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Short communication

Transcutaneous electrical nerve stimulation at different frequencies on heart rate variability in healthy subjects

Cinara Stein [a], Pedro Dal Lago [a], Janaína Barcellos Ferreira [a], Karina Rabello Casali [b], Rodrigo Della Méa Plentz [a,b,*]

[a] Universidade Federal de Ciências da Saúde de Porto Alegre, UFCSPA, Porto Alegre, RS, Brazil
[b] Instituto de Cardiologia/Fundação Universitária de Cardiologia, IC/FUC, Porto Alegre, RS, Brazil

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ABSTRACT

Sympathetic and parasympathetic nervous system imbalance has been strongly associated to sudden cardiac death. Among the non-pharmacological treatment, transcutaneous electrical nerve stimulation (TENS) represents a possible therapeutic intervention to reduce sympathetic excitation and improve the sympatho-vagal balance in different clinical conditions. We aimed to verify acute effects of high and low transcutaneous electrical nerve stimulation (TENS) frequencies by the evaluation of heart rate variability. Seven healthy volunteers received an application of low frequency (10-Hz) and high frequency (100-Hz) TENS. After 10-Hz, there was decrease of LF normalized units (n.u.) component (32.7 ± 5.9 *vs* 18.3 ± 3.4, $p < 0.002$) and increase of HF n.u. (60.9 ± 4.3 *vs* 72.6 ± 8.9, $p < 0.016$). In contrast, after 100-Hz there was increase of LF n.u. (31.5 ± 16.1 *vs* 41.6 ± 12.2, $p < 0.019$) and reduction of HF n.u. (63.9 ± 15.3 *vs* 53.7 ± 12.3, $p < 0.031$). In conclusion, TENS modulates sympathetic and parasympathetic activity in a frequency dependent manner.

1. Introduction

Sympathetic and parasympathetic nervous system imbalance has been strongly associated to sudden cardiac death (Vasegui and Shivkumar, 2008). Increased sympathetic activity is known to be related to the development of cardiac arrhythmias. Therefore, therapeutic correction of the autonomic imbalance is associated with substantial reduction of cardiovascular mortality (European Society of Cardiology, 1996; Rovere et al., 1998). The gold standard intervention to reduce sympathetic hyperactivity is the pharmacological blockade of the sympathetic nervous system by using beta-blockers (Adamson and Gilbert, 2006). However, many side effects have been reported during chronic use of these treatments (Naftchi, 1990). Non-pharmacological therapies such as physical exercise (Jurca et al., 2004; Raczak et al., 2006) and breathing exercise (Mourya et al., 2009), has shown effect in the setting of central nervous system in pathological situations such as hypertension and heart failure, in reducing the system nervous sympathetic and increase the system nervous parasympathetic (Naftchi, 1990).

Among the non-pharmacological treatment modalities, transcutaneous electrical nerve stimulation (TENS) represents a possible therapeutic intervention to reduce sympathetic excitation and improve the sympatho-vagal balance in different clinical conditions. The use of TENS (25 Hz) in patients with scleroderma improves upper gastrointestinal symptoms and the cardiovascular sympatho-vagal balance (Sallam et al., 2007). Another study reported that the periodic application of TENS (80 Hz) in both feet is sufficient to increase the baroreflex sensitivity in chronic heart failure (CHF) patients (Gademan et al., 2010). Moreover, the use of different frequencies of TENS (2 and 85 Hz) on upper extremities was tested in healthy subjects and showed an increase in sympathetic modulation. Although, the report was inconclusive regarding the effects of each frequency applied (Wong and Jette, 1984).

Another important aspect to be considered is the site where the TENS is applied. Diverse studies have used different application sites, such as: the anterior chest wall (Chauhan et al., 1994), upper limbs (Chen et al., 2007), and legs (Gademan et al., 2010), under different clinical situations, demonstrating different results in relation to central nervous system modulation. Recently, several surveys have used non invasive electrical stimulation in the treatment of refractory hypertension, with good results (Wustmann et al., 2009; Heusser et al., 2010). Another possible region to TENS application would be the paravetebral ganglionar area. It can be justified by the anatomical autonomic organization of the sympathetic nervous system to the heart and to the suprarenal gland and, vessels (Janes et al., 1986). We hypothesized that TENS application in this area may alter the feedback loop and outflow of autonomic modulation, which in turn, contribute to a decreases in sympathetic modulation and circulating catecholamine levels. Therefore, the aim of this study is to assess the acute effects of the application of TENS at high and low frequencies, in the paravertebral ganglionar region, on cardiovascular sympathetic and parasympathetic nervous system modulation in healthy subjects.

