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ORIGINAL RESEARCH

Effects of transcutaneous electrical diaphragmatic stimulation on the cardiac autonomic balance in healthy individuals: a randomized clinical trial

Efeitos da estimulação diafragmática elétrica transcutânea sobre o balanço autonômico cardíaco de indivíduos hígidos: ensaio clínico randomizado

Los efectos de la estimulación eléctrica transcutánea del diafragma en el balance autónomo cardiaco en individuos sanos: estudio clínico aleatorio

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ABSTRACT | The transcutaneous electrical diaphragmatic stimulation (TEDS) is a technique of respiratory muscle activation that affects breathing pattern and rhythm. In an attempt to evaluate changes in cardiac autonomic balance in response to TEDS in healthy individuals, we used a well-established TEDS model. Twenty-two volunteers aged between 22 and 35 years old, with no cardiac pathology history, were randomized into two groups (control, n = 8; TEDS, n = 14). The individuals were allowed to rest in supine position and were then subjected to the electrical stimulation protocol. The control group was subjected to electrical stimulation at perceptive level, whereas for the TEDS group the electric stimulus generated diaphragm contraction. Cardiac intervals (CI) were sampled by a Polar RS800CX monitor. Cardiac interval variability was studied in the time and frequency domains. In the control group, electrical stimulation did not change cardiac interval length and variability (CI: 761±44 vs. 807±39 ms; RMSSD: 37±9 vs. 42±13 ms ; LF: 69±6 vs. 67±5 nu; HF: 31±6 vs. 33±5 nu; all comparisons versus baseline). Nevertheless, as compared to baseline, TEDS group showed decreased sympathetic cardiac modulation (LF: 43±3 vs. 63±4 nu) and increased parasympathetic cardiac modulation (RMSSD: 109±10 vs. 41±6 ms; HF: 57±3 vs. 37±4 nu) during diaphragmatic stimulation. However, cardiac interval length was not changed by electrical stimulation (CI: 686±59 vs. 780±31 ms). It can be suggested that the use of TEDS stimulus leads to pronounced changes in the cardiac sympathovagal balance, with higher parasympathetic cardiac modulation, possibly induced by increased diaphragmatic excursion.

Keywords | Transcutaneous Electrical Nerve Stimulation; Respiratory Mechanics; Autonomic Nervous System; Cardiovascular Physiological Phenomena; Physical Therapy Specialty.

RESUMO | A estimulação diafragmática elétrica transcutânea (EDET) é uma técnica de mobilização da musculatura respiratória que interfere no padrão e no ritmo respiratório. Na tentativa de avaliar as alterações no balanço autonômico cardíaco à EDET em indivíduos saudáveis, foi utilizado um modelo já estabelecido de eletroestimulação diafragmática. 22 voluntários com idades entre 22 e 35 anos, sem histórico cardíaco, foram randomizados em dois grupos (controle, n=8; EDET, n=14). O protocolo de eletroestimulação foi aplicado nos indivíduos em repouso (posição supina). O grupo controle foi submetido a estimulação elétrica em nível perceptivo, enquanto no grupo EDET o estímulo gerava contração diafragmática. Os intervalos cardíacos (CI) foram registrados por cardiofrequencímetro Polar (RS800CX). A variabilidade do intervalo cardíaco foi estudada nos domínios de tempo e frequência. No grupo

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controle, a estimulação elétrica não alterou a duração do intervalo cardíaco e sua variabilidade (CI: 761±44 vs. 807±39ms; RMSSD: 37±9 vs. 42±13ms; LF: 69±6 vs. 67±5nu; HF: 31±6 vs. 33±5nu), em comparação às condições basais). No entanto, o grupo EDET apresentou diminuição na modulação simpática cardíaca (LF: 43 ±3 vs. 63±4nu) e aumento da modulação parassimpática cardíaca (RMSSD: 109±10 vs. 41±6ms; HF: 57±3 vs. 37±4nu) durante a eletroestimulação diafragmática. No entanto, a duração do intervalo cardíaco não foi alterada por estimulação elétrica (CI: 686±59 vs. 780±31ms). Pode-se sugerir que o uso da EDET promove mudanças acentuadas no balanço simpatovagal, resultando em maior modulação parassimpática cardíaca, possivelmente induzida pelo aumento da mobilidade diafragmática.

