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Original article

Nonlinear Conte-Zbilut-Federici (CZF) Method of Computing LF/HF Ratio: A More Reliable Index of Changes in Heart Rate Variability

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Key Words

acupuncture, autoregressive, autonomic modulation, exercise, fast Fourier transform, heart rate variability

Abstract

Objectives: Acupuncture treatments are safe and effective for a wide variety of diseases involving autonomic dysregulation. Heart rate variability (HRV) is a noninvasive method for assessing sympathovagal balance. The low frequency/high frequency (LF/HF) spectral power ratio is an index of sympathovagal influence on heart rate and of cardiovascular health. This study tests the hypothesis that from rest to 30% to 50% of peak oxygen consumption, the nonlinear Conte-Zbilut-Federici (CZF) method of computing the LF/HF ratio is a more reliable index of changes in the HRV than linear methods are.

Methods: The subjects of this study were 10 healthy young adults. Electrocardiogram RR intervals were measured during 6-minute periods of rest and aerobic exercise on a cycle ergometer at 30% and 50% of peak oxygen consumption (VO_{2peak}).

Results: The frequency domain CZF computations of the LF/HF ratio and the time domain computations of the standard deviation of normal-to-normal intervals (SDNN) decreased sequentially from rest to 30% VO_{2peak} ($P < 0.001$) to 50% VO_{2peak} ($P < 0.05$). The SDNN and the CZF computations of the LF/HF ratio were positively correlated (Pearson's r = 0.75, $P < 0.001$). fast Fourier transform (FFT), autoregressive (AR) and Lomb periodogram computations of the LF/HF ratio increased only from rest to 50% VO_{2peak}.

Conclusion: Computations of the LF/HF ratio by using the nonlinear CZF method appear to be more sensitive to changes in physical activity than computations of the LF/HF ratio by using linear methods. Future studies should determine whether the CZF computation of the LF/HF ratio improves evaluations of pharmacopuncture and other treatment modalities.

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1. Introduction

Evidence is emerging that acupuncture and pharmacopuncture are efficacious treatments for cardiovas-

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cular disease, as well as a variety of other diseases involving autonomic dysregulation [1-11]. Frequency-domain (spectral) methods for computing heart rate variability (HRV) are commonly used to evaluate the power of sympathetic-parasympathetic (sympathovagal) autonomic neural modulations of heart rates. Low-frequency power (LF) is a measure of mainly sympathetic influence, with some vagal baroreceptor influences, over relatively long time intervals while high-frequency power (HF) is a measure, mainly, of the vagal influences of respiratory sinus arrhythmia (RSA) over short time intervals [12]. The significance of very low frequency (VLF) power is disputable, but appears to be a mixture of sympathetic modulations with metabolic, thermogenic and emotional influences [13]. LF is usually evaluated in the frequency range 0.04 – 0.15 Hz, HF in the range 0.15 – 0.4 Hz [14, 15] and VLF in the range 0.0033 – 0.04 Hz [13, 14]. The LF/HF ratio is used to indicate the amount of sympathovagal modulation of the instantaneous heart rate [14, 16].

Linear spectral HRV analyses include the nonparametric fast Fourier transform (FFT) and the parametric autoregressive (AR) methods [17]. The AR spectrogram is smoother than the FFT spectral power density, thereby providing the advantages of better resolution with longer time segments and easily distinguishable peaks [18]. Combining frequency-domain methods with time-domain methods, the latter largely based on the standard deviation or root mean square of the standard deviation of the electrocardiogram RR interbeat intervals, have led to many breakthroughs in understanding HRV [18]. Altered HRV, measured by using both time-domain and frequency-domain analyses, are now known to occur physiologically. Aging has been characterized by no change in the overall LF/HF ratio, with complementary decrements in both the LF and the HF, and hypertension is characterized by an increase in the magnitude of the LF component and a decrease in the magnitude of the HF component compared to those components in normotensive individuals [19, 20]. Individuals with ischemic cardiovascular disease, including myocardial infarction, show similar signs of sympathetic upregulation as those with hypertension [19, 20]. Inaccuracies in the computation of the LF/HF ratio are known to occur when data are not segmented appropriately according to the physiological state and can be effectively eliminated by using the Lomb periodogram computation of the LF/HF ratio [21, 22].

