The contribution of preintervention blood pressure, VO₂max, BMI, autonomic function and gender to exercise-induced changes in heart rate variability

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ABSTRACT

Introduction The quantification of heart rate variability (HRV) is a tool to assess the interaction between exercise and autonomic control, as well as the pathophysiology of diseases affecting autonomic function. Little is known about the influence of genetically influenced physiology on exercise-induced changes in autonomic cardiac regulation. It was theorised that preintervention values for blood pressure, VO₂max, body mass index (BMI), autonomic function and gender contribute significantly to the exercise-induced changes in HRV.

Methods A 12-week, medium-to-high intensity exercise intervention was completed by 183 volunteers (18–22 years). Data were sampled at baseline and after 12 weeks. Standard time domain, frequency domain and Poincaré HRV quantification techniques were implemented. Regression analysis was performed to determine the influences of the predictors (baseline values for low frequency (LF), high frequency (HF), BMI, VO₂max, gender, blood pressure) on the exercise-induced response of the dependent variables (changes in HRV-indicator values).

Results Parameters found to be significant ($p < 0.05$) predictors of exercise-induced changes were LF, HF and systolic blood pressure in, respectively, 10, 5 and 2 of the 12 regressions performed. The results indicated that the independent variables contribute between 12.83% and 29.82%, depending on the specific HRV indicator, to the exercise-induced changes in the autonomic nervous system.

Conclusions Preintervention autonomic status, as represented specifically by LF, is the most important determinant of cardiac autonomic response to an exercise intervention in a healthy study population. Baseline autonomic function could thus be a significant confounder in the outcome of exercise study results.

INTRODUCTION

Heart rate variability (HRV) as an indicator of exercise-induced changes in autonomic cardiac regulation shows wide interperson SDs, as well as inconsistent study results.^{1–2} Vesterinen *et al*³ recently reported unexplained individual adjustments in performance ability as measured by VO₂max after exercise training. A review by Hautala *et al*⁴ showed a range from zero improvement to plus 40% improvement in exercise ability as measured by VO₂max without finding an explanation by physiological mechanisms.

Various factors can, in theory, contribute to the individual variations in adaptation to exercise as measured by HRV and VO₂max. In the case of HRV quantification, technical aspects such as

length and period of sampling times, choice of analytical techniques and non-standardisation of the populations investigated may play a role.^{1–4} However, little is known about the influence of preintervention physiology and genetic influence on autonomic cardiac changes, as measured by HRV, in response to exercise adaptation.⁴

Since 2005 publications seem to concur on the effects of medium to long term (12 weeks and longer) exercise programmes. Increased resting vagal cardiac control is visible in many reports,^{5–10} with an overall increase in HRV,^{11–14} accompanied by a possible decrease in sympathetic.^{15–17} Studies reporting no effect on HRV markers are few and seem to be linked to the exercise-intervention intensity and also the specific type of exercise intervention.^{18–20}

A fundamental question unanswered in literature is on the role of the preintervention physiological characteristics and genetics of the participants/patients or athletes on exercise-induced autonomic change and performance. This information is a critical knowledge for the athlete coach in the prevention of over-reaching/overtraining and also for clinicians, as exercise is widely recommended to induce positive changes in the cardiac autonomic control of clinical populations.²¹ Indicators of physiological status identified by the literature as possible confounders included blood pressure, fitness, body mass index (BMI) and baseline autonomic function.^{1–2}

In this preliminary study, the focus was on baseline physiological factors that may influence exercise-induced autonomic changes in cardiac control as measured by HRV. The independent variables tested were baseline/preintervention systolic blood pressure (SBP), diastolic blood pressure, aerobic fitness (VO₂max), BMI and HRV-indicator values. The dependent variables were the change (Δ) in the HRV-indicator values observed. The Δ HRV indicator values were calculated as the postintervention HRV indicator value minus the preintervention HRV indicator values. It was hypothesised that the preintervention independent variables (blood pressure, VO₂max, gender, BMI and status of the autonomic nervous system (represented by low frequency (LF) and high frequency (HF) power), contribute significantly to the exercise-induced changes in the dependent variables (HRV indicators).