Descritores | Estimulação Elétrica Nervosa Transcutânea; Mecânica Respiratória; Sistema Nervoso Autônomo; Fenômenos Fisiológicos Cardiovasculares; Fisioterapia.

RESUMEN | La estimulación eléctrica transcutánea del diafragma (EETD) es un método que moviliza la musculatura respiratoria que interfiere en el patrón y en la frecuencia respiratoria. Para evaluar las alteraciones en el balance autónomo cardiaco por la EETD en individuos sanos, se empleó un modelo prestablecido de estimulación eléctrica muscular del diagrama. Han participado 22 voluntarios con edad entre 22 y 35 años, sin enfermedades cardiacas, puestos en grupos aleatorios: Grupo control (n=8) y EETD (n=14). Se aplicó el protocolo de estimulación eléctrica en individuos en posición decúbito supino. Al grupo control se lo sometió a la estimulación eléctrica a nivel perceptual, mientras que en el EETD la estimulación le generaba contracción del diafragma. Los intervalos cardiacos (CI) se registraron a través del monitor de ritmo cardiaco polar (RS800CX). Se estudió la variabilidad del intervalo cardiaco en los dominios tiempo y frecuencia. En el grupo control, la estimulación eléctrica no presentó alteraciones en la duración del intervalo cardiaco y su variabilidad (CI: 761±44 vs. 807±39ms; RMSSD: 37±9 vs. 42±13ms; LF: 69±6 vs. 67±5nu; HF: 31±6 vs. 33±5nu; comparado con las condiciones de base). Pero si comparado las condiciones de base en el grupo EETD presentó una disminución en la modulación simpática cardiaca (LF: 43±3 vs. 63±4nu) y un aumento en la modulación parasimpática cardiaca (RMSSD: 109±10 vs. 41±6ms; HF: 57±3 vs. 37±4nu) durante la realización de este método. Sin embargo, la duración del intervalo cardiaco no presentó alteraciones por la estimulación eléctrica del diafragma (CI: 686±59 vs. 780±31ms). Se puede concluir que el empleo de la EETD promueve cambios significativos en el balance simpático, resultando en una modulación parasimpática cardiaca más grande, posiblemente inducida del aumento de la movilidad del diafragma.

Palabras clave | Estimulación Eléctrica Transcutánea del Nervio; Mecánica Respiratoria; Sistema Nervioso Autónomo; Fenómenos Fisiológicos Cardiovasculares; Fisioterapia.

INTRODUCTION

Under physiological conditions, the proper functioning of the respiratory system depends on appropriate strength and endurance of respiratory muscles[1]. Any dysfunction that compromise the functional excursion of the diaphragm, the main inspiratory muscle, will reduce the operational lung volume and lead to changes in ventilation/perfusion ratio, which is crucial for appropriate gas exchange[1,2].

Inspiratory muscle weakness reduces lungs' inflation capacity, leading to decreased overall lung capacity. However, the literature shows that endurance and strength training[3] of inspiratory muscles could be helpful in reversing the dyspnea and exercise intolerance arising from respiratory muscle weakness[4,5].

The transcutaneous electrical diaphragmatic stimulation (TEDS) is one of the techniques used for respiratory muscle training, aiming an increase in strength and endurance of respiratory muscles[6-8]. In brief, the TEDS consists on applying rhythmic electrical stimuli with a short duration biphasic waveform pulse through electrodes placed on the surface of the skin, i.e., diaphragm area, causing an inspiratory contraction of the diaphragm muscle[9,10]. It is noteworthy to mention that this is a noninvasive technique that allows normal diaphragmatic breathing patterns, with no damage to muscle fibers[11].