* Corresponding author at: Universidade Federal de Ciências da Saúde de Porto Alegre, UFCSPA, Porto Alegre, RS, Brazil.
E-mail address: roplentz@yahoo.com.br (R.D.M. Plentz).

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2. Methods

2.1. Subjects and design

A prospective, controlled trial was conducted with seven healthy subjects (four women), mean age 23.3 ± 4.3 years old, weight 63.9 ± 15.4 and body mass index 22.6 ± 3.5 kg/m^2. All volunteers were interviewed to collect personal data, clinical and family history of cardiovascular diseases as well as life style. The subjects should be sedentary or engage in light activity (exercise frequency, less than 3 times/week). All the participants were forbidden to perform exhaustive exercises and intake caffeine at least two hours before the intervention and instructed to have a meal before the assessment. Obesity, smokers, alcohol consumption, hypertension, diabetes, pulmonary and/or kidney diseases were exclusion criteria.

The protocol was approved by the Ethics Committee of Federal University of Health Sciences of Porto Alegre, and all subjects signed an informed consent form.

2.2. Interventions

All volunteers participated in one session of electrical stimulation with low frequency (TENS, 10 Hz/200 μs) and one session with high frequency (TENS, 100 Hz/200 μs). TENS (QUARK®, Brazil) was applied with self-adhesive electrodes (size 9 × 5 cm,), on two consecutive days in the paravertebral ganglionar region (from T1 to L2). The order of the interventions was randomly determined (by raffle). The sessions took place at the same time of the day, lasted 30 min, in an acclimatized room (23 °C) and the intensity of the current was delivered at sensory-level intensity, adjusted every 5 min by the sensory threshold, during the 30 min as tolerated by each subject, but without motor contraction or pain reported by the subject.

Throughout the protocol, the participants were comfortably accommodated in a supine position, head elevation of 30º with knees resting on a wedge. Before TENS application, the participants had their skin cleaned with alcohol solution (70%), to avoid any interference to the electrical current conductivity.

2.3. Outcomes

2.3.1. Heart rate variability

All signals were blindly analyzed. The acquisition of electrocardiogram signal (ECG) was performed immediately before and after the interventions for a 10-minute period. It was done using a protocol with three derivations, with the subject at rest, comfortably laid in the supine position, head elevation of 30°, knees resting on a wedge and controlled breathing. The breathing control was conducted through sound incentives in which the respiration rate was set at 12 breaths per minute (I:E/2:3).To assess the heart rate variability (HRV), the temporal series of RR intervals, obtained from the continuous ECG signal (sample rate – 1 kHz) registered by the MP150 system (Biopac, California, USA) were analyzed by means of spectral analysis, using autoregressive modeling.

Temporal series from the tachogram, related to each selected segment were quantitatively evaluated considering the values for the HR, total and normalized powers (n.u) of low frequency (LF – 0.04 to 0.15 Hz) and high frequency (HF – 0.15 to 0.40 Hz) components of HRV and the sympatho-vagal index (LF/HF). Normalized units (n.u.) were obtained by dividing the power of a given component by the total power (from which VLF has been subtracted) and multiplying by 100 (Montano et al., 2008).

2.3.2. Statistical analysis and sample size

Data were analyzed using the Statistical Package for Social Sciences (version 10.0, SPSS, Chicago, Illinois). We estimated that a sample size of 7 individuals in each group would have a power of 80% to detect a 20% difference between means of LF component (n.u.), for an $\alpha = 0.05$. Descriptive data are presented as mean ± SD. The effects of the interventions on continuous variables were compared using two-way analysis of variance for repeated measures (ANOVA), with randomized blocks, and post-hoc analysis was conducted using the Tukey test.

3. Results

3.1. Heart rate variability

Although there was no in difference in total heart rate variability after TENS at either stimulation frequency, the pattern of oscillation was changed indicating an alteration in autonomic control after the interventions. Moreover, the normalized parameters related to sympathetic and parasympathetic cardiac modulations were changed (Table 1).

There was decrease of LF n.u. after low frequency (10 Hz) TENS (LF: 32.6 ± 5.9 *vs* 18.3 ± 3.4, $p < 0.002$). In contrast, after high frequency (100 Hz) TENS, there is an increase of the LF n.u. (LF: 31.5 ± 16.0 *vs* 41.5 ± 12.2, $p < 0.019$). (Fig. 1A). These components were related to sympathetic and parasympathetic cardiac modulation, respectively. It was also observed an increase of HF n.u. (HF: 60.9 ± 4.3 *vs* 72.6 ± 8.9, $p < 0.016$) when low frequency TENS was applied and reduction of the HF n.u. (HF: 63.9 ± 15.3 *vs* 53.7 ± 12.3, $p < 0.031$) after application of high frequency TENS (Fig. 1B). Moreover, sympatho-vagal balance, expressed by the LF/HF index, was higher after high frequency TENS, indicating an increase in sympathetic respect to parasympathetic modulation (Fig. 1C).