METHODOLOGY

The study consisted of a 12-week medium-to-high intensity exercise intervention, in a group of 100

male and 83 female recruits of the South African National Defence Force (SANDF) between the ages of 18 and 22. The study protocol was approved by the SANDF Ethics Committee as well as the Research Ethics Committee of the Faculty of Health Sciences, University of Pretoria. All participants gave written informed consent before the start of the intervention. Exclusion criteria included refusal to give voluntary written informed consent; a history of cardiovascular, hepatic, respiratory or renal impairment, as well as pulmonary, metabolic and orthopaedic diseases requiring medical attention; lung/respiratory tract infection in the previous 2 weeks; and medication that could influence cardiovascular control and psychological disorders. None of the participants were professional athletes or high-level sport participants, and all the participants were subjected to the same, strictly standardised, 24 h routine (exercise, diet and sleep) for the duration of the 12-week exercise intervention. The calculated average basal metabolic rate for participants, taking weight and age into account, was 6371 kJ/day. This, in addition to the energy expenditure of the training and exercise activities, resulted in a calculated average energy expenditure of 8485 kJ/day, which can be classified as a medium-to-high intensity exercise programme.²²

DATA SAMPLING AND STATISTICAL ANALYSIS

Baseline values for the independent variables were collected at the start of the training period, while the autonomic cardiac control was determined with HRV quantification at baseline and again after the 12-week exercise intervention. Standard time domain, frequency domain and Poincaré HRV quantification techniques were implemented. The HRV indicator values obtained were then used to calculate the dependent variables (postintervention HRV values minus the preintervention HRV values). This information was then used in a regression analyses to test the study hypothesis. This type of statistical analysis is used when investigating the relationships between variables to determine causal effect of the one on the other.²³ In the current study, linear regression was used to determine the influences of preintervention BMI, VO₂max, gender, blood pressure and autonomic function (LF, HF), on the exercise-induced autonomic response measured by HRV-indicator values (postintervention HRV value minus preintervention HRV value).²³

Measurements

The participants were weighed on a calibrated medical scale wearing underwear, running shorts and a t-shirt. The height was measured with a stadiometer whereafter their BMI was calculated: mass (kg)/height (m²). Blood pressure was recorded after the participant had rested quietly for 5 min. A mercury sphygmomanometer, cuff and stethoscope were used to determine the blood pressure of each participant. Owing to the large number of participants in the current study, aerobic capacity was indirectly calculated by using the statistically significant negative correlation between the 2.4 km run time of the recruits and their VO₂max. Burger *et al*²⁴ reported that that the 2.4 km timed out and back run test reliably predicts the directly measured VO₂max. The running time to complete a distance of 2.4 km on a flat surface was recorded and used to calculate the VO₂max of participants.

During HRV quantification, a minimum tachogram length of 1 min is essential to assess the HF components, and at least 2 min for the LF components.²⁵ Data from a 180 s tachogram in the supine position were used for HRV quantification and for the regression analysis. During the HRV data sampling periods, attention was given to the standardisation of temperature, luminosity, noise and the consumption of caffeine and alcohol.²⁶ No strenuous activities were undertaken during the preceding 48 h. Data were sampled after a good night’s rest and a standard breakfast in the morning hours before 11:00 at 22°C. POLAR RS800 heart rate monitors were used to obtain the intervals between successive QRS complexes (RR/NN intervals). Tachograms from participants were registered after a 2 min stabilisation period in the supine position. The RR/NN intervals were analysed with Polar software obtained from the University of Kuopio, Finland.

The HRV techniques used for the evaluation of the cardiac autonomic control were grouped into three categories: time domain, frequency domain and non-linear analysis of variability. HRV indicators determined are listed in table 1 with an explanation of the efferent source of stimulation (sympathetic or parasympathetic branch of ANS).^{25 27}

RESULTS

Baseline values for independent variables sampled at the start of the training period are shown in table 2. The HRV indicator

Table 1 HRV indicators including the origin of efferent stimulation (sympathetic or parasympathetic branch of ANS)

Indicator and unit	Origin of efferent stimulation
HR (s)	The mean heart rate influenced by vagal (short term) and sympathetic (long term) branch of ANS
RR or NN (s)	The mean of the intervals between successive QRS complexes, influenced by vagal (short term) and sympathetic (long term) branch of ANS
SDRR or SDNN (s)	SD of intervals between successive QRS complexes, indicator of vagal (short term) and sympathetic (long term) influence on HRV (overall HRV)
RMSSD (ms)	Root mean square of the SD between RR/NN intervals, indicator of vagal influence (short term)
pNN50 (%)	The percentage of successive RR/NN interval differences larger than 50 ms computed over the entire recording, indicator of vagal influence (short term) on HRV
SD1 (ms)	Indicator of the SD of the immediate, or short-term, RR/NN variability due to parasympathetic efferent (vagal) influence on the sino-atrial node
SD2 (ms)	Indicator of the SD of the long-term or slow variability of the heart rate. It is accepted that this value is a representative of the global variation in HRV
LF power (ms ²)	Indicator of sympathetic influence including a parasympathetic component
HF power (ms ²)	Indicator of only parasympathetic influence
LF/HF	Indicator of autonomic balance
LFnu	LF in normalised units (LF/LF+HF), influenced by vagal (short term) and sympathetic (long term) branch of ANS
HFnu	HF in normalised units (HF/LF+HF), indicator of only parasympathetic influence

HF, high frequency; HRV, heart rate variability; LF, low frequency.