The influence of the breathing fluctuation on the heart rate variability (HRV) is described in clinical trials[8]. Studies show that fluctuations in the respiratory frequency have major effect on heart rate (HR) and its variability, a physiological phenomenon known as respiratory sinus arrhythmia (RSA)[12-14]. The increase in the intrathoracic negative pressure induced by diaphragm contraction during the respiratory cycle leads to changes in cardiac output because of an increased cardiac preload. Therefore, the atrial and pulmonary stretch receptors transmit afferent impulses that reach the brain stem through vagal afferents[15,16]. Then, efferent impulses to the heart modulate cardiac rhythm during the respiratory cycle, producing a tachycardic response during the inspiratory phase and a bradycardic response during the expiratory phase[12]. These coupled fluctuations are known as RSA[14].

The RSA reflects the synchronism between HRV and respiration by the cardiac vagal outflow shortened during inspiration and prolonged during expiration[14]. This phenomenon seems to be commanded by two major mechanisms involving respiratory and circulatory centers in the brainstem. First, the inhibition of cardiac vagal efferent activity by lung inflation, which evokes tachycardia by stimulating the pulmonary C-fiber afferents, i.e., pulmonary stretch receptors[14,15,17]; second, the acetylcholine-mediated inhibitory postsynaptic potential in the cardiac vagal preganglionic neurons by central respiratory drive, which makes neurons less responsive to excitatory inputs during inspiration[18-20].

Over the last years, the analysis of HRV has been extensively used to evaluate the autonomic modulation of the cardiovascular system[21-23]. The information regarding the cardiac autonomic modulation obtained from HRV analysis has been proven to be accurate and feasible[24]. HRV can be examined in the time and frequency domains. Among the various existing time domain measures of HRV, we can mention the RMSSD (root mean square of successive differences), which is correlated with rapid changes in the HR and reflects the parasympathetic modulation of the heart[25]. Furthermore, HRV can be evaluated in the frequency domain by spectral analysis. HR oscillations at low frequency (i.e., when expressed in normalized units) are accepted as an index of cardiac sympathetic modulation, whereas high frequency oscillations of HR are considered to reflect parasympathetic modulation of the heart[22]. The LF/HF ratio has been used to assess sympathovagal balance[22].

Therefore, this study was carried out to evaluate the effects of TEDS, a technique used for respiratory muscle training on the cardiac autonomic modulation of healthy individuals.

METHODOLOGY

Individuals and experimental design

A convenience sample (n=30) was invited to participate and was tested for the inclusion criteria. Eight subjects were excluded and the remaining 22 were assigned into the study. Experimental protocols were conducted at the Rehabilitation Center of Tiradentes University (UNIT), Aracaju, Sergipe, Brazil. Inclusion criteria were as follows: (1) aged from 22 to 35 years old; (2) enrolled in a moderate physical exercise program (no more than once a week); (3) absence of cardiovascular diseases. We excluded individuals who were taking drugs known to influence the cardiac autonomic modulation, as well as individuals taking tobacco and alcohol. Eligibility standards were not changed throughout the whole study.

Those who met the eligibility criteria were randomly assigned into two groups as follows: Control group (subjected to electrical stimulation at perceptive level; n=8; 2 men, 6 women) and TEDS group (electric stimulus generated diaphragm contraction; n=14; 4 men, 10 women). The unbalanced randomization between groups (1:1.75) was preferred, since individuals assigned to the TEDS group could present low acceptability to the electrical stimulation protocol, leading to leave the study. The flowchart of participants through the study is shown in Figure 1.

Intervention and data collection

One day before the beginning of the experimental protocol, the individuals underwent a session of habituation to the procedures (i.e., synchronizing the breathing rate to the electrical stimulation frequency and resting in supine position during the whole experimental protocol) to reduce stress. Participants were asked to avoid drinking caffeinated beverages or taking strenuous exercise in the 12 hours prior to the test. Research trials were conducted in the morning (8 a.m. to 12 p.m.), in the months of May and June of 2010. Prior to investigation, the research protocol was verbally explained and volunteers were given written information. All participants signed the informed consent form. All experimental protocols performed in this study were approved by the Research Ethics Committee of Tiradentes University – UNIT (Protocol #070510; CEP/UNIT).

