

The effect of passive lower limb training on heart rate asymmetry

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Research

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Abstract

Background: Heart rate asymmetry (HRA) is an approach for quantitatively assessing the uneven distribution points of RR intervals of sinus rhythm. We aimed to investigate whether the automatic regulation lead to HRA alternation during passive lower limb training.

Methods : Several variance-based HRA variables derived from Poincaré plot were established. Thirty healthy participants were recruited in this study. The protocol included baseline (Pre-E) and three passive lower limb training trials (E1, E2 and E3) with a randomized order. Heart rate variability (HRV) frequency-domain parameters (LF (n.u.), HF (n.u.) and VLF (ms²)) and HRA variables (SD1a, SD1d, SD2a, SD2d, SDNNa and SDNNd) were calculated by using 5-min RR time series.

Results : Our results showed that the performance of HRA distinguished. The HRA was observed with significant changes in E1, E2 and E3 compared to Pre -E. Moreover, HRA variables correlated with HRV parameters in all trials, which indicated that HRA might benefit in assessing autonomic alteration in passive lower limb trainings.

Conclusions: In summary, this study suggested that passive training led to significant HRA alternation and the application of HRA gave us the possibility for autonomic assessment.

Background

Heart rate variability (HRV) has been extensively studied in clinical settings as it is modulated by the cardiovascular regulatory mechanisms, especially the interplay between sympathetic and parasympathetic activities[1, 2]. HRV is a non-invasive approach to studying heart rate by measuring the variation of RR intervals, which beat at a non-constant frequency. There are different methods specifically for the purpose of studying the variance of RR time series, such as frequency methods and nonlinear dynamic methods[3, 4].

Heart rate asymmetry (HRA), which is defined as the asymmetric distribution of heartbeat fluctuations, has been gaining momentum for the last few years. It takes into account the directionality of the RR intervals, so that heart rate accelerations and decelerations can be distinguished[5, 6]. It turns out that HRA is useful for quantifiable interpretations of chronic diseases[7, 8].

Several measures have been developed to assess the asymmetry of heart rate, e.g., Guzik's index (GI) and Slope index (SI) uncovers the distance and phase angle information in the plot, respectively[5, 9], while area index(AI) combines these two characteristics to perform the asymmetry[2]; Other measure to HRA includes the monotonic runs, Piskorski and Guzik proposed that RR intervals could be partitioned into acceleration and deceleration runs to count the numbers separately[6]. All these measures are aiming at exploring the difference between accelerations and decelerations and interpreting the physiological meanings.

Despite literatures regarding effects and associations between HRA metrics and pathological factors[8], few studies examined the HRA alterations respond to passive limb training. Several studies suggested that passive trainings elicited increased femoral blood flow and cardiac output, as well as a great change in HRV, which implied a great effect of passive training on cardiovascular and autonomic modulation[10–12]. However, the HRA mechanism in passive training remained unclear. The examination of changes of HRA measures with passive training can help better understanding the modulation of heartbeat, providing opportunities to comprehend the knowledge of how to standardize the training and make training effective for hemiplegia patients. In other words, HRA can be of great help to interpret how well the underlying control mechanism works and provide information in clinical settings.

In the present study, we focused on elucidating whether HRA distinguishes between passive trainings and baseline. In addition, we explored how HRA alteration is related to HRV indices and measures of physiology responding to different passive limb training trials. This study can contribute to a more comprehensive understanding of the asymmetrical properties of heart rate and to provide validity of HRA in passive lower limb training.

Heart Rate Asymmetry

HRA observed from Poincaré plot represents the presence of complex dynamics in physiological signal. There were several effective measures established to assess HRA[13]. In this part, we introduced the definitions of HRA variables and the basic descriptors used in this study.