Table 2 Baseline values for independent variables

Variable	Mean	SD
BMI (kg/m ²)	22.27	3.05
VO ₂ max (ml/kg/min)	40.17	10.57
Systolic blood pressure (mm Hg)	118.86	8.92
Diastolic blood pressure (mm Hg)	75.17	9.57
LF(ms ²)	361.00	396.9
HF(ms ²)	415.8	391.3

BMI, body mass index; HF, high frequency; LF, low frequency.

values (determined at baseline and again after the 12-week exercise intervention) used to calculate the dependent variables (postintervention minus preintervention HRV indicator values) are summarised in table 3.

Linear regression analysis was performed to determine the influence of baseline values for LF, HF, BMI, VO₂max, gender and blood pressure (systolic and diastolic), on the exercise-induced changes measured in each of the HRV indicators (table 4). Regression models were fitted and were significant ($p < 0.05$) in all the cases except for HF ($p = 0.48$) and LF/HF ($p = 0.13$). The F-statistic is an indication of how the model fits. The p value (significance of the predictor) is also reported in table 4.

DISCUSSION AND CONCLUSION

This study is among the first to investigate the influence of the preintervention physiological status on exercise-induced autonomic responses in a large, healthy group of participants. Results indicated that the combined influence of baseline LF,

HF, BMI, VO₂max, gender and blood pressure on exercise-induced changes in HRV (RR/NN interval, SDRR/NN, HR, RMSSD, pNN50, SD1, SD2, LF, HF, LF/HF, LFnu and HFnu) were significant in 10 of the 12 regression models tested. The model did not fit the exercise-induced changes in LF/HF and HF. Novel information obtained was the fact that LF, an HRV indicator influenced by the sympathetic and parasympathetic branch of the ANS, seems to influence exercise-induced autonomic changes the most, as it was a significant ($p < 0.05$) predictor in 10 regression models. HF, an indicator of vagal influence, was significant in only 3 of the 12 models and SBP in one of the regression models.

According to Hautala *et al*²⁸, the large interindividual variation to training response as well as wide intersubject variation found in cardiac autonomic regulation may be due to a common denominator other than factors such as blood pressure, blood cholesterol, cardiac dimensions, BMI and smoking. In combination, these explained together only ~10% of the variation in autonomic regulation, while genetic factors determine a much larger proportion (more than 20%) of the interindividual variation of the R–R interval variability. In our study, the baseline values for LF, HF, BMI, VO₂max, gender and blood pressure appears to explain between 12.83% and 29.82% of the exercise-induced changes in HRV indicator values (table 4). Parameters found to be significant predictors of exercise-induced changes were LF, HF and SBP.

New information gained from the current study is the fact that the LF HRV indicator was the one HRV parameter that was consistently a significant predictor ($p < 0.05$) of the exercise-induced changes in the HRV indicators, followed by HF. The HRV indicator, LF, although considered by some as an indicator of pure sympathetic cardiac control, is in fact of mixed origin, that is, influenced by the sympathetic and parasympathetic branches of the ANS.²⁵ This is in contrast to some of the results reported by Hautala²⁸ indicating that it is especially the vagally mediated HF HRV indicator which is associated with increased aerobic power (VO₂max) when measured by a 24-h tachogram. Differences in populations may be the reason, as our population was a young, healthy group between 18 and 22 years old. Thus, the results of the study are relevant, specific to individuals within quite a restricted age band of 18–22 years of age. We used daytime supine HRV and not a 24 h tachogram. It may also be that the physiological mechanisms determining exercise ability, as measured by VO₂max, differ from exercise-induced changes in autonomic function measured by HRV.

Additionally, we suggest that the preintervention physiological aspects may have a more visible influence on the exercise-induced changes of HRV measured during a stressor such as standing and also during recovery directly after exercise. In the supine position, HR is primarily regulated by parasympathetic influences, while rising and standing trigger the sympathetic branch of the ANS as seen by the increases in HR. A previous study by our group indicated that exercise-induced changes in sympathetic and parasympathetic ANS control differ, depending on posture, that is supine, rising and standing.²⁹ For this reason, the determination of the influence of baseline physiological indicators on exercise-induced changes in HRV measured during rising and standing periods may provide new insights. Finally, the fact that VO₂max was only indirectly measured may also have influenced the reported results.

