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Autonomic Function in Individuals with Slow Heart Rate Response following an Exercise Stress Test

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Abstract

Objective: To examine the autonomic function using HRV measures in apparently healthy individuals undergoing exercise stress test (EST) and demonstrating slow HRR response. **Methods:** HRV was measured with 12 lead ECGs during graded EST and analyzed via a post-processing method. Autonomic function was determined by Power Spectral Analysis of the very low frequency (VLF), low frequency (LF), high frequency (HF), and the ratio of LF/HF. We correlated HRV indices with resting, exercise, and recovery data. **Results:** No differences were found in anthropometric measurements, peak EST HR, and METS between individuals with slow HRR (below 18 b/min) compared with controls (HRR > 18 b/min). Only the VLF component of the HRV indices was statistically different ($p = 0.03$) at one-minute post-exercise compared with controls. Additionally, a significant correlation between HRR and resting LF and HF indices was found in the individuals with slow HRR but not in the controls. **Conclusion**: In apparently healthy individuals with slow HRR post-EST, autonomic function did not demonstrate any differences at any phase of the EST, including at one minute of recovery. However, a significant correlation was found between resting LF and HF powers and HRR in individuals with slow vagal reactivation post-exercise. The clinical and prognostic implications of such observation deserve further investigation.

Keywords

Heart Rate, Heart Rate Recovery, Heart Rate Variability, Exercise Stress Test

1. Introduction

Heart rate recovery (HRR) is defined as the difference in heart rate (HR) from peak effort to that record at a 1-minute post-exercise stress test (EST) [1] [2]. Normally, a cutoff point above 18 b/min measured during active recovery and a cutoff point of 12 b/min measured during a passive recovery period are categorized as normal HRR responses [3] [4]. Low HRR (≤18 b/min) correlates with a high risk of mortality [5] and could be detected by measuring HR variability (HRV) indices during EST [6] [7].

Autonomic function plays a significant role in the physiological changes associated with exercise in general and during EST in particular. During the recovery period from an EST, parasympathetic/vagal tone reactivates, and sympathetic tone is gradually withdrawn [8] [9]. These changes can be measured using HRV indices. The sympathovagal balance is reflected by the very low frequency (VLF) domain, the overall sympathetic activity is reflected by the low frequencies (LF) domain, and the parasympathetic tone is reflected by the high frequency (HF) domain, and by the ratio between the LF/HF [10] [11] [12] [13]. HRR and HRV are used to evaluate, among other things, post-exercise autonomic, sympathetic, and parasympathetic functions [14]. These indices have also been used to indicate physical performance and recovery, mostly in normal activities, and competitive athletes [15].

The vagal nerve activity increases the HF and VLF powers during recovery following exercise and decreases the LF/HF ratio [10]. Nunan *et al.* 2010 have shown that HRV consistently differs between healthy individuals based on their HRR. Individuals who demonstrated slow HRR had a significantly lower total power of HF, suggesting that a greater modulation in vagal activity is essential for a better HRR [16]. Chen *et al.* 2011 demonstrated a significant correlation between HRR and short-term HRV frequency domains, presented by the total power of LF and HF, during the recovery period [17].

In the current study, we aimed to examine autonomic function using HRV measures, in apparently healthy individuals undergoing EST and demonstrating slow HRR response.

2. Methods

The protocol was approved by the local IRB Committee in Sheba Medical Center (approval No. SMC-9871-12). The study included healthy inactive volunteers that approved their participation by signing the informed consent form.

The ESTs were carried out at the Institute for Medical Screening, Sheba Medical Center, Tel Hashomer. EST was performed on a running treadmill by a highly professional technician, using the Bruce protocol. 12-lead ECG was recorded at rest, during each exercise stage, and during the entire 5 min recovery period. The test was stopped when the participant reached HR > 85% of age-predicted HRmax. Individual characteristics and ESTs' data were analyzed. HRR was determined based on a cut-off point of 18 b/min measured during the

first min of active recovery.