Poincaré plot is a tool for depicting and quantifying the distribution of RR intervals on a 2D coordinates. There are two important lines: the first one is the identity line, which goes across all points representing no change in the duration of consecutive RR intervals ($RR_n = RR_{n+1}$); the second line is perpendicular to the identity line, and it crosses the centroid of the whole plot. According to these two lines, SDNN is extracted by calculating the total variance of all RR intervals

$$SDNN^2 = \frac{1}{n} \sum_{i=1}^n (RR_i - \overline{RR})^2 \quad (1)$$

where n is the total number of RR intervals, and RR is the mean RR time series.

As described by Piskorski and Guzik[14, 15], short-term variability SD1 is the variance of projection of points along the identity line, and perpendicular projection of points leads to long-term variability SD2. Combining the two variables, there is a known formula[14]

$$SDNN^2 = \frac{1}{n} (SD1^2 + SD2^2) \quad (2)$$

By the lines, the two descriptors can be partitioned into parts on accelerations and deceleration in the following way

$$SD1^2 = SD1_a^2 + SD1_d^2 \quad (3)$$

$SD1_a$ is calculated from the perpendicular distance of points above the identity line and $SD1_d$ is calculated from the perpendicular distance of points below the identity line, representing short-term variance of contributions of accelerations and decelerations, respectively.

Consequently, $SD2$ is separated in the same way by referencing the perpendicular line

$$SD2^2 = SD2_a^2 + SD2_d^2 \quad (4)$$

where $SD2_a$ and $SD2_d$ represent long-term variance of the contributions of accelerations and decelerations, respectively.

Using the formulas above, $SDNN$ can be partitioned into two parts, too

$$SDNN^2 = SDNN_a^2 + SDNN_d^2 = \frac{1}{2} [(SD1_a^2 + SD1_d^2) + (SD2_a^2 + SD2_d^2)] \quad (5)$$

with

$$SDNN_a^2 = \frac{1}{2} (SD1_a^2 + SD2_a^2), SDNN_d^2 = \frac{1}{2} (SD1_d^2 + SD2_d^2) \quad (6)$$

This partition can detect a more specific asymmetry resulting from acceleration and deceleration of sinus heart rate.

Results

As shown in Fig. 2, frequency-domain HRV parameters were calculated in baseline (Pre-E) and three passive movement trials (E1, E2, E3). Compared to Pre-E, the LF (n.u.) and VLF (ms^2) in E1, E2 and E3 were decreased, whereas only E2 and E3 showed statistical significance ($p < 0.05$). For HF (n.u.), increased values were observed in E1, E3 and E3 compared to Pre-E, whereas E1 and E2 showed statistical significance ($p < 0.05$).

The HRA variables including $SD1_a$, $SD1_d$, $SD2_a$, $SD2_d$, $SDNN_a$ and $SDNN_d$ were examined and compared in Fig. 3. In Pre-E, no asymmetry was observed for these HRA variables, suggested that the behavior of

heart rate acceleration and deceleration had no difference in the baseline. While in E1, E2 and E3, the HRA changes were observed with higher deceleration than acceleration. Significant difference was found between SD2a and SD2d in E1 ($p < 0.05$). For SDNNa and SDNNd, significant difference existed in E1 and E3 ($p < 0.05$).

Additionally, 24 participants (80%) with SD1a < SD1d and 19 cases (63%) with SD2a < SD2d were observed and 21 participants (70%) exhibited SDNNa < SDNNd in E1, E2 and E3. Furthermore, ICC in Table 1 showed that all HRA variables produced higher reproducibility with ICC > 0.8 ($p < 0.001$).

Table 1
Interclass correlation coefficients (ICC) for HRA variables

	SD1 _a	SD1 _d	SD2 _a	SD2 _d	SDNN _a	SDNN _d
ICC	0.890	0.888	0.828	0.832	0.863	0.899
p	< 0.001**	< 0.001**	< 0.001**	< 0.001**	< 0.001**	< 0.001**
ICC > 0.75 means that the effect of reproducibility of HRA variables is good.						