Group randomization was performed by the sealed envelope technique[26,27]. In order to keep group randomization unbalanced (1:1.75), the investigator shuffled and put into a box 22 identical sealed opaque envelopes, each one containing a paper (15×15cm) with a written code designating CONTROL (8 envelopes) or TEDS (14 envelopes). On the day of the experimental trial, the researcher opened an envelope revealing the allocation to each group. We asked the participants' age, measured their height and weight to calculate their body mass index, and kept them blind to the group assignment. Then, they were instrumented with a wrist HR monitor (RS800CX, Polar Electro Inc., Lake Success, New York, USA), equipped with a transmitter (Polar Electro Inc., Lake Success, New York, USA) that was tied around their chests. For implementation of TEDS, skin electrodes (5×5 cm) were bilaterally placed (Figure 2A) in the sixth to eighth intercostal space, between the anterior axillary line and the midaxillary line[10]. Using an electrical stimulator (FesVif® 995 Dual, Quark, Piracicaba, São Paulo, Brazil), TEDS was performed with the following parameters: pulse frequency of 30 Hz, pulse width of 2 ms, ON time 2 s, OFF time 3 s. We have chosen the minimum current capable of eliciting palpable contraction of the diaphragm muscle, and participants were instructed to keep their BR constant at 12 cpm during the TEDS protocol (Figure 2B) by following a metronome. Individuals in the Control group had their BR monitored and counted by the researcher.