Inaccuracies can be amplified by physical activity [23] and might produce erroneous interpretations with respect to evaluating sympathovagal modulations of the heart rate associated with exercise [24]. The present study was, therefore, designed to test the hypothesis that, across different levels of physical activity from rest to 50% of peak oxygen consumption (VO_{2peak}), a nonlinear method of computing the LF/HF ratio may overcome the methodological inconsistencies associated with linear computations of that ratio for quantifying the autonomic effects of acupuncture and pharmacopuncture therapies.

2. Material and Methods

Ten healthy, young-adult, African-American participants, 6 females and 4 males, volunteered for this study. All subjects were free of cardiac and pulmonary disease. The anthropometric and the physiological characteristics of the study subjects are presented in Table 1. Before participation, each subject was familiarized with the experimental procedure and risks. Approval was obtained from the Institutional Review Board at Howard University, and written informed consent was obtained from all participants.

The subjects performed two laboratory sessions of exercise approximately one week apart in the upright position on an electronically-braked bicycle ergometer (Ergoline 800, Sensormedics Corp., Loma Linda, CA). In the first session, the subjects performed an incremental test to determine the peak oxygen uptake (VO_{2peak}). The initial power was set at 20 W and was increased by 20 W every 3 minutes to volitional fatigue. VO_{2peak} was defined as the VO_2 obtained during the last minute of the incremental exercise test. The VO_{2peak} test results were used to determine the subjects' specific work rates corresponding to 30% and 50% VO_{2peak} for the second session. During the second session, the subjects rested on the ergometer for 10 minutes, followed by 10 minutes of work both at 30% VO_{2peak} and at 50% VO_{2peak}.

Height and weight were measured using standard laboratory procedures. Percent body fat was determined using Hologic QDR 4500/W dual-energy X-ray absorptiometry scans (Hologic, Inc., Marlborough, MA). Beat-to-beat electrocardiogram RR intervals were recorded using a BIOPAC MP150 high-speed data-acquisition system (BIOPAC Systems, Inc., Aero Camino, CA), with a sampling frequency of 1,000 Hz from the ECG signal, providing an accuracy of 1 ms for each RR interval. RR interval recordings were visually inspected for undesirable beats and noise by using BIOPAC Systems Acknowledge 9.6 Software. The RR intervals for the last 6 minutes at rest and during submaximal work at 30% VO_{2peak} and at 50% VO_{2peak} were analyzed. Expired gas fractions of VO_2 and VCO_2 and minute ventilation were measured using the Physio-Dyne Max II metabolic system (Physio Dyne Instrument Corp., Massapequa, NY). Expired gases were measured and averaged every 60 seconds. Before the VO_{2peak} test, the O_2 and the CO_2 analyzers were calibrated with medical grade 21.0% and 5% O_2 and CO_2, respectively. Calibration of the turbine flow meter of the metabolic system was performed with a 3-L syringe.

A spectral power density analysis of HRV was used to derive measures of autonomic modulation [25]. Frequency-domain HRV features followed the guidelines of the European Task Force [12]. HRV in the time domain was evaluated by using the standard deviation of the normal-normal electrocardiogram RR intervals (SDNN), and that in the frequency domain was evaluated by using the linear FFT, AR and Lomb periodogram methods and the nonlinear conte-zbilut-federici (CZF) method to compute the LF/HF ratio by using Nevrokard HRV software (Nevrokard, HRV, Medistar, Ljubljana, Slovenia). The power spectrum of electrocardiogram RR intervals within the 0.15- to 0.4-Hz range was defined as the HF component and primarily represented the parasympathetic (vagal) modulation of respiratory sinus arrhythmia. The LF component (0.04 – 0.15 Hz) is considered to be a mixture of both vagal and

