comparing an inter-repetition rest set versus a set to failure during the first postexercise minutes. On the contrary, and in line with our results, Mayo et al. (2015) showed that a long set configuration with a high intensity of effort (8/10, i.e., 80%) and a short set (4/10, 40% intensity of effort) elicited higher reductions of cardiac parasympathetic modulation than a session with a very short set (1/10, i.e., 10%). These findings, along with those of the present study, indicate that the type of set configuration used determines the reductions of the cardiac parasympathetic modulation.





**Fig. 3** Cardiac baroreflex control and vascular tone before (baseline) and after a long set configuration session (LSC, in squares), a short set configuration session (SSC, in circles), and a control session (CON, in triangles). **a**  $BRS_{count}$ : number of baroreceptor sequences detected [ramps simultaneous in systolic blood pressure (SBP) and pulse intervals]; **b**  $BRS_{slope}$ : magnitude of the baroreflex sensitiv-

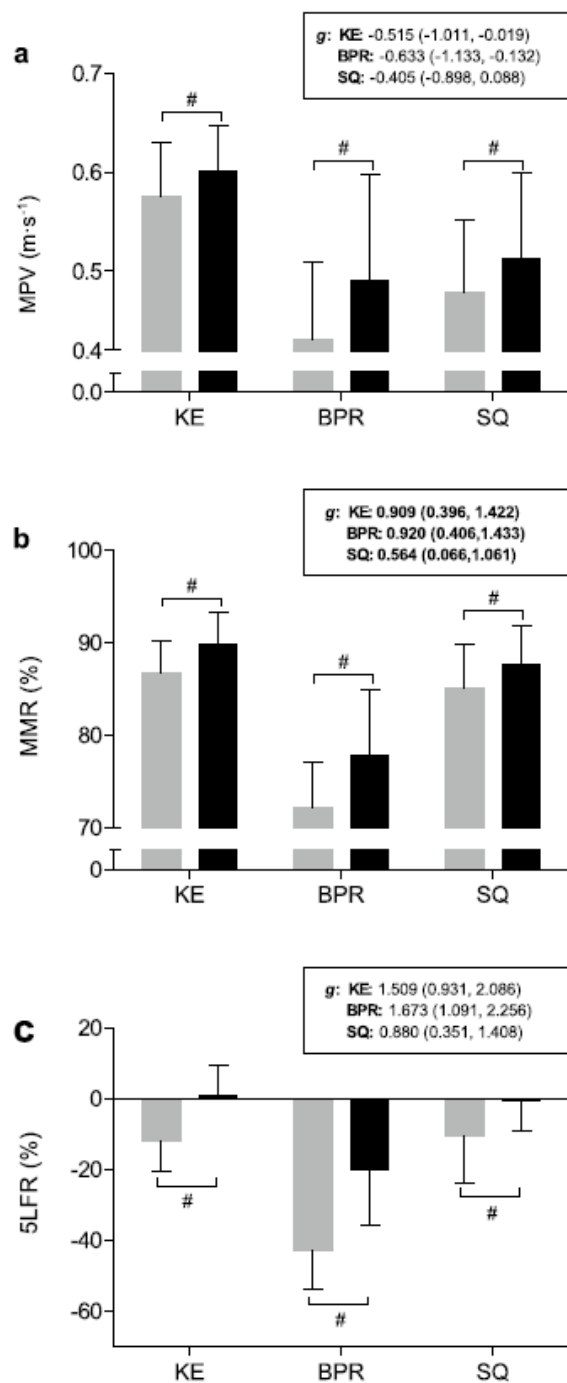
ity; **c** BEI: Baroreflex effectiveness index; **d** LFsPA: low frequency of SBP. \*Within session differences in comparison with baseline, @differences between epochs, #differences between training sessions at a specific time-period and \$differences in comparison with CON at a specific time-period. Data are displayed as means  $\pm$  SD ( $n=32$  excepted for BEI,  $n=24$ )

Previous investigations have reported that HR is, by itself, a surrogate of autonomic activity (Lahiri et al. 2008) both at rest (Hjalmarson 2007) and during recovery (Jouven et al. 2005). Thus, both are good indexes of increased risk of a cardiac event. In our study, HRV and HR results showed a similar trend. In fact, HR values were higher even after 20 min of the long set configuration, suggesting a slower HR recovery (i.e. a slower parasympathetic reactivation). This reinforces the findings of the effect of set configuration on the autonomic response.

