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# CARDIOVASCULAR AUTONOMIC RESPONSES TO WHOLE BODY ISOTONIC EXERCISE IN NORMOTENSIVE HEALTHY YOUNG ADULT MALES WITH PARENTAL HISTORY OF HYPERTENSION

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**Abstract :** The objective of this study was to assess blood pressure and autonomic activity during rest and recovery in young adult normotensives offsprings of hypertensives. A total of 49 healthy normotensive males with BMI of 18.5–24.9 kg/m$^2$ chosen for the study and classified into two groups based on their parental history of hypertension underwent a sub maximal cycle ergometry exercise test. ECG and heart rate were recorded at baseline, during the exercise test and during recovery period of ten minutes while blood pressure was recorded at baseline and during recovery. Spectral analysis of HRV was performed. The basal systolic blood pressure and the recovery systolic blood pressures at the 1st and 3rd minute of recovery after exercise test were significantly higher in the study group than the control group. The basal LFnu and LF/HF ratio were significantly higher while the basal HFnu was significantly lower in the study group than the control group. A difference in basal systolic blood pressure, a higher LFnu and a lower HFnu found in offspring of hypertensive parents may be an early marker of cardiovascular change in subjects with a genetic predisposition to hypertension.

**Key words :** blood pressure heart rate variability isotonic exercise

## INTRODUCTION

Exercise tests bring about changes in hemodynamics of cardiovascular system. An increase in systolic blood pressure and a normal or low diastolic blood pressure is the normal response to isotonic exercise (1). Studies have shown that normotensives with a high normal resting blood pressure or unusually high blood pressure response to exercise tests are prone to develop hypertension (2). Those with a parental history of hypertension also show a high blood pressure response known as an exaggerated response, to exercise testing (3).

During the last few decades, researchers have recognized the significance of the relationship between autonomic system and cardiovascular mortality. Studies have shown that there is an association between an increased likelihood for lethal arrhythmias and signs of either increased sympathetic or reduced vagal activity. This has encouraged the development of quantitative markers of functions for autonomic nervous system like heart rate variability (4). Heart rate variability is the amount of heart rate

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fluctuations around the mean heart rate. It is a valuable tool to investigate sympathetic and parasympathetic function of the Autonomic Nervous System (5).

We hypothesize that normotensive young adults, with and without parental family history of hypertension show a difference in blood Pressure at rest and during post-exercise recovery. We also hypothesize that normotensive young adults, with and without family history of hypertension may show a difference in autonomic activity at rest and during post-exercise recovery.

## MATERIALS AND METHODS

Before initiation of the study, approval was obtained from ethics committee of St Johns Medical College, Bangalore. A total of forty-nine male subjects in the age group of 18–30 years were recruited from the student and staff population of St Johns Medical College and Hospital. A brief history was taken and general and systemic examinations were performed and healthy subjects were recruited based on the inclusion and exclusion criteria.

Study Group : with parental history of hypertension. (18 subjects)

Control group : without parental history of hypertension. (31 subjects)

*Inclusion criteria (common to both study and control groups)*

1. Males in the age group of 18-30 years
2. Non-smokers
3. Normal range of body mass index (BMI)(18.5–24.9 kg/m$^2$)
4. Fasting overnight.

*Exclusion criteria :*

1. Any acute illness
2. Diabetes mellitus
3. Anti-hypertensive medication
4. History of chest pain, breathlessness, orthopnoea
5. Physical disability like arthritis of the knee, which may impair cycling
6. Any recent illness during the past two weeks or so.

Parental history of essential hypertension was ascertained from the medical prescription of the parents who were hypertensive and the anti hypertensive medication prescribed, along with the dosage was noted in the data sheet.

Subjects were interviewed the previous day and a detailed description of the protocol was explained to them. Experiments were conducted in the morning in the fasted state. Subjects were instructed to complete their evening meal by 8 pm, refrain from caffeinated beverages 12 hours prior to the experiment and to avoid strenuous physical activity from the previous evening. A written informed consent was also obtained on the day of the experiment.

A mechanically braked cycle ergometer powered by electricity was used for the experiment. The ECG was recorded on Biopac MP30 which is an acquisition system. The blood pressures were recorded at rest and during recovery using the blood pressure monitor AT-987 (M-1) which is a fully automatic, digital blood pressure monitor. Weight of the subject was measured to the nearest 100 grams using an electronic weighing scale and height was measured to the nearest 0.1 cm using a stadiometer (Holtain limited, Crymych, Dyfed, Made in Britain).