The Spearman correlation coefficients between HRA variables and HRV frequency-domain parameters were summarized in Table 2. A considerable part of the coefficients was statistically significant ($p < 0.05$). A negative correlation was found between LF (n.u.) and SD1_a and SD1_d while a positive correlation between LF (n.u.) and others. A positive correlation was found between HF (n.u.) and SD1_a, SD1_d, while a negative correlation between HF (n.u.) with others. For VLF (ms²), it had stronger positive correlation with SD2_a, SD2_d, SDNN_a and SDNN_d compared with SD1_a, SD1_d.

Table 2
Summary of Spearman correlation coefficients between HRA variables and HRV frequency-domain parameters

	SD1 _a	SD1 _d	SD2 _a	SD2 _d	SDNN _a	SDNN _d
LF(n.u)	-0.425**	-0.525**	0.380*	0.449**	0.358*	0.286
HF(n.u)	0.430**	0.530**	-0.382*	-0.445**	-0.358*	-0.281
VLF(ms ²)	0.374*	0.372*	0.708**	0.661**	0.769**	0.683**
*: $p < 0.05$. **: $p < 0.001$.						

Discussion

In this study, we elucidated the response of HRA to passive lower limb training and explored the correlation between HRA variables and HRV frequency-domain parameters. Three passive training trials were performed in a randomized order to examine the HRA alternation compared to the baseline. Six

established HRA variables, i.e., $SD1_a$, $SD1_d$, $SD2_a$, $SD2_d$, $SDNN_a$ and $SDNN_d$ were examined. Additionally, the response of autonomic mechanism to passive lower limb training was assessed by HRV parameters, i.e., LF (n.u.), HF (n.u.) and VLF (ms^2).

Marked reduction in LF (n.u.) and VLF (ms^2) of HRV parameters was found during passive lower limb exercise while HF (n.u.) significantly increased compared with baseline. These findings were in agreement with previous researches[10, 22] that parasympathetic activity performed a dominant role and vagal tone was withdrawn caused by passive training. In this study, the relationships between HRA variables and HRV frequency-domain parameters were investigated, which indicated that HRA correlated with changes in sympathetic and parasympathetic activities (see Table 2). Accordingly, a lower HRA variables correlated with lower LF (n.u.) and VLF, while with higher HF (n.u.). This suggested that the effect on HRA was parallel to the response in HRV, and meanwhile the reduction in $SD1_{a/d}$, $SD2_{a/d}$ and $SDNN_{a/d}$ resulted from suppression of parasympathetic activity. However, this conclusion must be drawn cautiously in the future work due to a considerable part of the weak coefficients, which indicted that HRA and HRV were correlated but had distinct metrics in assessing intricate and nonlinear autonomic system. Another reason for the weak correlation might due to the hemodynamic responses to passive training, i.e., passive training led to heart rate increase and an enhancement in cardiac output[23–25].

Physiologically, HRA was related to sinus node innervated by autonomic nervous system, which modulated heart rhythm through neurotransmitter release[26]. This was the reason that the disturbed HRA could provide diagnostic evidences for many pathologies[7, 8, 27]. In this study, more participants (80%) exhibited short-term asymmetry with $SD1_d > SD1_a$, which showed consistency with some researches. For example, Piskorski et al [20, 28] suggested that most subjects showed the HRA phenomenon with $SD1_d > SD1_a$, $SD2_d < SD2_a$ and $SDNN_d < SDNN_a$ in 420 young healthy participants. However, more participants with $SD2_d > SD2_a$ and $SDNN_d > SDNN_a$ were found for long-term and total asymmetry, which was different with Piskorski et al 's research. This difference may partially result from different lengths of the data used in the present study. Another reason may due to a compensation mechanism in HRA, which was that a larger contribution of decelerations to short-term asymmetry was compensated by a larger contribution of accelerations to long-term asymmetry[14, 20]. It could be physiologically interpreted that the prolongations of AH and HV intervals contributed larger than the shortenings to short-term variability of the intervals[29]. On the other hand, the respiratory maneuvers had influence on HRA property. Klintworth et al found an increased HRA with inspiration/expiration ratio = 1:1 or 2:1 by recording 5-min ECGs[30].

