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Original Article

Physiology Section

Relationship between Autonomic Functional Status and Maximal Aerobic Capacity

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ABSTRACT

Introduction: Modern autonomic function tests can assess the degree and spread of autonomic dysfunction non invasively. Cardiovagal, pseudomotor and adrenergic autonomic functions could be assessed in standard laboratory tests. Cardio-respiratory Fitness (CRF) also known as aerobic fitness or maximal aerobic power is typically reported as VO_2 max.

Aim: To find the relationship between autonomic functional status and maximal aerobic capacity (VO_2 max).

Materials and Methods: This observational study was conducted in the Research laboratory of Department of Physiology at RUHS College of Medical Sciences, Jaipur Rajasthan, India, from December 2020 to May 2021. The study included 100 apparently healthy students between 18-25 years of age and not practicing any form of exhaustive physical training (cycling, aerobic, skating, scuba diving, professional sports, track and field, water jogging, walking at 5 mph, competitive gymnasium). Autonomic functional status was assessed by various parasympathetic and sympathetic tests. VO_2 max was assessed by treadmill test using Graded exercise protocol. To found a correlation between VO_2 max and autonomic function test parameters, Pearson's Pearson correlation test was done.

Results: The subjects had a mean age of 21.03±2.45 years, mean height of 1.64±0.08 m, mean weight of 59.66±11.15 kg and mean Body Mass Index (BMI) of 22.08±3.75 kg/m^2. Mean height was 1.69±0.06 metre for male subjects and 1.58±0.06 metre for female subjects; mean weight was 62.52±9.52 kg for male subjects and 56.80±11.64 kg for female subjects. Mean BMI was 21.57±3.06 kg/m^2 for male subjects and 22.59±4.3 kg/m^2 for female subjects. Weak positive correlations were found between VO_2 max and autonomic function test parameters, such as Valsalva ratio and hand grip blood pressure response, whereas weak negative correlations were found between VO_2 max and Expiration/Inspiration (E/I) ratio ratio. VO_2 max had a weak positive association (r-value=0.024) with Valsalva ratio and Blood pressure response to hand grip test (r-value=0.111), but a weak negative correlation (r-value=-0.019) with E/I ratio in males.

Conclusion: Regular aerobic exercise appears to be associated with decrease in sympathetic responses and increase in parasympathetic responses. The present study indicated the existence of gender differences in autonomic function tests in young adults of 18-25 years of age due to difference.

Keywords: Expiration/Inspiration ratio, Hand grip test, Valsalva ratio

INTRODUCTION

The autonomic nervous system regulates important bodily functions as Blood Pressure (BP), heart rate, thermoregulation, respiration, gastrointestinal, bladder, and sexual function. Autonomic dysfunction can occur as a result of many diseases that affect autonomic pathways [1]. Autonomic function tests can assess the severity and spread of autonomic dysfunction non invasively. Cardiovagal, psudomotor, and adrenergic autonomic functioning could be evaluated in standard laboratory tests [1]. The need for autonomic function tests lies in the fact that patients with autonomic failure shows an increase in mortality [2]. With the development of non invasive cardiovascular reflex function tests, now there is more systematic range available that is optimised for early diagnosis of autonomic neuropathy. These non invasive tests are, sensitive, specific, reproducible, quantitative, clinically relevant and less time consuming [3]. The omnipresent nature of the autonomic nervous system has allowed tests to be described in various systems like-cardiovascular, gastrointestinal, urogenital, pupillary, sudomotor and neuroendocrine [4].

"Physical fitness" is a multi-dimensional state of being that usually refers to two aims: Performance that incorporates six skill-related fitness components and health that incorporates five health-related fitness components, each of which contributes to total quality of life. Among its components, great emphasis has been given to CRF, also known as aerobic fitness or maximal aerobic power [5]. It is the overall capacity of the cardiovascular and respiratory systems and the ability to carry out prolonged strenuous exercise [6]. Amongst various other factors, regular physical activity is the key aspect to achieve optimal physical fitness. Insufficient physical activity is the risk factor for non communicable diseases such as cardiovascular diseases, diabetes mellitus, stroke, cancers and health outcomes such as mental health injuries and obesity [7].

Cardiovascular fitness has a pertinent role in not only athletic performance but also everyday activities such as walking, running and climbing stairs. In adults, fitness is a strong and independent predictor of cardiovascular disease and all-cause mortality and morbidity. Studies suggest that Cardiorespiratory Fitness (CRF) in young people is declining. Accurate measurement of CRF is essential to determine fitness levels and to monitor effects of intervention. The CRF is typically reported as VO_2 max, the maximal oxygen uptake that can be achieved during maximal intensity exercise [8]. A person's maximum aerobic power (VO_2 max) can be estimated by using direct or indirect methods. Direct method (laboratory method) measures VO_2 max through direct analysis of the gases involved in pulmonary ventilation, while performing progressive and maximal exercise tests. Indirect methods estimate a person's aerobic capacity based off their heart rate, their distance covered, and or their time of trial when using a certain protocol [9].