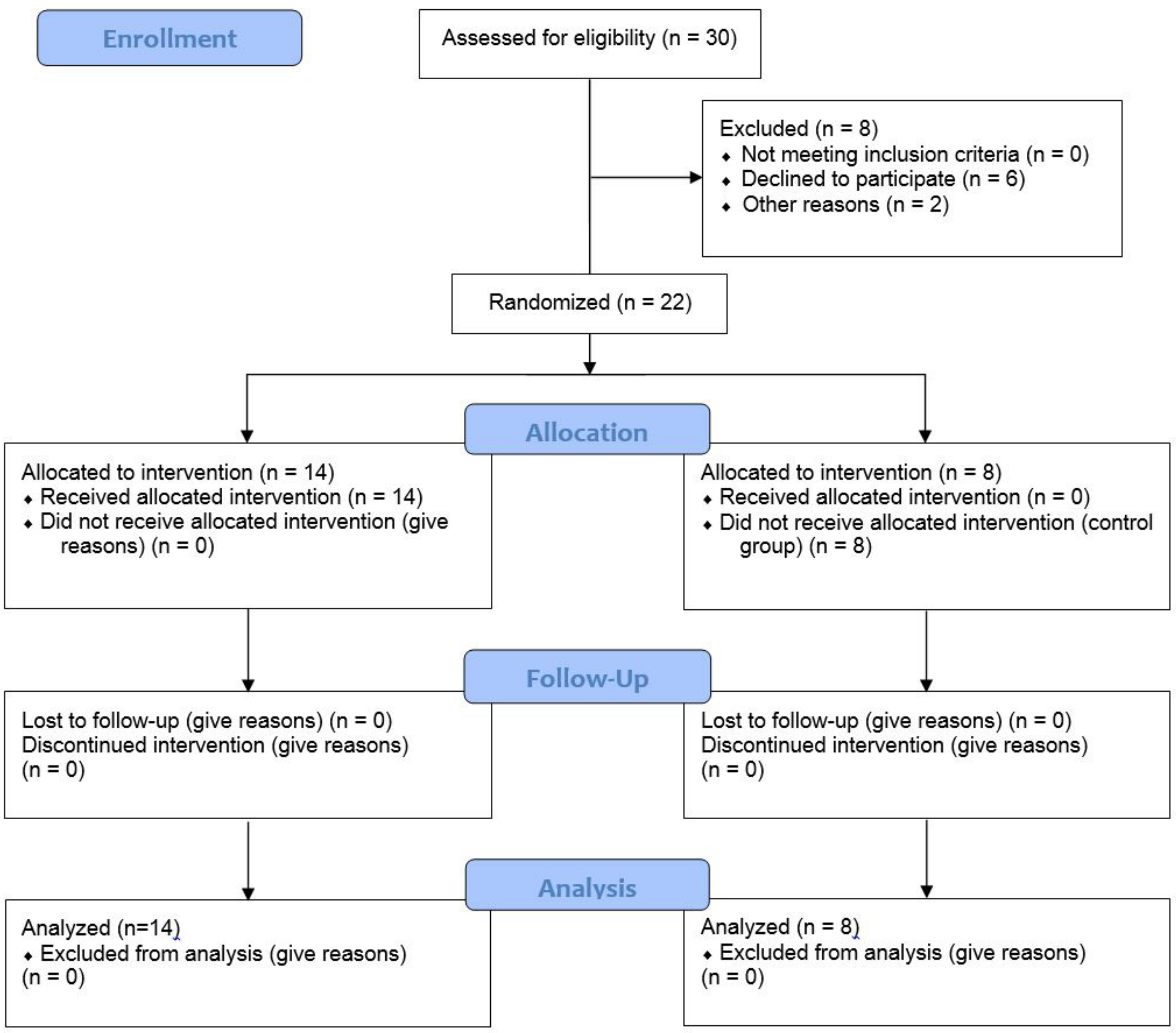

Figure 1. Flowchart of participants through the trial

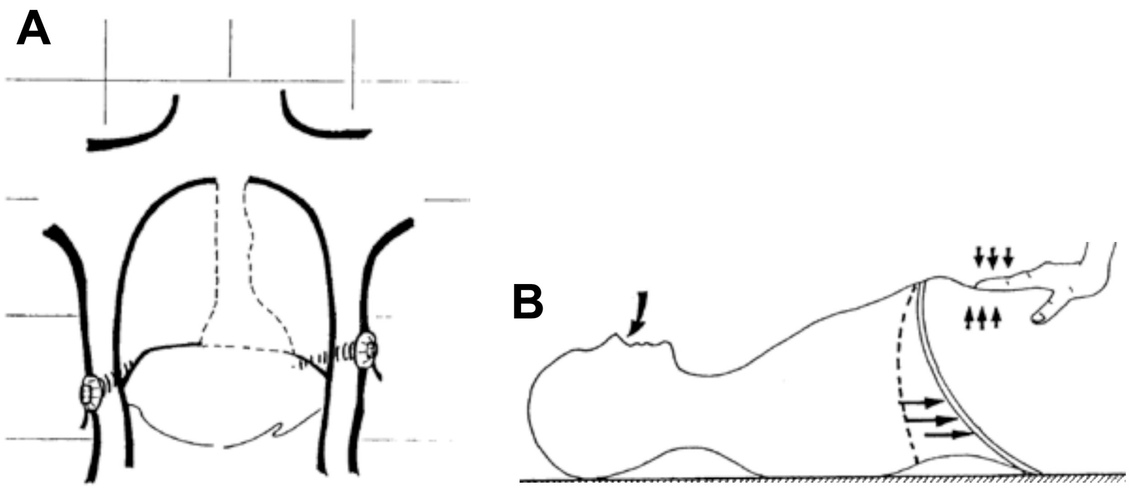

Figure 2. Adapted from Cuello and colleagues (1991)10. A. access to the costal diaphragm fibers. B. Evaluation of the diaphragm excursion

Data analysis

We evaluated cardiac autonomic balance by cardiac interval variability (CIV) analysis. For that purpose, cardiac intervals were sampled through a HR monitor (RS800CX, Polar Electro Oy, Kempele, Finland) during the 5 minutes prior to TEDS therapy, in the course of TEDS (12 minutes), and during the next 5 minutes following TEDS.