**Study protocol**

All experiments were performed at the

Human Experiments Laboratory in the department of physiology at St John's Medical College between 6:30 AM and 8:30 AM. The subjects were explained in detail about the experimental procedure. Experiments were done in a quiet room during which subjects lay supine, awake and breathing normally. After instrumentation, subjects were given a 30 minutes mandatory rest period. At the end of 30 minutes rest period, the ECG (II lead) recordings were started along with Blood Pressure recording every 5 minutes for the next 10 minutes. Three Blood Pressure readings were obtained during this period at an interval of 5 minutes between two consecutive blood pressure recordings. Least baseline Heart Rate and Blood Pressure were determined and noted in the data sheet.

The target Heart Rate was then calculated. Target heart rate was calculated as basal heart rate plus 60% of heart rate reserve.

Maximum Heart Rate (6) = 220 – Age

Heart Rate Reserve (7) = Maximum Heart Rate – Basal Heart Rate

Target Heart Rate = (60% x Heart Rate Reserve) + Basal Heart rate

The subject was instructed to sit on the cycle ergometer and start cycling at 60 revolutions per minute. The workload was gradually increased to 50 Watts at increments of 10 watts every minute. The subject was told to continue cycling till he reached the target heart rate and the stop watch was started when he reached target heart rate. He was instructed to continue at the same intensity of work for the next 3 minutes. The ECG was continuously recorded during this period. At the end of the 3 minutes of exercise after reaching target heart rate, he was instructed to stop (8).

Post-Exercise recovery period began from the cessation of exercise and lasted for the next 10 minutes. During the recovery period, subjects continued to sit on the cycle ergometer. The blood Pressure was recorded every alternate minute during the recovery period. The ECG was continuously recorded during the recovery period. The recording was stopped at the end of 10 minutes and the data was saved in the Biopac MP 30. The Heart Rate was determined at the end of each minute of exercise and recovery from the ECG and noted in the data sheet. The ECGs of all the subjects were analyzed by Power Spectral analysis using the software by Juha-Pekka Niskanen, Mika P. Tarvainen and Perttu O. Of the 18 normotensive subjects with a parental history of hypertension, the ECG of one subject could not be analyzed as there were too many artifacts which could not be manually edited. Hence, we had only 17 subjects with family history of hypertension in our HRV analysis.

**Estimation of physical fitness index:**

The Harvard step test was used for estimating the physical fitness index of our subjects (9). Studies have shown that this protocol is suitable in Indian males.

**Statistical analysis of data**

The data were examined for normality. Wherever the data was not normally distributed, non-parametric tests were used. Mean±SDs were used to describe normally distributed data while median and interquartile ranges were used to describe the non-normally distributed data. The student Independent t test has been used to find significance between subjects with and without parental history of hypertension. The Mann Whitney U test was used to assess differences in heart rate variability parameters between the two groups since those were not normally distributed.

Friedman test – non-parametric test for repeated measurement was used to find the significance of recovery changes within each group. The null hypothesis was rejected at $P<0.05$. SPSS version 14.0 and Microsoft Excel were used for analysis of data.

## RESULTS

There was no significant difference in age, BMI and physical fitness index between the two groups (Table I). While the Mean Basal systolic blood pressure was significantly higher in the study group than in the control group, there was no significant difference in the basal diastolic blood pressure, heart rate in the two groups (Table I).

There was no significant difference in maximal heart rate, heart rate reserve and target heart rate between the study and control groups (Table II).

There was no significant difference in the exercise heart rate during the first, second and third minutes of exercise between the two groups (Table III). This is expected as the study design required the subjects to achieve their target heart rate (basal heart rate + 60% of heart rate reserve).

TABLE I: Age, body mass index (BMI), physical fitness index and basal cardiovascular parameters of both control and study subjects.

| *Parameters* | *Control group (n=31)* | *Study group (n=18)* | *P-values* |
|---|---|---|---|
| Age in years | 19.45±1.71 | 20.94±2.94 | 0.061 |
| BMI in kg/m$^2$ | 21.17±2.15 | 22.13±1.91 | 0.127 |
| Physical fitness index | 108.59±12.69 | 105.36±13.46 | 0.406 |
| Mean basal heart rate | 63.1±8.73 | 65.43±9.46 | 0.387 |
| Mean basal systolic blood pressure | 106.87±6.98 | 113.67±7.21 | 0.002** |
| Mean basal diastolic blood pressure | 65.68±4.91 | 68.44±6.16 | 0.09 |

Results are expressed as Mean±SD; **P<0.01.