Note that our results suggested a symmetry in baseline (see Fig. 3) which was not in line with previous study[2, 5]. We assumed that it was the different uses of reference points that led to this consequence. It was reported that the performance of HRA, i.e., SI and AI, varied a lot when using different reference points[31]. Yan et al 's study demonstrated that using the minimum of RR interval time series as reference points could achieve optimization of the result [31]. In the present study, the origin of the global coordinate was used. Therefore, there was no evidence that $SDNN_{a/d}$ was lack of sensitivity to vagal

withdrawal during passive movement and this result remained more investigations. Furthermore, we also used AI and SI to assess the asymmetry phenomenon in response to passive training in this study as Yan et al did[31], however, no asymmetric phenomenon was observed in four trials and there was no statistical significance ($p > 0.1$). The outcomes proved that these variance-based HRA variables performed better than SI and AI in assessing autonomic regulation for passive lower limb training. Additionally, the ICC results underlined the suitability of HRA for application.

Previous studies revealed that men and women had different automatic response to passive training[10, 32]. In addition, it was verified that HRA could be perturbed by pathologies[2, 27]. Hence, the gender influence on HRA should be taken into account in further studies, and also a larger population of healthy participants and patients from different age groups are required to confirm and extend these conclusions.

Conclusion

To sum up, this study investigated the influence of passive movement on HRA and demonstrated that HRA was useful in assessing autonomic response to passive training. The asymmetry of accelerations and decelerations was a universal phenomenon during three passive training trials in this study. The variance-based HRA variables performed well in detecting asymmetric phenomenon and suggested a suppression of vagal activity responded to passive movement. The correlations between HRA and HRV parameters reinforced the point.

Methods

1. Participants

Thirty healthy, physically active participants (15 males, 15 females) without history of cardiovascular or neurological disorder were included in the study. The average age was 23 ± 2.3 years and body mass index (BMI) was between 19 to 24 kg/m². All participants were nonsmokers, normotensive, and asymptomatic for respiratory disease. None of them were taking any medication. Caffeine and alcohol were refrained approximately 48 hours prior to the data collection, as well as intense exercise. None of participants had received professional lower limb strength training. The study conformed to the Declaration of Helsinki and was approved by ethics committee at University of Shanghai for Science and Technology, Shanghai, China. All participants gave written informed consent to participate in this study.

2. Experimental protocol

All the measurements were undertaken in a quiet and temperature-controlled (25 ± 3 °C) room free from external distractions. For each participant, ECG signal was first recorded for 10 min as a baseline (Pre-E) following a rest period of at least 15 min prior to exercise sessions. Then, ECG signals were recorded for three 10-min trials with the passive cycling machine (Mode: ZP-K600A, Tianjin Zepu Technology Co., Ltd, China) adjusted to 5cycs/min (E1), 10cycs/min (E2) and 15cycs/min (E3), respectively (Figure. 1). These three trials were performed in a random order. Each trial was separated by at least a 10-min period. Before

the experiment, the participant conducted a sufficient number of practice sessions so that they could flex their leg to a comfortable range of motion and keep the body stable to avoid any motion artifacts.

3. Data acquisition and processing

In the experiment, the PowerLab/16sp system (Castle Hill, AD Instruments, Australia, 2002) was used to record and amplify ECG signal. Three electrodes for the lead \AA ECG signal were respectively placed on right wrist, left wrist and right leg for each participant. Sampling frequency was set at 1 kHz and ECG signal filtered by a 1 Hz high-pass filter and a 40 Hz low-pass filter. After removing abnormal R peaks on the QRS complexes, the values of normal-to-normal cardiac interval corresponding to sinus rhythm were automatically measured and were subsequently exported for further analyses. All ECG datasets used for subsequent analysis were free of any form of morphologically abnormal beats. To eliminate the effect of muscular compensation and ensure steady state conditions, only last 5-mins ECG signal of each session was analyzed.