Autonomic function indices were measured using "Embletta Gold" (Embla USA), by HR recording and signal sampling at 200 Hz and analyzing ECG records offline. Power spectral measurements, with a standard available importer, were calculated using software HC1000P—HypnoCore Ltd. Israel. HRV measurements included monitoring of the average power; at the first minute of resting in a supine position (all maintained their normal breathing patterns), during each phase of the EST until peak exercise, and during the first minute of active recovery. HRV indices were analyzed by frequency domains method and included "very low frequency" (VLF, 0 - 0.03 Hz; an index of the overall activity of slow mechanisms of sympathetic function including respiration and the sympathovagal balance), "low frequency" (LF, 0.04 - 0.15 Hz; an index of sympathetic activity), "high frequency" (HF, 0.15 - 0.40 Hz; an indicator of vagal activity), and the ratio between the "LF to HF power" (LF/HF; a reflection of sympathovagal balance), as previously reported [18] [19]. The analysis was based on the recorded ECG signals sampled, and the location of R peaks was detected using the peak detection algorithm offline. The R-R interval series transformed into a consistently HRV signal valid for estimating the power spectral algorithms. Spectral analysis was performed on each frequency; VLF, LF, HF, and the ratio between the LF/HF on each EST stage. Irregular R-R intervals point event series was automatically or visually removed to reduce artifacts. Data of the individuals demonstrating slow HRR response (those individuals having HRR below 18 b/min) was compared with controls demonstrating HRR above 18 b/min.

3. Statistical Analyses

Statistical analyses included comparisons for all study outcomes; at rest, peak exercise, and at first-minute of recovery using Graph-Pad Prism (version 9.2). All HRV indices were log-transformed (ln), and are presented by the absolute integral (ln) power values of the VLF, LF, HF, and the LF/HF ratio, as we previously performed [20], and were normally distributed according to D'Agostino & Pearson omnibus normality test [21].

Parametric Independent t-test was performed for all anthropometrics data, HR at rest, peak exercise and recovery, maximal METs, and HRV indices including the VLF, LF, HF, and the LF/HF ratio during all ESTs phases, and LF/HF at rest. A non-parametric Mann–Whitney test was performed for the total number of ESTs and maximal HR age-predicted (%), according to D'Agostino & Pearson omnibus normality test [21]. Pearson correlations were also performed to analyze the relationship between resting HRV indices and HRR. Data are presented as Mean ± SD. A p-value ≤ 0.05 considered significant.

4. Results

All individuals were apparently healthy, with no medications while undergoing the annual checkups. They had normal EST with no clinical symptoms or signs of ischemia, hypertension, or arrhythmia. Demographic characteristics, medical

history, and health-related habits, including regular physical activity, were subjectively reported without any differences during the previous 3 years.

Anthropometric data, blood, and lipid profile of the slow HRR response (n = 11) were not different from controls (n = 17) and were all within the normal range, Table 1.

4.1. ESTs Results

Significantly, higher absolute resting HR and HR at one-minute post-EST were found in individuals with slow HRR compared with controls ($p = 0.03$ and $p < 0.001$, respectively). The HRR, as expected, in the slow HRR response was below 18 b/min and significantly lower compared with control ($p < 0.0001$). Nevertheless, no significant differences were found in peak-exercise HR ($p = 0.90$) and maximal METS achieved in the ESTs' between both slow and fast HRR responses, ($p = 0.83$). The EST results demonstrated similar physiological exercise parameters presented both in the slow HRR response and control, Table 2.

4.2. HRV Indices

Despite a significantly higher power of VLF found at one-minute post-exercise in individuals with slow HRR compared with control ($p = 0.03$), and borderline higher values at peak exercise, $p = 0.08$, there was non-significant HF power at rest and at one-minute post-exercise ($p = 0.06$ and $p = 0.07$, respectively). Additional, no significant differences were found in all other HRV measures (VLF, HF, LF, and LF/HF ratio) during all ESTs' phases; rest, peak exercise, and during one minute of recovery, between both, slow and fast HRR response, $p > 0.05$, Table 3.

Table 1. Anthropometric characteristics.