TABLE II: Maximal heart rate, heart rate reserve and target heart rate of subjects in the two groups.

| *Parameters* | *Control group (n=31)* | *Study group (n=18)* | *P-values* |
|---|---|---|---|
| Maximal Heart Rate (Beats per minute) | 200.5±1.7 | 199.05±2.94 | 0.06 |
| Heart rate reserve (beats per minute) | 138.38±9.68 | 135.77±8.96 | 0.346 |
| Target Heart Rate (beats per minute) | 148.5±7.51 | 149.41±8.39 | 0.7 |

Results are expressed as Mean±SD.

TABLE III: Heart rate change during whole body exercise in 49 normotensive male subjects.

| *Exercise HR (in beats per minute)* | *Control group (n=31)* | *Study group (n=18)* | *P-values* |
|---|---|---|---|
| At 1 minute | 147.23±5.50 | 147.83±7.25 | 0.742 |
| At 2 minute | 149.87±7.95 | 150.61±7.63 | 0.751 |
| At 3 minute | 151.68±7.83 | 153.33±4.42 | 0.511 |

Results are expressed as Mean±SD.

Post-exercise recovery systolic blood pressure was significantly higher in the study group than control group during the 1st and 3rd minute of recovery after Bonferroni correction. However, there was no significant difference between the two groups after adjusting for baseline systolic blood pressure. There was no significant difference in post-exercise recovery diastolic blood pressure between the two groups during the 10 minutes (Fig. 1).

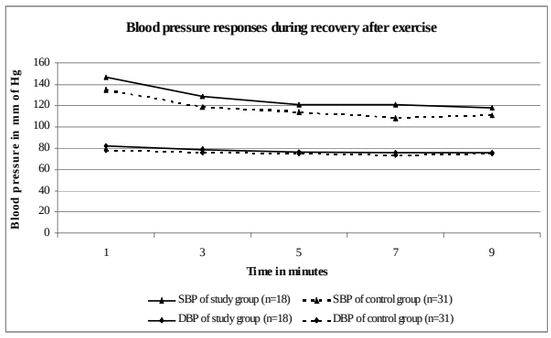


Fig. 1: Recovery systolic blood pressure (SBP) and diastolic blood pressure (DBP) in the study and control groups.

There was no significant difference between the two groups in the heart rate during the 10 minutes post-exercise recovery period (Fig. 2).

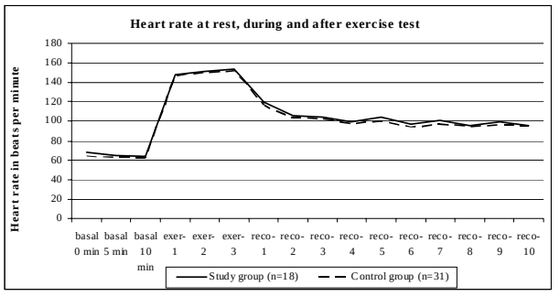


Fig. 2: Recovery heart rate at rest, during exercise test and recovery after exercise in the study and control groups.

Exer - x: Heart rate at the end of x minutes of exercise after reaching target heart rate.

Reco - x: Heart rate at the end of x minutes after exercise is stopped.

Area under the curve for heart rate during post-exercise recovery of 10 minutes was not significantly different between the two groups. However, Area under the curve for post-exercise recovery systolic blood pressure was significantly higher in the study group than the control group. Area under the curve for diastolic blood pressure during

TABLE IV: Summary measures (area under the curve) of heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP) during post-exercise recovery spanning 10 minutes calculated using a formula.

| *Area under the curve during recovery* | *Control group (n=31)* | *Study group (n=18)* | *P-values* |
|---|---|---|---|
| HR during recovery (in beats per min) | 99.30±9.90 | 101.81±12.53 | 0.442 |
| SBP during recovery (in mm of Hg) | 116.93±9.03 | 125.71±9.66 | 0.002** |
| DBP during recovery (in mm of Hg) | 75.02±6.82 | 77.75±5.30 | 0.150 |

Results are presented in Mean±SD. *P<0.05; **P<0.01.