4. HRV and HRA measures

Short-term HRV analysis has been proved to overcome high non-stationarities problem and is suitable for studying short-time autonomic response[16, 17]. In this study, frequency domain parameters were derived from power spectral analysis of last 5-min RR time series by using fast Fourier transform (FFT) algorithm. The power spectrum is typically parsed into three frequency ranges[18]: very low frequency (VLF, 0.003–0.04 Hz); low frequency (LF, 0.04–0.15 Hz); high frequency (HF, 0.15–0.4 Hz). LF and HF components were measured in normalized units(n.u.) to minimize the inter-participant variation[19]. VLF was presented in absolute values of power (ms^2).

For HRA, six well-established variables ($\text{SD1}_{a/d}$, $\text{SD2}_{a/d}$, $\text{SDNN}_{a/d}$) derived from Poincaré plot were calculated, which were introduced in Sect. 2 (Heart rate asymmetry). For these variance-based variables, SD1_a and SD1_d were the contributions of acceleration and deceleration to short-term variance, respectively; SD2_a and SD2_d were to long-term variance; SDNN_a and SDNN_d were to total variance[20]. It was worth noting that this interpretation referred to the construction of variables rather than length of analyzed time series[20, 21]. Taken together, the combined HRV and HRA analysis of time series offered an in-depth insight into dynamics of the heart.

5. Statistical analysis

All quantitative variables were presented with means \pm standard deviation (SD). Shapiro-Wilk test was used to investigate if the normality assumption was satisfied. For the comparison of normally distributed HRV indices, one-way repeated measures ANOVA incorporating a Bonferroni adjustment was used to compare characteristics in four trials (Pre-E, E1, E2, E3), followed by post hoc analysis. The paired HRA variables between trials were compared using paired sample T-test. Additionally, interclass correlation coefficient (ICC) was used for evaluating the reproducibility of HRA variables in different trials. Nonparametric Spearman correlation test was performed to analyze the relation between HRA variables and the most often used HRV frequency-domain parameters (VLF, LF, HF). All test results yielding p-value

< 0.05 were considered statistically significant, and analyses were conducted by using SPSS statistical software (Version 24).

Abbreviations

HRA

heart rate asymmetry

HRV

Heart rate variability

HF

high frequency component

LF

low frequency component

VLF

very-low frequency

SDNN

standard deviation of NN intervals

ECG

electrocardiogram

GI

Guzik's index

SI

Slope index

AI

area index

Declarations

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Contributions

Liang Wu and Ping Shi: proposed the idea and designed the method; Liang Wu and Anan Li performed experiments and analyzed the data. They made discussions and composed the manuscript together with Hongliu Yu and Yang Liu. All authors read and approved the final manuscript.

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Ethics declarations

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the ethics committee of University of Shanghai for Science and Technology, Shanghai, China (Ref. No. 2013-9010-14YZ091).

Consent for publication

All authors gave their consent for publication.

Competing interests

The authors declare that they have no competing interests.