Anthropometrics data:	Controls (n = 17)	slow HRR response (n = 11)
Age (years)	57.7 ± 8.5 (39 - 67)	51.5 ± 11.2 (27 - 70)
Weight (kg)	80.8 ± 18.3	80.6 ± 16.6
Height (cm)	173.6 ± 8.6	175.6 ± 8.8
BMI (kg/cm^2)	26.6 ± 4.2	25.9 ± 3.9
Hb (g/dL)	14.1 ± 1.2	14.0 ± 1.3
HbA1C (%)	5.4 ± 0.6	5.7 ± 0.7
TG (d/L)	101.8 ± 33.5	114.6 ± 26.2
LDL (mmol/L)	115.2 ± 25.6	119.0 ± 20.8
HDL (mmol/L)	48.7 ± 12.1	50.6 ± 11.5

Controls; HRR > 18 b/min; male (n = 11); 65%, female (n = 6); 35%. Slow HRR response ≤ 18 b/min; male (n = 9); 82%, Female (n = 2); 18%). Hb; Hemoglobin concentration. HbA1C; Hemoglobin A1C. TG; Triglycerides. LDL; Low Density Lipoprotein Cholesterol. HDL; High Density Lipoprotein Cholesterol. Data are presented as Mean ± SD. No differences were found between groups.

Table 2. Resting, exercise, and recovery data of both groups (n = 28).

ESTs results (mean ± SD)	Controls (n = 17)	slow HRR response (n = 11)
Resting SBP (mmHg)	130.6 ± 18.9	127.3 ± 12.7
Resting DBP (mmHg)	80.0 ± 10.6	79.8 ± 7.6
Resting HR (b/min)	75.0 ± 7.4	*81.9 ± 7.8
Maximal HR (b/min)	158.2 ± 7.4	158.7 ± 14.5
Maximal HR age predicted (%)	98.1 ± 5.8	93.7 ± 7.1
Maximal METs (ml/kg/min)	12.1 ± 1.5	12.2 ± 2.3
Maximal SBP (mmHg)	165.2 ± 23.0	171.8 ± 20.5
Maximal DBP (mmHg)	77.3 ± 6.8	79.8 ± 7.6
HR at 1 min post exercise (b/min)	129.4 ± 7.9	**148.2 ± 13.8
HRR (Delta; b/min)	28.8 ± 7.0	***10.5 ± 3.1

ESTs; individuals' last exercise stress tests (n = 28). Data are presented as Mean ± SD. * Denote significant differences between groups using an unpaired t-test (* p = 0.03, ** p < 0.001, *** p < 0.0001).

Table 3. Differences in HRV indices at rest, maximal exercise, and during the 1-min recovery period.

EST phases	Controls (n = 17)	slow HRR response (n = 11)
Rest		
In (VLF)	7.02 ± 0.69	7.07 ± 0.79
In (LF)	6.99 ± 1.07	7.44 ± 1.41
In (HF)	7.50 ± 1.48	8.57 ± 1.14
LF/HF (ratio)	0.81 ± 1.08	1.26 ± 0.57
Maximal exercise		
In (VLF)	9.20 ± 0.75	9.66 ± 0.39
In (LF)	11.65 ± 0.59	11.47 ± 1.31
In (HF)	11.38 ± 1.06	11.18 ± 1.48
LF/HF (ratio)	0.27 ± 0.69	0.29 ± 0.61
One minute post-exercise		
In (VLF)	8.85 ± 0.73	*9.40 ± 0.42
In (LF)	10.58 ± 0.56	11.03 ± 0.89
In (HF)	11.18 ± 0.73	11.88 ± 1.08
LF/HF (ratio)	0.60 ± 1.10	0.85 ± 0.84

HRR; Heart rate recovery; HRR > 18 b/min (group1; n = 13); HRR >< 18 b/min (group 2; n = 11). All HRV indices were log-transformed (ln), and are presented by the absolute integral (ln) power values of the VLF, LF, HF, and the LF/HF ratio [20]. Data are presented as Mean ± SD. * Denote significant differences between groups using an unpaired t-test, p = 0.03.

4.3. Correlations between Resting HRV and Post-Exercise HRR

Resting LF and HF powers were positively correlated to HRR only in the slow HRR response. However, the resting VLF did not correlate with HRR in the slow HRR response, yet did significantly correlate in the controls. No correlations were found between resting LF and HF and HRR in the controls, nor in the resting LF/HF ratio and HRR in both groups, Table 4.

5. Discussion

The present study aimed to examine autonomic function in apparently healthy individuals who demonstrated slow HRR response during the first-minute post-active recovery following EST using HRV indices. We found that despite the slow HRR response, there were no significant differences in the spectral measures of HRV presented by the absolute values of the LF, HF, and the LF/HF ratio at rest, peak exercise, and recovery between individuals having slow HRR response compared with controls. Furthermore, only the slow HRR group presented a correlation between the resting LF and HF indices and HRR, which was not found in the controls, despite having a fast HRR response.