Table 1 Characteristics of the study subjects

Variable	Subjects (n = 10)
Age (year)	20.5 ± 0.7
Height (cm)	167.7 ± 3.2
Weight (kg)	70.5 ± 4.8
Body fat (%)	30.1 ± 4.7
Systolic blood pressure (mm Hg)	119.0 ± 2.8
Diastolic blood pressure (mm Hg)	76.8 ± 2.2
HR_{peak} ($b.min^{-1}$)	186.9 ± 2.6
VO_{2peak} ($mL.kg^{-1}.min^{-1}$)	30.1 ± 2.4

HR_{peak}, peak heart rate; VO_{2peak}, peak oxygen consumption. Data are means ± standard errors.

3. Results

The anthropomorphic and the physiological characteristics of the study group show that they represent healthy, sedentary, young adults (Table 1). The effects of using the FFT, AR, Lomb periodogram, and CZF methods to compute the HRV parameters at each of the three levels of physical activity were determined (Table 2). CZF computations of the LF/HF ratio were found to be significantly smaller sequentially across the resting control (0.62 ± 0.04), the 30% VO_{2peak} (0.41 ± 0.03, $P < 0.01$ *vs.* control) and the 50% VO_{2peak} (0.34 ± 0.02, $P < 0.001$ *vs.* control and $P < 0.05$ *vs.* 30% VO_{2peak}) conditions. The activity-related changes in the CZF-computed LF/HF ratio were also found for the SDNN values from rest (62 ± 9 ms) to 30% VO_{2peak} (30 ± 4 ms, $P < 0.001$ *vs.* control) to 50% VO_{2peak} (25 ± 4 ms, $P < 0.0001$ *vs.* control and $P < 0.05$ *vs.* 30% VO_{2peak}). The SDNN values for the LF/HF ratio and the ratios computed by using the CZF method were significantly correlated (Pearson's r = 0.75, $P < 0.001$). The LF/HF ratios at 50% VO_{2peak} computed by using the FFT, AR, and Lomb periodogram methods were significantly greater than the value obtained using the control computations (FFT and AR $P < 0.01$, Lomb $P < 0.05$), but were not significantly different from the LF/HF ratio computed for the 30% VO_{2peak} condition($P > 0.1$).

Whereas all the linear computations of the LF/HF ratio (FFT, AR and Lomb) were unable to differentiate between the two levels of exercise, 30% and 50% VO_{2peak}, the AR computations were the only linear computations that differentiated between the resting control and 30% VO_{2peak} conditions. The SDNN time-domain measurement and the nonlinear CZF computation of the LF/HF ratio, both indicators of the RR interbeat interval variability, differentiated between the three levels of activity.

Table 2 LF/HF-activity relationships computed by using the FFT, AR, Lomb and CZF Methods

Activity	FFT	AR	Lomb	CZF	SDNN (ms)
Rest LF/HF	2.5 ± 0.9	2.6 ± 0.9	2.9 ± 1.0	0.62 ± 0.04	62 ± 9
(LF, nu)	(51 ± 7)	(83 ± 15)	(32 ± 4)	(38 ± 2)	
30% VO_{2peak}	4.6 ± 1.6	5.2 ± 1.5*	4.3 ± 1.0	0.41 ± 0.03†	30 ± 4‡
LF/HF (LF, nu)	(54 ± 7)	(100 ± 13)	(22 ± 8)	(29 ± 1)	
50% VO_{2peak}	7.2 ± 2.6†	6.5 ± 2.0†	6.0 ± 1.9*	0.34 ± 0.02§	25 ± 4§
LF/HF (LF, nu)	(52 ± 7)	(87 ± 12)	(11 ± 2)	(25 ± 1)	

*Significantly different from the resting control measurement at $P < 0.05$, †different from the resting control at $P < 0.01$, ‡different from the resting control at $P < 0.001$, and §different from the 30% VO_{2peak} measurement at $P < 0.05$. All values are LF/HF ratios, LF/HF, and LF (in normalized units, nu) expressed as means ± standard errors.