4. Discussion

To the best of our knowledge, this is the first study conducted to investigate the effects of different frequencies of TENS application in the paravertebral ganglionar region on cardiac sympathetic and parasympathetic nervous system. TENS applied in the paravertebral ganglionar region presents novel results when compared with TENS

Table 1
Spectral analysis results.

	Low frequency TENS ($n = 7$)		High frequency TENS ($n = 7$)	
	Before	After	Before	After
HR (bpm)	69.7 ± 11.2	73.3 ± 11.4	71.7 ± 10.8	71.6 ± 7.5
HRV var (ms^2)	4191.5 ± 3414.7	4278.2 ± 3870.7	2679.0 ± 1916.0	3680.8 ± 2249.1
LF (ms^2)	1101.1 ± 1099.5	417.4 ± 467.6*	668.9 ± 582.3	933.9 ± 337.1
LF nu	32.6 ± 5.9	18.3 ± 3.4*	31.5 ± 16.0	41.5 ± 12.2*£
HF (ms^2)	2136.4 ± 2434.3	1613.6 ± 1677.6	1274.2 ± 999.2	1348.4 ± 785.1
HF nu	60.9 ± 4.3	72.6 ± 8.9*	63.9 ± 15.3	53.7 ± 12.3*£
LF/HF	0.5 ± 0.1	0.3 ± 0.1	0.6 ± 0.6	0.9 ± 0.4£

Values reported as mean ± SD. Heart Rate = HR; HRV = Heart rate variability; VLF = very low frequency component; LF = low frequency component; HF = high frequency component; * statistical difference ($p < 0.05$) related to before condition and £ related to low frequency TENS.

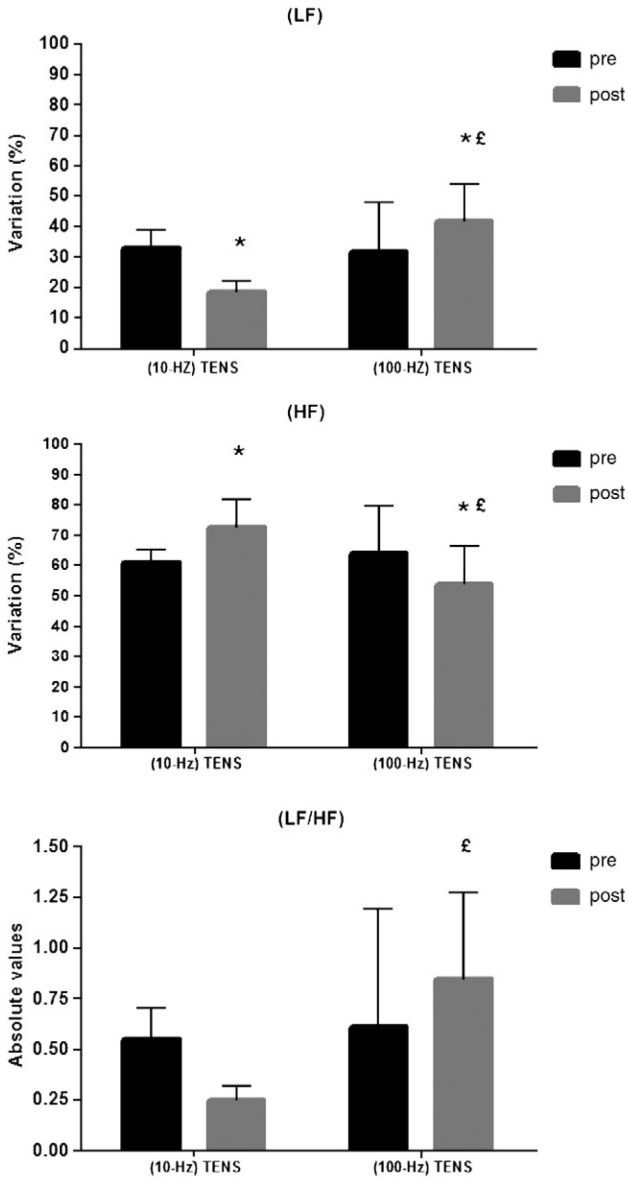

Fig. 1. Heart rate variability pre and post TENS: panels of spectral parameters of low frequency normalized component (LF), high frequency normalized component (HF) and sympathovagal balance (LF/HF).Values reported as mean ± SD. * statistical difference ($p < 0.05$) related to before condition and £ related to low frequency TENS.

applied in other sites. In the present study, we observed that application of low frequency TENS decreases sympathetic and increases parasympathetic modulation. On the other hand, high frequency TENS promotes an increase in the sympathetic and decrease in the parasympathetic modulation. Probably, the anatomical organization of the sympathetic and parasympathetic systems could be associated with the results presented here.