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Figures

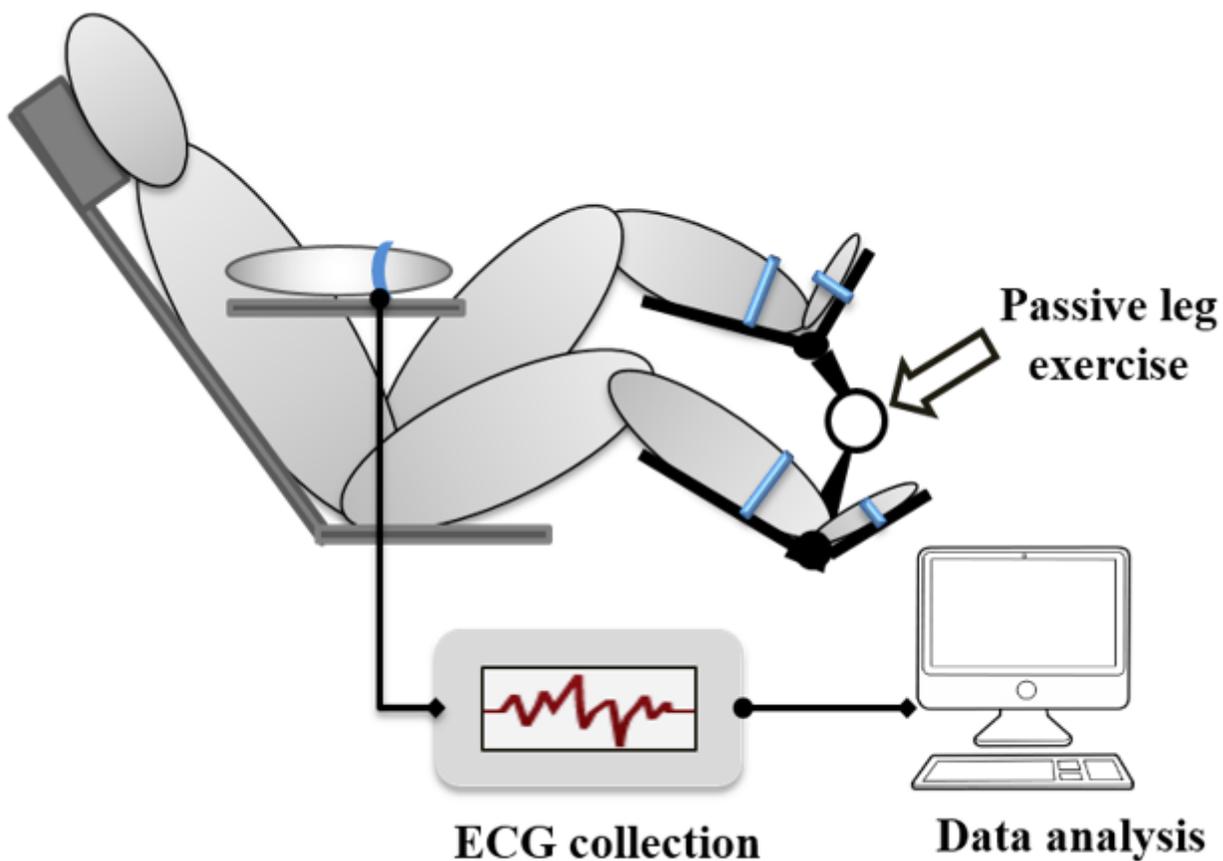


Figure 1

Experimental setup for passive lower limb training. The ECG signals were collected with physiological signal recording system. HRV and HRA variables extracted from ECG signals were analyzed peripheral device software.