LF/HF, low frequency/high frequency; FFT, fast Fourier transform; AR, autoregressive; Lomb, Lomb periodogram; CZF, Conte-Zbilut-Federici; SDNN, standard deviation of normal- normal electrocardiogram RR (interbeat) intervals; VO_{2peak}, peak oxygen consumption; nu, normalized units.

sympathetic signals [26, 27].

Differences between the time-domain SDNN and the frequency-domain linear FFT, AR, and Lomb periodogram methods and the nonlinear CZF method for computing the LF/HF ratio, expressed in normalized units (nu), were evaluated at the following three levels of steady-state physical activity: resting conditions, aerobic exercise under 30% VO_{2peak} conditions, and aerobic exercise under 50% VO_{2peak} conditions.

Descriptive statistics were expressed as means ± standard errors. The statistical significances of the differences between the methods of computing the LF/HF ratio were evaluated by using an analysis of variance (ANOVA) at each level of physical activity. Statistical significance was set at $P \leq 0.05$.

4. Discussion

Current noninvasive, linear computations of the LF/HF ratio, a useful index of sympathovagal balance, are often inconsistent from day to day in the same individuals under the same environmental conditions and are often exaggerated during aerobic exercise [21-24]. Exercise stress testing is the most widely-used method for assessing cardiovascular health, and the ability to quantify the LF/HF ratio during exercise stress testing may provide a robust tool for assessing the effects of acupuncture, pharmacopuncture, and other treatment modalities. The main purpose of t6his study was to determine whether a novel nonlinear (CZF) method for computing the LF/HF ratio, a reliable measure of sympathetic-parasympathetic influences on the heart rate that has been extended to a general assessment of autonomic neural signaling, was superior to the linear FFT, AR and Lomb methods.

This is the first study to compare FFT, AR, Lomb and CZF computations of the LF/HF ratio across the range of activity from rest to 30% to 50% of peak oxygen consumption. The main finding of this study is that only CZF computations of the LF/HF ratio, which decreased sequentially, thereby indicating less variability of the RR interbeat interval, were significantly different across the three levels of activity. FFT, AR and Lomb computations of the LF/HF ratio increased from rest to 50% of peak oxygen consumption, but were not significantly different from 30% to 50% of peak oxygen consumption, thereby reliably indicating increased sympathetic modulation of heart rates only from rest to 50% of peak oxygen consumption. This finding on linear computations of the LF/HF ratio agrees with that of a study comparing only FFT and AR computations of the LF/HF ratio in healthy, young adults across four conditions of physical activity: resting to 20% of peak oxygen consumption to recovery and resting to 40% of peak oxygen consumption to recovery [23].

In the present study, the mean LF/HF ratio at rest, computed by using the FFT, AR and the Lomb methods, were skewed toward greater sympathetic modulation than expected, as evidenced by three of the ten study subjects exhibiting a resting LF/HF ratio ≥ 3. This higher-than-expected level of sympathetic modulation at rest was accepted because it did not translate to higher-than-normal blood pressures. A resting LF/HF ratio < 1 is expected during both preprandial, overnight fasting and postprandial states resting in bed for a group of healthy young adults similar to those in the present study [28, 29]. In the present study, the subjects were all postprandial, and this condition was not controlled. The resting LF/HF ratio was also not controlled because inclusion of subjects exhibiting a wide range of resting LF/HF ratios was thought to make these results relevant to both research laboratories and medical clinics. Moreover, some normal study subjects were likely to have increased sympathetic modulations because of a "white-coat syndrome" [30]. Sympathetic influences are reported to be exaggerated in an African-American subpopulation like the one comprising the present study group [31].