In relation to the use of low frequency TENS (4 Hz) applied to the upper limb, there are some reports that suggest a reduction in sympathetic nervous system after the use of TENS (Cramp et al., 2000; Olyaei et al., 2004). Here we found similar results, i.e. there was a reduction in sympathetic nervous system coupled with an increase in parasympathetic nervous system. Several mechanisms could be linked with these results. There are indications that TENS increases baroreflex sensitivity via somatosensory impulse mediated by A-δ nerve fibers (Gademan et al., 2010). It is well recognized that an improvement in baroreflex sensitivity can reduce sympathetic outflow (Gademan et al., 2010). The region where the TENS is applied could also stimulate large-diameter afferent fibers which in turn modulate efferent sympathetic nervous system (DiCarlo and Rosian-Ravas, 1999). Additionally, the increase in peripheral blood flow associated to electrical stimulation can activate peripheral ergoreceptors and modulate sympathetic outflow (Andersson and Lundeberg, 1995). In this sense, there is evidence that the excitation of peripheral nerves promoted by TENS can induce the production of substance P in the sensitive terminals, which is associated with vasodilatation (Chen et al., 1991).

Regarding the effects of high frequency TENS on the sympathetic and parasympathetic nervous system, previous studies have reported increased sympathetic tone (Wong and Jette, 1984; Casale et al., 1985) during its application, which is in agreement with our findings. There are several hypotheses associated with these results, Wong and Jette (1984) believe that: firstly the increase in sympathetic tone could be related to vasoconstrictor sympathetic fiber stimulation during high frequency TENS stimulation and, secondly, the occurrence of a vasoconstrictor response (autoregulation theory of blood flow) generated by the increase in blood flow demand, due to the muscle contraction during high frequency TENS application. However, is noteworthy that our study, compared with others, present methodological differences, such as the application site and the used stimulus intensity. Although some authors have demonstrated decrease in sympathetic activity after TENS use (Sanderson et al., 1995; Hollman and Morgan, 1997) or no modification the neural control to the heart (Buonocore et al., 1992), there is a lack of investigation about the effects of low frequency TENS, on cardiac sympathetic and parasympathetic modulation evaluated by HRV, which is difficult in the interpretation of these results.

Despite of it, many studies failed to show differences related to the TENS features (Nolan et al., 1993; Scudds et al., 1995; Cramp et al., 2000; Reeves et al., 2004; Chen et al., 2007), or have not compared both methods, high and low frequencies. (Indergand and Morgan, 1994; Sanderson et al., 1995; Hollman and Morgan, 1997). Our study was able to compare and demonstrate the effects of different applications of this electrical current on the outflow of the cardiovascular sympathetic and parasympathetic nervous systems, evaluated by heart rate variability, being a well established non-invasive method, capable of obtaining information in the matter of autonomic modulation, which is important in the diagnosis of heart disease, especially in humans (Montano et al., 1994).

The effects of TENS on central nervous system modulation may also be related to the production of endogenous opioids and the gate control mechanisms. Several studies have demonstrated that low frequency TENS increases the release of endogenous opioids, which have modulatory effects on the nucleus of the solitary tract (NTS) and consequently, on the central nervous pathway of cardiovascular control (Sluka et al., 1999, Kalra et al., 2001). On the other hand, some authors report that high frequency TENS acts by stimulating large-diameter afferent fibers, inhibiting second-order neurons in the dorsal horn and preventing impulses carried by small-diameter fibers from being transmitted (Collins and DiCarlo, 2002). This theory proposes that unmyelinated C fibers and thinly myelinated A-δ fibers transmit information to the spinal cord, resulting in stimulation of reflex sympathetic vasoconstrictor. Its effects are associated with one main mechanism in which this electrical current produces pain relief, the "gate control theory" (Melzack and Wall, 1967).

The results of this investigation suggests that low frequency TENS may be a noninvasive, non-pharmacological approach to reduce sympathetic modulation. We recognize one limitation of the present study: we did not perform direct measurements of sympathetic nervous system by assessment of muscle sympathetic nerve or by evaluation of plasma catecholamine, which should be conducted to clarify the effects of TENS on sympathetic outflow.

This might be a good target for future research to explore possible clinical uses of TENS in the field of rehabilitation, especially for patients who present sympathetic hyperactivity, by studying the biochemical mechanisms involved in this modulation.

In conclusion, TENS at low frequencies is able to reduce sympathetic nervous system and increase parasympathetic nervous system when applied in the paravertebral ganglionar region in healthy subjects. In contrast, high frequency TENS promotes increased sympathetic modulation.

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