Following data acquisition, we exported beat-to-beat series of cardiac intervals and HR from the HR monitor to a computer **software (Polar Pro Trainer 5,** Kempele, Finland**) by an infrared interface.** The cardiac interval variability was assessed in the time-frequency domain by a software (**HRV Kubios, Department of Physics, University of Kuopio, Kuopio, Finland**), which allowed the precise adjustment of parameters related to the time-frequency domain analysis (e.g. time period for analysis, interpolation rate, segment length, and boundaries of frequency bands). Non-interpolated beat-by-beat time series of cardiac intervals were used for RMSSD evaluation. However, for the assessment of cardiac interval variability in the frequency domain, the time series were converted to data points every 250 ms using cubic spline interpolation (4 Hz). The interpolated series were divided into half-overlapping sequential sets of 256 data points (64 s). A Hanning window was used to attenuate side effects and all segments had the spectrum calculated using a direct Fast Fourier Transform (FFT) algorithm for discrete time series. Finally, the spectra were integrated in low-frequency (LF; 0.04 – 0.15 Hz) and high-frequency (HF; 0.15 – 0.4 Hz) bands, and results were obtained in normalized units (nu). To assess the sympathovagal balance, the LF/HF ratio was calculated[21].

Statistical analysis

The results are shown as mean±SEM (standard error of the mean). Demographic and hemodynamic characteristics were compared between groups using Student's t test. The effects of TEDS on cardiac autonomic modulation were assessed by one-way analysis of covariance (ANCOVA). When appropriate, post-hoc comparisons were performed by Bonferroni's test. Differences were considered significant when $p < 0.05$. All statistical tests were performed with SigmaPlot software v13.0 (Systat Software Inc., San Jose, California, USA).

RESULTS

The studied groups showed no differences in the demographic and hemodynamic characteristics (Table 1). Table 2 shows the HR and breathing rate (BR) values obtained before, during, and after electrical stimulation on control (n=8) and TEDS (n=14) groups. No differences were observed in HR and BR between groups.

Figure 3 shows the RMSSD; the power of the LF and HF bands of the cardiac interval spectrum; and the LF/HF ratio before, during, and after electrical stimulation in control (n=8) and TEDS (n=14) groups. Before the electrical stimulation, both groups showed equivalent values for all parameters. We observed no differences in the RMSSD, LF, HF, and LF/HF ratio following electrical stimulation in the control group. Conversely, we observed an increase in RMSSD and HF power, and a decrease in LF power and LF/HF ratio in TEDS group after electrical stimulation. After ceasing electrical stimulation, all parameters were restored to baseline levels in TEDS group.

Table 1. Demographic and hemodynamic characteristics

Variables	Control (n=8)	TEDS (n=14)	p
Gender (M/F)	2/6	4/10	----------
Age (y)	27±1.7 (23–30)	27±1.3 (24–29)	0.908
BMI (Kg/m²)	22±0.9 (20–24)	23±0.7 (22–24)	0.527
SBP (mmHg)	111±4.0 (103–119)	107±2.9 (102–113)	0.416
DBP (mmHg)	70±3.3 (64–76)	69±2.7 (63–74)	0.742

M – male; F – female; BMI – body mass index; SBP – systolic blood pressure; DBP – diastolic blood pressure. Values are expressed as mean±standard error of mean (95% confidence interval)

Table 2. Heart rate and breathing rate values obtained before, during, and after electrical stimulation in Control and TEDS groups

	Before	During	After
Control HR (bpm; n=8)	76±3.5 (69–82)	81±5.0 (71–91)	74±2.5 (69–79)
TEDS HR (bpm; n=14)	78±2.6 (73–83)	78±2.5 (72–83)	75±2.2 (71–80)
Control BR (cpm; n=8)	13±0.8 (11–14)	12±0.0	12±0.8 (11–14)
TEDS BR (cpm; n=14)	12±0.4 (12–13)	12±0.0	12±0.3 (11–12)

HR – heart rate; BR – breathing rate; bpm – beats per minute; cpm – cycles per minute. Values are expressed as mean±standard error of mean (95% confidence interval)