TABLE V: HRV parameters at rest (basal), during early recovery (1-3 minutes after completing exercise test), mid recovery (4-6 minutes after completing exercise test) and late recovery (7-9 minutes after completing exercise test) in the control and study group.

| *Heart rate variability parameters* | *Control group (n=31)* | | *Study group (n=18)* | | *P-values* |
|---|---|---|---|---|---|
| | *Mean* | *SD* | *Mean* | *SD* | |
| Basal LF | 583.80 | 363.29 | 766.88 | 460.57 | 0.184 |
| Early recovery LF | 35.03 | 33.84 | 33.18 | 24.45 | 0.706 |
| Mid recovery LF | 47.35 | 34.90 | 47.53 | 35.44 | 0.806 |
| Late recovery LF | 71.03 | 53.28 | 62.24 | 47.26 | 0.438 |
| Recovery changes – P value | <0.001** | | <0.001** | | – |
| Basal HF | 770.97 | 534.84 | 590.76 | 404.84 | 0.382 |
| Early recovery HF | 14.10 | 14.35 | 20.29 | 24.60 | 0.658 |
| Mid recovery HF | 11.16 | 10.43 | 14.18 | 14.60 | 0.689 |
| Late recovery HF | 22.94 | 26.71 | 14.35 | 11.76 | 0.331 |
| Recovery changes – P value | 0.003** | | 0.559 | | – |
| Basal LF/HF ratio | 0.92 | 0.47 | 1.79 | 1.24 | 0.008** |
| Early recovery LF/HF ratio | 4.31 | 3.97 | 4.26 | 4.63 | 0.612 |
| Mid recovery LF/ HF ratio | 6.49 | 4.36 | 6.18 | 5.04 | 0.690 |
| Late recovery LF/ HF ratio | 5.46 | 4.48 | 5.67 | 3.89 | 0.597 |
| Recovery changes – P value | 0.023* | | 0.113 | | – |
| Basal LFnu | 44.48 | 12.44 | 57.84 | 17.05 | 0.006 |
| Early recovery LFnu | 71.88 | 17.65 | 68.34 | 18.96 | 0.603 |
| Mid recovery LFnu | 80.21 | 13.63 | 79.85 | 11.16 | 0.690 |
| Late recovery LFnu | 76.54 | 14.64 | 80.26 | 10.37 | 0.568 |
| Recovery changes – P value | <0.001** | | <0.001** | | – |
| Basal HFnu | 54.92 | 13.19 | 42.16 | 17.05 | 0.009 |
| Early recovery HFnu | 28.12 | 17.65 | 31.66 | 18.96 | 0.605 |
| Mid recovery HFnu | 19.79 | 13.63 | 20.15 | 11.16 | 0.690 |
| Late recovery HFnu | 22.97 | 14.47 | 19.75 | 10.37 | 0.643 |
| Recovery changes – P value | 0.023* | | 0.113 | | – |

Results are presented in Mean±SD. *P<0.05; **P<0.01.

post-exercise recovery period of 10 minutes was not significantly different between the two groups (Table IV).

Basal LF/HF ratio and basal LFnu were significantly higher in the study group than the control group while the basal HF was significantly higher in the control group than the study group (Table V).

There were significant changes in all HRV parameters during recovery after exercise except in LF/HF, HF and HFnu in the study group (Table V).

## DISCUSSION

Our finding that basal systolic blood pressure is significantly higher in the study group than the control group is consistent with other studies (10, 11). Studies have shown that those with a parental history of hypertension show a higher resting diastolic blood pressure (11). In our study, the basal diastolic pressure between the two groups was not significantly different (P=0.09). Larger sample size might have showed significant results.

Julius et al. suggested that those who have a positive family history of hypertension frequently exhibit hyperactive sympathetic nervous system (SNS). The consequences of SNS stimulation are peripheral vasoconstriction, an increase in heart rate, resulting in increase in peripheral vascular resistance with rise in systemic blood pressure (12). In our study, however, we did not find a difference in the basal heart rate between the two groups. Almost all our subjects, being in the age group of 18–30 years were physically fit and had a Physical fitness Index which was graded as excellent or good. Hence, almost all of them had a low resting heart rate.