The length of the cardiac parasympathetic modulation reduction lasted up to 40 min after both experimental sessions. Our results partially agreed with Kingsley et al. (2016), who indicated that parasympathetic activity might not be fully recovered up to 30 min after an RT session composed of upper- and lower-body exercises. However, Mayo et al. (2015) reported a shorter time of reduced cardiac parasympathetic modulation for short set configurations. These discrepancies may be due to several reasons. On the one hand, the whole-body multi-exercise nature of

our design, that included both single- and multi-joint exercise, in comparison with the one-exercise model employed by Mayo et al. (2015), might partially explain the differences observed. On the other hand, the differences in the intensity of effort magnitude and total volume performed in each study might also determine the recovery of cardiac parasympathetic modulation. Whereas previous studies used less repetitions per session (e.g. the 40 repetitions used by Mayo et al. 2015 or the 90 repetitions by Kingsley et al. 2016), our sessions had each participant complete a total of 200 repetitions. In this sense, a previous study (Figueiredo et al. 2015a) showed that an RT session with a greater volume promotes longer reductions in parasympathetic activity compared to sessions with a lower volume, which is in agreement with our findings..

In addition, even though in our study the time differences only were observed until 40 min postexercise, the magnitude of the reductions suggests that the recovery length in the long set configuration could be longer in comparison with the short structure, but this is speculation. The recovery time



**Fig. 4** Mechanical responses during a long set configuration session (LSC, grey bars) and a short set configuration session (SSC, black bars) for the knee extension (KE), bench press (BPR) and parallel squat (SQ) exercises. **a** MPV: average mean propulsive velocity. **b** MMR: mean respect to maximum propulsive velocity ratio. **c** 5LFR: the last five respect to the first five propulsive velocity ratio. #Differences between sessions; g: Hedge's *g*. Data displayed as means  $\pm$  SD ( $n=32$ )

differences between protocols may be due to the incapacity of the baroreflex to synchronise the BP responses to changes in HR. Despite that both RT protocols promoted a reduction in BRS during recovery, the long set configuration caused a higher reduction and a slower recovery to the baseline values than the short one, suggesting that this incapacity might be particularly important in more strenuous protocols (Heffernan et al. 2008; Queiroz et al. 2013; Kingsley et al. 2016, 2019). These results are partially in agreement with Mayo et al. (2015). They reported BRS reductions after both long and short intra-set rest configurations but not after the inter-repetition rest training session. Nevertheless, in that particular study, the reductions in comparison with baseline were significant up to 40 min for both set configurations. This may be due to the differences between studies in the intensity of effort used (Mayo et al. 2015). This points out the suitability of managing the set configuration to attenuate the impact on cardiac parasympathetic modulation after RT and to promote a faster recovery whilst maintaining the rest of the loading parameters equated. Thus, shorter sets should be recommended when the aim is to mitigate the effects of RT on cardiac parasympathetic modulation.

The reductions in cardiac baroreflex activity may also be produced by an increase in arterial stiffness triggered by the higher sympathetic tone of central arteries (Heffernan et al. 2007). Our analysis did not detect significant changes in sympathetic vascular tone, which is coincident with Queiroz et al. (2015). In their study, they did not find differences in LFSBP after an RT protocol in healthy men. Conversely, other studies showed increments of LFSBP after RT sessions (Heffernan et al. 2007; Niemelä et al. 2008; Kingsley et al. 2019). Niemelä et al. (2008) compared three different exercise protocols (i.e. aerobic exercise, light resistance exercise, and heavy resistance exercise), and only heavy resistance exercise produced significant increases in LFSBP. These findings suggest that intensity may be a factor affecting the vascular tone, and thus modulating arterial stiffness. Further studies are needed to elucidate the effect of the RT variables on vascular sympathetic tone and how the set configuration might modulate this response in high-intensity protocols.