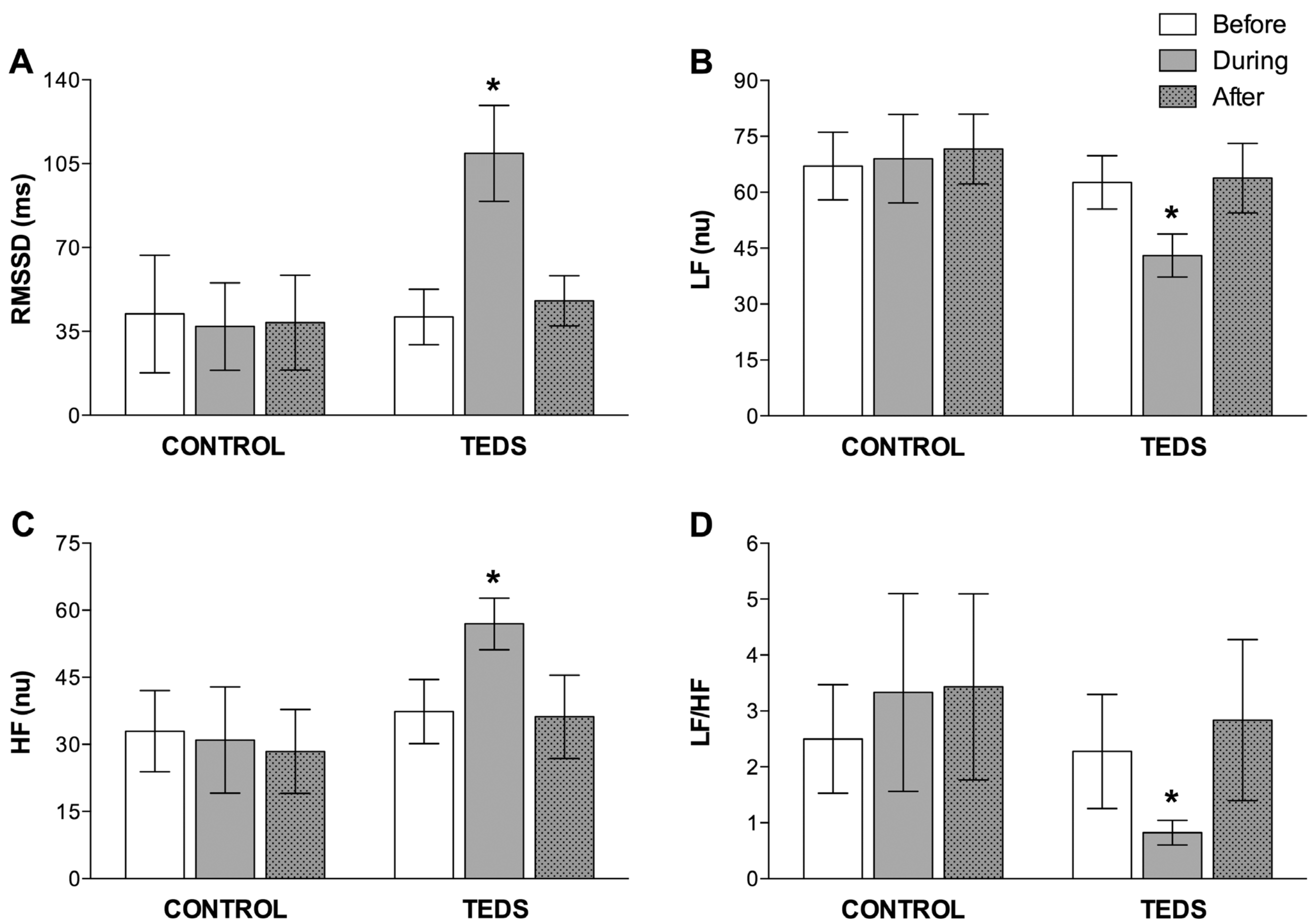

Figure 3. Cardiac interval variability. Root mean square of successive differences (RMSSD; Panel A); power of the low frequency (LF; Panel B) and high frequency (HF; Panel C) bands of the cardiac interval spectrum; and LF/HF ratio (Panel D) before, during, and after electrical stimulation in Control and TEDS groups. Values are expressed as mean and 95% confidence intervals. * $p<0.05$ vs. TEDS before

DISCUSSION

The results of this study show that TEDS elicited different changes in the CIV parameters in both groups studied. control groups presented no changes in CIV following electrical stimulation at perceptive level. However, electrical stimulation produced changes in CIV seen by decreased cardiac sympathetic modulation and reduced cardiac parasympathetic modulation. It is noteworthy that, after cessation of electrical stimulation, all CIV parameters were restored to baseline.