The present study evaluated the different linear computations of the LF/HF ratio in normalized units, which served to eliminate the computational variations associated with expressing HRV spectral powers in raw ms^2. Normalized units are used to express the LF and the HF on a proportional scale that compensates for the within- and the across-subject variability found for measures of raw ms^2 spectral powers, are reported to have smaller coefficients of variation than raw ms^2 units, and are more repeatable between studies [32]. The calculated LF/HF ratios and LF values were presented in data tables values so that one could appreciate how activity-related changes in the LF, commonly used as the main indicator of sympathetic modulation, affected the computations of the LF/HF ratio. Because of the inverse proportionality between the LF and the HF expressed in normalized units, increases in the LF in normalized units are equivalent to decreases in the HF in normalized units, and *vice versa* [32]. Thus, the LF/HF ratio is thought to be a more useful index of autonomic (sympathetic-parasympathetic, sympathovagal) interactive modulation of the heart rate than the LF, a specific indicator of sympathetic modulation, and the HF, a specific indicator of vagal parasympathetic modulation, [32].

Linear FFT, AR and Lomb computations of the LF/HF ratio are reported to be reliable HRV spectral indicators of the power of the sympathovagal interactive modulations, with greater values being indicative of greater sympathetic influences [33]. On the other hand, the LF/HF ratio computed by using the nonlinear CZF method has been shown to be a spectral indicator of the variability in the RR interbeat intervals [33]. Decreases in the variability of RR intervals, also indicated in this study by using the time-domain SDNN measure, together with increases in the LF/HF ratio found by using FFT and AR computations, are widely-used indicators of autonomic responsiveness to aerobic exercise [23]. In the present study, the nonlinear CZF computations of the LF/HF ratio were found to decrease sequentially and significantly from rest to 30% to 50% of peak oxygen consumption. The time-domain SDNN computations of the LF/HF ratio exhibited the same activity-related pattern of change as the CZF computations, and those measurements were significantly correlated. We also observed that the differences between the CZF-computed values of the LF/HF ratio and the values of the LF/HF ratio in the time-domain SDNN computations between rest and 30% of peak oxygen consumption were significantly greater than those between 30% and 50% of peak oxygen consumption. This finding is consistent with previous research indicating that the largest cardiovascular perturbations occurred at the beginning of aerobic exercise [32]. On the other hand, the LF/HF ratios computed by using the linear FFT, AR and Lomb methods were found to be increased significantly only from rest to 50% of peak oxygen consumption. These findings suggest only the variability in the RR interbeat intervals may be measured reliably, not the power of the associated sympathovagal modulations from rest to 30% to 50% of peak oxygen consumption. These findings have important implications for HRV evaluations involving autonomic dysregulation and cardiovascular disease commonly performed using exercise stress testing protocols such as the one employed in the present study [24]. Exercise stress testing is a widely-used method for assessing patients and evaluating the effects of pharmacological and alternative medical treatments for cardiovascular disease on the cardiovascular system. Improvements in exercise stress testing, such as increased HRV, are important clinical outcomes of acupuncture treatments [34].

5. Conculsion

Greater sensitivity to activity from rest to 30% to 50% of peak oxygen consumption was demonstrated by using nonlinear CZF computations of the LF/HF ratio rather than linear FFT, AR, and Lomb periodogram computations. We conclude that sequential the decreases in the variability of electrocardiogram RR interbeat intervals associated with changes in activity from rest to 30% to 50% of peak oxygen consumption can be reliably measured by using CZF computations of the LF/HF ratio. Future studies should determine whether the nonlinear CZF method improves assessment of the changes in the sympathovagal influences on heart rate and other autonomic functions that result from acupuncture, pharmacopuncture, and other medical treatments.

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Conflict of interest

The authors declare that there are no conflict of interest.

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