We questioned if the slow HRR response is due to inherited autonomic dysfunction and could be expressed by HRV indices at rest, peak exercise, or during the recovery period post-exercise testing. Only the VLF power at one-minute post-exercise was significantly higher in individuals who demonstrated a slow HRR response compared with the individuals who demonstrated a fast HRR response ($p = 0.03$), as previously discussed by Shaffer *et al.* 2014, and which did not differ at rest and peak-exercise [22].

The borderline higher VLF at peak exercise found in the slow HRR response ($p = 0.08$), correlates with a normal and high exercise capacity as reported by Lu *et al.* 2016 [23]. Furthermore, as previously reported [8] [10], the vagal nerve activity increases the VLF band parallels an increase in the HF and a decrease in the LF/HF ratio during peak exercise and recovery [20], as we also observed in our current study. We assume that the significant differences in VLF ($p = 0.03$) and the borderline higher HF ($p = 0.07$) during recovery might indicate a normal parasympathetic response in individuals who presented a slow HRR response, despite their significantly lower HRR.

Table 4. Correlations between resting HRV and HRR in both study groups (n = 28).

	Controls (n = 17)	slow HRR response (n = 11)
Resting VLF to HRR	***r = −0.53**	r = 0.48
Resting LF to HRR	r = −0.10	r = 0.56
Resting HF to HRR	r = 0.12	***r = 0.62**
Resting LF/HF to HRR	r = 0.37	r = −0.21

All HRV indices were log-transformed (ln), and are presented by the absolute integral (ln) power values of the VLF, LF, HF, and the LF/HF ratio. HRR; Heart rate recovery (b/min). * Denote significant correlation ($p < 0.05$).

We also found a non-significant higher HF power at rest and during recovery in individuals with slow HRR compared with fast HRR, which means that both responses might represent a normal parasympathetic post-EST behavior.

Resting HRV reflects the ability to respond to physiological demands during exercise [24] [25] [26]. A higher resting HRV indicates a higher parasympathetic tone and therefore greater recovery status, while lower resting HRV values reflect an increase in sympathetic tone leading to a lower recovery status [7] [24].

Several studies highlighted a lack of significant correlations between resting HRV and HRR following a maximal EST on a treadmill, for example in well-trained athletes [27], healthy population [28] [29], and normal college-age men [30].

Our results emphasized that despite having a slow HRR response, there was a significant correlation to a higher resting HF. Nevertheless, the relationship between resting HRV and HRR has not been well established and remains controversial. For example, Bechke *et al.* demonstrated a positive relationship between resting HRV and HRR in apparently healthy females [13]. Cunha *et al.* 2015, reported that the parasympathetic reactivation following EST, (as assessed by HRR), depends on exercise modality and cardiac autonomic control at rest [31]. HRR seems to be dependent on parasympathetic reactivation after almost total withdrawal during exercise, different from parasympathetic modulation at rest when both sympathetic and parasympathetic releases provide the natural variation of HR [7]. This paper shows, to the best of our knowledge, for the first time the correlations between HRV and HRR in individuals with slow HR response post-EST, and found a significant correlation with HF power.

The strength of the current study is the examination of a healthy population demonstrating both fast and slow HRR, which presented a normal autonomic function and a correlation to resting HRV only in the slow response individuals. Therefore, it should be taken into account in the autonomic function evaluation measured in a single EST.

One of the limitations relates to the small sample size (n = 28) and the fact that only healthy individuals participated in the current study. The HRV results are based on the current individuals' ESTs with no follow-up over repeated ESTs. We can assume that the autonomic function in the first-minute post-exercise might have a large variation between individuals and therefore should be examined in repeated ESTs. Further studies are needed to evaluate the relationship between HRR and HRV indices post-ESTs in other populations.

6. Conclusion

Despite having slow HRR in a single EST, there were no significant differences in the spectral measures of HRV presented by the absolute values of the LF, HF, and the LF/HF ratio at rest, peak exercise, and recovery compared to individuals with fast HRR. Additionally, a significant correlation was found between resting HF power and HRR only in the slow HRR response, but not in the controls. This data demonstrates that a slow HRR might not present an abnormal vagal reacti-

vation following a single EST and might question the significant direct impact of LF and HF indices on HRR post-EST. Further studies are needed to investigate the relationship between HRV and HRR in non-healthy individuals.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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