The efferent vagal activity is a major contributor of the High frequency component as seen in clinical and experimental observations of autonomic maneuvers such as electrical vagal stimulation, muscarinic receptor blockade and vagotomy (13, 14). The LF component is considered by some (14, 15) as a marker of sympathetic modulation (especially when expressing it as normalized units) and by others as a parameter that includes both sympathetic and parasympathetic influences. Studies have shown that normotensives with a family history of hypertension exhibit altered sympathovagal balance with decreased parasympathetic activity at the cardiac level (14). In accordance with these studies, Basal High frequency power is lesser in the study group than the control group. The LF/HF ratio was significantly higher in the study group than the control group (P=0.008). LF/HF ratio is considered by some to mirror sympathovagal balance. The ratio of sympathetic to vagal activity was higher in the study group than the control group. The LFnu, which represented sympathetic activity, was significantly higher in the study group than the control group while the HFnu, which represented parasympathetic activity, was significantly lower in the study group than the control group.

Our finding during recovery is that there is no significant difference in the recovery heart rate between the two groups. The systolic blood pressure during recovery was significantly higher at the first and third minute of post exercise recovery after Bonferroni correction in the study group than in the control group. However, there was no significant difference between the two groups after adjusting for baseline systolic blood pressure. This means that the difference in the recovery blood pressure between the two

groups is as a result of baseline differences. The Area under the curve for systolic blood pressure during recovery is significantly higher in the study group than the control group (P=0.002). This indicates that the fall of blood pressure from 1st minute of recovery to the 9th minute of recovery is slower or more gradual in the study group than the control group. Controlling for baseline and age, the area under the curve for systolic blood pressure during recovery is showing a trend towards significance between the two groups (P=0.126). Further research is required for confirmation of this finding. Use of larger sample size may yield a significant p value. Summary measures like area under the curve were preferred to Repeated Measures analysis of variance (ANOVA) because results obtained from summary measures were both easy to understand and interpret. One consequence of replacing the serial measurements on a subject by a single summary measure is that what seemed like a lot of data suddenly seems rather small. The summary measures will give a more honest indication of the amount of information that has been collected (16).

We could not determine the Heart rate variability parameters during exercise due to non stationarity of the ECG during exercise. During recovery, there was no difference in the heart rate variability parameters between the two groups. Friedman's test was done to find out whether there were any significant changes in the three recovery groups (Early recovery, mid recovery and late recovery). We can deduce from the results that there is a significant change during recovery in the LF in both groups and in HF in the group without parental history of hypertension. However, in the study group, there is no significant change in HF, LF/HF and HFnu during recovery. HF represents the parasympathetic component. When a person begins to exercise there is parasympathetic withdrawal and sympathetic activation. On cessation of exercise, there is parasympathetic reactivation. That is, theoretically HF should increase. However, we find a poor vagal reactivation or in other words, poor parasympathetic reactivation in the study group. Mezzacappa et al conducted a study where subjects performed cold pressor and mental arithmetic tasks. They found that vagal rebound after the tests was poor in the group with parental history of hypertension. Probably, a similar mechanism is operating in our subjects with parental history of hypertension (17).

We gave thirty minutes of rest to each subject before beginning to record the basal parameters. Hence, the results of basal period are characteristic of the sample and have given us significant information.

We could not record the blood pressure during the exercise due to the limitations of the automated blood pressure monitor. This resulted in missing out valuable data that could have yielded conclusive results. Similarly, improvement in the technique of recording ECG and probably, using software that would help to analyze the ECG recorded during exercise would yield valuable data. The sample size was of modest size because of difficulty in recruiting subjects due to restrictions like including only male subjects and subjects with normal body mass index. A larger sample size would have resulted in better results. Simultaneous recording of beat to beat heart rate and blood pressure would have given valuable information about baroreceptor sensitivity.

The finding that the basal systolic blood pressure and LFnu are higher and HFnu is lower in the study group than in control group in the age group of 18–30 years, may be an early marker of cardiovascular autonomic change in subjects with a genetic predisposition to hypertension. Further research needs to be done in age groups lesser than 18 years old to find out how early the changes are seen in the cardiovascular and autonomic parameters in the offsprings of hypertensives. The ability to detect cardiovascular autonomic changes in younger age groups will help us to identify those prone to develop hypertension later in life. Moreover, physicians could start interventions in the form of exercise, diet and avoiding smoking and others to delay or avoid the onset of hypertension.

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