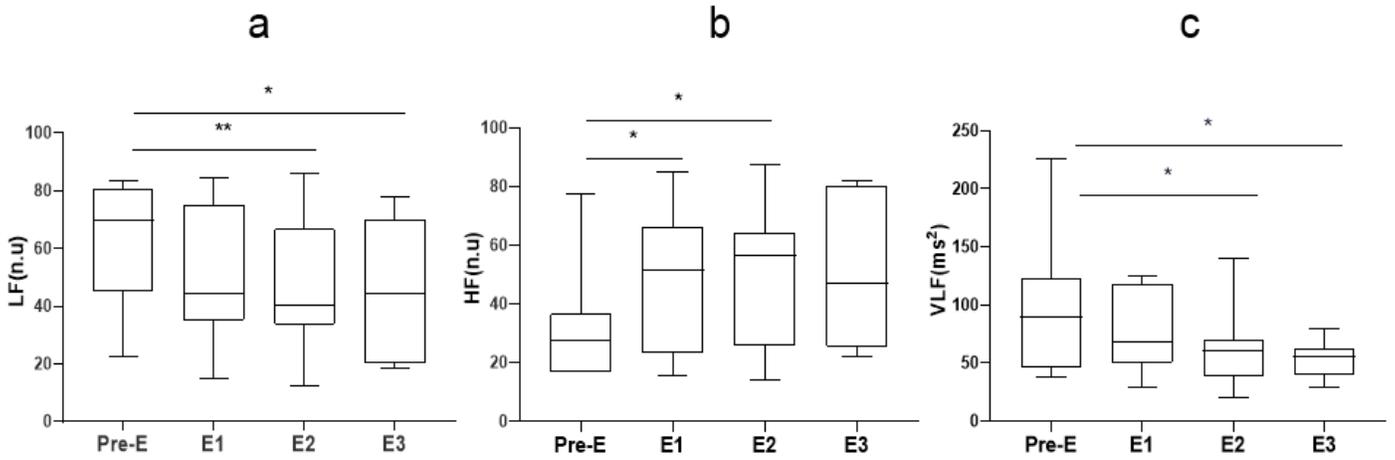


Figure 2

The frequency-domain HRV parameters in Pre-E, E1, E2 and E3. *: $p < 0.05$; **: $p < 0.01$.

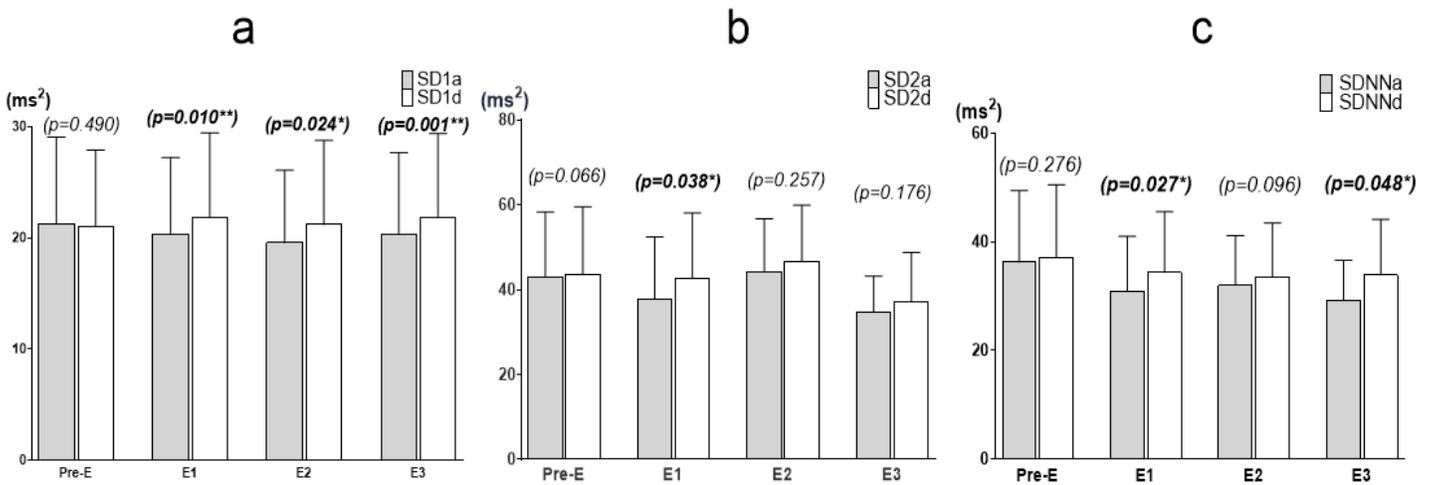


Figure 3

Comparison of HRA between accelerations and decelerations in all trials. a, b and c corresponded to relative short-term asymmetry (SD1a, SD1d), long-term asymmetry (SD2a, SD2d) and total asymmetry (SDNNa, SDNNd), respectively.