The studied groups showed no differences in the demographic and hemodynamic characteristics (Table 1). We observed no differences in HR and BR before, during, and after electrical stimulation in both groups (Table 2).

In our study, TEDS was able to reduce cardiac sympathetic modulation (43±3 vs. 63±4 nu) and increase cardiac parasympathetic modulation (57±3 vs. 37±4 nu). The results suggest that transcutaneous electric stimulation of the diaphragm at perceptive level (control group) does not change cardiac autonomic balance. In addition, we observed a decrease in LF/HF ratio (0.82±0.11 vs. 2.28±0.52) during electrical stimulation in TEDS group, as compared to data obtained in baseline conditions, suggesting a shift of sympathovagal balance towards parasympathetic predominance.

The large variety of HR monitors has aroused the curiosity of the comparison of its reproducibility with the conventional electrocardiogram (ECG). Wrist-worn models are worldwide employed because of their practical use and low-cost, in addition to the advantage of being used during free movement or dynamic physical activity in exercise and sports practice. On the clinical setting, data acquisition should be performed using a controlled, reliable, and practical method. Riscili et al.[28] have shown that HR data acquisition by Polar heart monitors is a safe and feasible method that can be used without any interference in cardiac functionality. The literature show that R-R interval (period between two successive R waves in the ECG) data samples with 5 minutes of duration, obtained with HR monitors, can be used for HRV analysis[29,30]. Some studies have already shown that HRV analysis, i.e., frequency domain, performed on data sampled with HR monitors over a short period (short-term) or with ECG devices over a long period (long-term), produces comparable and accurate results[31-34]. In addition, Pimentel et al.[34] showed that HR monitors can be used for R-R interval sampling during exercise, a condition marked by pronounced changes in the sympathovagal balance.

Our findings clearly showed that TEDS produces changes in the cardiac autonomic modulation with a shift towards parasympathetic predominance, i.e., decrease in the LF/HF ratio.

This suggests that the perception of electric current applied is not responsible for changes in CIV, but the negative pressure of inflation triggered by diaphragm contraction after the application of the stimulus on motor points[35]. The cardiac rhythmicity is continually modulated by the autonomic nervous system, leading to oscillations in the cardiac interval length that can be evaluated on a beat-by-beat basis[21,22].

Since the power of the HF band of the cardiac interval spectrum and the HF peak location at the spectrum are associated with respiration, we can say that they are influenced by changes in RSA. From our results, we can speculate that TEDS stimulus possibly increased inspiratory volume without noticeable changes in BR, contributing to changes in RSA.

Studies in the literature[36,37] show that changes in respiratory parameters can influence markedly the RSA amplitude. In addition, increases in RSA contribute to an extended action of acetylcholine on muscarinic receptors in the sinoatrial node, slowing down the nerve conduction during expiration[38]. In this study, BR remained unchanged during and after TEDS, as compared to baseline values. Hence, it is suggested that the changes in the CIV observed in this study may be due to an increase in depth of breathing generated by diaphragmatic electrical stimulation.

Corroborating our findings, studies conducted on chronic obstructive pulmonary disease patients revealed that, when BR is acutely reduced, changes in the cardiac sympathovagal balance are observed, i.e., reduced sympathetic activity and a trend to an increased baroreflex sensitivity[39].

Study limitations and implications

The current trial had a small sample size and the methodology for BR assessment could be improved by using a respiration monitor belt around the individuals' chest. However, our findings contribute to a better understanding of the autonomic cardiac modulation during TEDS in healthy adults.

CONCLUSION

The use of TEDS stimulus for respiratory muscles training leads to pronounced changes in the cardiac sympathovagal balance, with a shift towards parasympathetic predominance. These changes are possibly induced by greater breathing depth, i.e., increased diaphragmatic excursion, observed after

TEDS. Thus, it can be suggested that TEDS stimulus can be effectively used not only for respiratory muscles training, but also as a technique to improve the cardiac sympathovagal balance in patients.

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