In conclusion, it seems that the preintervention ANS status (specifically LF) is the most important determinant of the response in the supine position to an exercise intervention in a normal, healthy study population.

Table 3 HRV-indicator values determined at baseline (preintervention) and after 12 weeks of exercise

HRV indicator	Mean	Median	SD	Minimum	Maximum
PreHR	72.81	72.58	10.94	45.38	102.73
PostHR	61.38	60.39	9.96	43.75	90.48
PreRR/NN	0.85	0.83	0.13	0.59	1.33
PostRR/NN	1.01	1.00	0.16	0.66	1.40
PreSDRR/NN	0.05	0.05	0.02	0.01	0.13
PostSDRR/NN	0.07	0.07	0.03	0.01	0.19
PreRMSSD	62.82	57.35	33.36	9.40	164.70
PostRMSSD	89.98	83.95	44.72	9.10	223.20
PrepNN50	33.72	34.55	21.83	0.00	78.00
PostpNN50	52.48	58.45	22.03	0.00	90.20
PreSD1	44.72	40.85	23.74	6.70	117.20
PostSD1	64.61	60.10	31.58	6.50	158.80
PreSD2	79.43	72.80	36.95	13.50	215.90
PostSD2	94.42	86.10	47.15	20.40	300.30
PreLF	361.0	243.0	396.9	0.0	2423.0
PostLF	517.6	329.5	873.2	0.0	9113.0
PreHF	415.8	288.5	391.3	7.0	1892.0
PostHF	779.4	525.5	729.8	11.0	5023.0
PreLF/HF	1.53	0.96	3.13	0.00	34.97
PostLF/HF	2.38	0.64	10.13	0.00	94.10
PreLFnu	44.99	46.45	19.99	0.00	86.20
PostLFnu	38.07	38.20	19.16	0.00	88.80
PreHFnu	49.98	50.10	19.28	2.10	117.30
PostHFnu	56.89	58.95	20.38	0.00	101.00

HF, high frequency; HRV, heart rate variability; LF, low frequency; Post, postintervention; Pre, preintervention.

Table 4 Summary of regression analyses

Regression model number	Dependent variable	Does the regression model fit significantly? (F-statistic)	R ² %	Significant predictors	p Value (significance of predictor)
1	HR	p=0.001	19.52	LF	0.009*
2	RR/NN	p=0.027	12.83	LF	0.028*
3	SDRR/NN	p<0.001	24.94	LF	<0.001*
4	RMSSD	p=0.003	17.14	LF	0.002*
5	pNN50	p<0.001	25.73	LF	0.004*
				HF	0.005*
6	SD1	p=0.005	15.98	LF	0.004*
7	SD2	p<0.001	29.82	LF	<0.001*
8	LF	p=0.002	17.61	LF	<0.000*
9	HF	p=0.488	Na	Na	Na
10	LF/HF	p=0.131	Na	Na	Na
11	LFnu	p=0.001	22.73	LF	0.001*
				HF	0.001*
				SBP	0.012*
12	HFnu	p=0.004	16.56	LF	0.005*
				HF	0.001*

*A priori statistical significance was set at $p \leq 0.05$.

HF, high frequency; LF, low frequency; SBP, systolic blood pressure.

What are the new findings?

Investigation of a relatively large, homogeneous group of participants during a strictly standardised training programme, indicated the following:

- Preintervention physiological aspects play a significant role (between 12.83% and 29.82%) in the exercise-induced changes in heart rate variability (HRV).
- Baseline autonomic function may thus be a significant confounder in the outcome of exercise study results.
- The LF HRV indicator was the one HRV parameter that was consistently a significant predictor ($p < 0.05$) of the exercise-induced changes in the HRV indicators, followed by HF.
- Preintervention physiological aspects may have a pronounced influence on the exercise-induced changes of HRV measured during a stressor such as rising and standing and also during recovery directly after exercise.

How might it impact on clinical practice in the near future

- These findings are crucial factors to consider during the planning and evaluation of exercise interventions in patients, athletes and healthy participants.
- An individual's baseline values for low frequency (LF) variability may be used as an indication of the exercise-induced changes that can be expected. Recognition of this fact will result in realistic and attainable individualised goals.
- In clinical research studies, standardisation of these factors may remove a significant % of bias not recognised before.
- Results imply that participant's inclusion criteria have to include predetermined criteria/cut-off points for HRV indicator values.

Contributors Data discussed in this article is from a PhD study by CCG (2011), who was responsible for the planning, conduct and reporting of results. DCJvR made contributions through the whole process and critically revised the article. All contributors are thus also authors.***

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- References to this paper are available online at <http://bjsm.bmj.com>

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