A possible explanation for the differences in the magnitude of the reduction of the cardiac parasympathetic modulation between sessions may be the different glycolytic involvement of both protocols, since parasympathetic activity is negatively related to lactatemia (Simões et al. 2010; Okuno et al. 2014). Our data demonstrated that the long set configuration produced higher lactate values in comparison with the shorter one. Similar results were observed in previous studies, where sets with a continuous pattern promoted greater lactate response than a work-equated set with an intra-set rest design (Goto et al. 2005; Girman et al. 2014) and a slower recovery to the baseline values (Denton and Cronin 2006).



Regarding the BP analysis, negligible changes were observed after both RT sessions. However, a meta-analysis by Casonatto et al. (2016) demonstrated that a single bout of RT decreases the BP from 60 min up to 24 h after the session. Furthermore, Mayo et al. (2016) only reported BP reductions after session when an RT protocol leading to failure was performed. Therefore, muscular failure may be a key factor in promoting BP reductions and may be a plausible reason why it was not found in our study. Possibly and according to Figueiredo et al. (2015a, b), other loading parameters in our study were not suitable to induce the postexercise hypotension observed in other studies, such as the total volume performed or the intensity selected. On the other hand, it has been suggested that the hypotensive effect is mostly observed in hypertensive people (Kenney and Seals 1993; Queiroz et al. 2015). Thus, the profile of our sample might not be suitable for inducing a hypotensive effect after an acute RT session.

Finally, mechanical measurements' analysis showed a lower velocity loss during the short set configuration exercises performed versus the long set design. These results are coincident with the findings of a recent meta-analysis (Latella et al. 2019), that showed how short set configurations maximise the neuromuscular performance, and in particular, attenuate the loss of velocity during an RT session.

There are some limitations in to the present study that should be considered. First, all women were using oral contraceptive pills and performed the protocols during the mid-follicular to the late luteal phase of their menstrual cycle. In this regard, previous studies suggested that the use of oral contraceptive pills does not affect HRV during the menstrual cycle in healthy women (Teixeira et al. 2015). However, the effects of the menstrual cycle on cardiac autonomic modulation have not been clarified completely (von Holzen et al. 2016). Second, despite the evidence on the validity and reliability of the cardiovascular device used in this study (Fortin et al. 2001), it only provides an indirect assessment of cardiac autonomic modulation. There is extensive debate regarding the relationship between changes in cardiac variability and the activity of a particular branch of the autonomic nervous system (Parati et al. 2006). To improve the physiological interpretation of autonomic data, the study design was developed controlling the possible confounding variables such as respiratory rate, steady-state, participant, or environmental conditions. In this sense, we controlled breathing frequency to avoid the effect of the increased respiratory rate after exercise on HRV measures (Penttila et al. 2001). This is because the respiratory activity is involved in the change in power spectral density distribution, particularly the measures of parasympathetic modulation (HF and HFnu.) (Brown et al. 1993; Weippert et al. 2015). Whilst breath control might have removed some experimental effects (Berntson et al. 1997), the changes are presumed

to be similar between protocols based on data that paced breathing and spontaneous breathing may result in similar effects (Wang et al. 2013); however, more research on this topic is pertinent. Furthermore, due to the technical limitations regarding the time spent to apply the instrumentation and calibrate the device, from the end of the session to 20 min, HR and BP were not evaluated. Further investigations with measurements during and immediately after the exercise must be carried out to assess the effect of set configuration on HR kinetics. Last, our participants were healthy and active young adults and performed two protocols with specific load characteristics, limiting the extrapolation of our results to other protocols or other population profiles. Further studies are needed to explore the acute and chronic effects of different set configurations on the cardiac autonomic modulation and cardiac baroreflex in populations at cardiovascular risk.

## Conclusions

In summary, our findings suggest that a moderate-intensity high-volume RT session using a long set configuration during several exercises produces a higher cardiac parasympathetic withdrawal in comparison with a short set configuration design. Based on these findings, a short set configuration should be prescribed to design safer RT sessions with lower reductions of cardiac parasympathetic modulation whilst the mechanical performance of the session is optimised.

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**Author contributions** EIS, MR, and XM conceived and designed research. MRA and EIS conducted experiments. MRA and EIS analysed data. MRA, EIS, XM, JM, and JDK drafted and critically revised the manuscript.

## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable standards.

**Informed consent** Written informed consent was obtained from all individual participants included in the study.



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