One of the mechanisms for the association between autonomic functions and maximal aerobic capacity (VO_2 max) may be alterations in cardiac autonomic nervous system functions, which can be assessed by sympathetic and parasympathetic tests [10]. Modulation of autonomic functions mainly cardio-vagal response to aerobic exercise in term of VO_2 max observed by many previous studies [11]. Higher levels of moderate-to-vigorous physical activity were linked to improve cardiac autonomic nervous system function in children and adolescents, according to a recent comprehensive

literature review [12]. However, the literature review pointed out that the evidence for an association between maximal aerobic capacity and autonomic nervous system function is still limited, and it called for more research into the full range of autonomic functions and VO_2 max and other physiological mechanisms for the link, such as muscle mass, biological maturation [12]. In previous studies indirect method for observing maximal aerobic capacity (VO_2 max) is being used very frequently due to its easy, safe, quick and feasible approach. In contrary, direct method by gas analyser can be more reliable [13,14]. Hence, the present study was designed to find association between autonomic functions and maximal aerobic capacity (VO_2 max) by using direct method.

MATERIALS AND METHODS

This observational study was conducted in the Research laboratory of Department of Physiology at RUHS College of Medical Sciences, Jaipur Rajasthan, India, from December 2020 to May 2021. The ethical clearance was obtained by Institutional Ethical Committee (EC/P-31/2020). An informed consent was obtained from all participants after adequate explanation of the procedure to be followed during the study. A total of 100 healthy young adults were enrolled in the study by convenience sampling.

Inclusion criteria: Apparently healthy young adult subjects (50 males and 50 females) aged between 18-25 years and not practicing any form of exhaustive physical training (cycling, aerobic, skating, scuba diving, professional sports, track and field, water jogging, walking at 5 mph, competitive gymnasium) were recruited for study.

Exclusion criteria: Subjects with history of hospitalisation in the last three months, smokers and alcoholic, individuals suffering from hypertension, diabetes and other psychological disorders, cardiac disorders, respiratory disorder such as asthma, Chronic Obstructive Pulmonary Disease (COPD), pneumothorax, respiratory tract infection and musculoskeletal disorders and those on medications that affect cardiovascular control were excluded.

Study Procedure

Basic demographic parameters including height, weight, gender and age were taken from all participants. Prior to the measurement, all subjects were instructed to fast overnight and refrain from exercising for 48 hours. They were requested to abstain from drinking tea and coffee or consuming caffeine for the preceding 24 hours. To assess the autonomic functional status, various parasympathetic and sympathetic tests were done.

Valsalva maneuver test: Subject was asked to blow in rubber tube of mercury manometer and maintain the pressure of 40 mmHg for 15 second. Continuous Electrocardiogram (ECG) was recorded 1 min before the strain, during strain and 45 sec after the strain. The ratio was taken as maximum R-R interval after maneuver to that of shortest R-R interval during the strain [15].

Deep breath test Expiration/Inspiration (E/I) ratio: The participant was asked to breathe deeply in sitting position at the rate of 6 breaths/min allowing 5 sec each for inspiration and expiration. Continuous ECG was recorded during this period and the ratio was calculated as maximum R-R interval for expiration to that of shortest R-R interval during inspiration [16].

Hand grip test: the participant was asked to hold the hand grip dynamometer in the dominant hand and press it with maximum effort. The tension developed, taken as the maximum isometric tension (T max). The subject was asked to maintain 30% of the T max for 35 minutes. The blood pressure was recorded from the non exercising arm every 30 sec before the release of hand grip. Maximum increase in BP before the release of hand grip was noted [17].

Maximal aerobic capacity (VO_2 max): VO_2 max was measured by using treadmill test in accordance with graded exercise protocol [18]. Following a 3 min walking (warm up stage) at 0% elevation, subject was asked to brisk walk at self-selected speed (between 4.3-7.5 mph) at same incline for three minutes and then with a constant speed, treadmill grade was increased by 2.5% every minute until a steady state Heart Rate (HR) of 180 beats per minute was achieved or subject become fatigue and was unable to continue the exercise. During the procedure, equipment was connected to a monitor screen, which showed various values such as Volume of oxygen (VO_2), Volume of carbon dioxide (VCO_2), Resting Energy Expenditure (REE), Respiratory Exchange Ratio (RER), Metabolic Equivalent of Tasks (METs) for every 10 seconds. However only VO_2 max was evaluated in the study.

Global Physical Activity Questionnaire (GPAQ): The GPAQ [19] collected information on sedentary behaviour and physical activity participation [19]. Metabolic Equivalents (METs) are evaluated in the analysis of GPAQ data. The intensity of physical activities is commonly expressed as METs. The GPAQ consists of 16 questions (P1-P16) in three domains of activity at work; travel to and from places and recreational activities. While using GPAQ data to calculate a person who was moderately active is allocated four METs, while for the person who spent time in vigorous activities was assigned eight METs.

Total time spent and energy expenditure in MET is calculated in all three domains of activity. Total time spent in physical activities per week is the sum of the time spent in all five settings in one week, whereas total energy expenditure or MET per week is the sums of the energy spent in one week.

- A person is said to be having sedentary lifestyle if the total activities performed by a person in a week are less than any of the conditions:

  -150 minutes of moderate-intensity physical activity

  OR

  -75 minutes of vigorous-intensity physical activity

  OR

  -An equivalent combination of moderate-intensity and vigorous-intensity physical activity achieving atleast 600 MET-minutes.
- Adult can be categorised in physically active category if MET minutes per week are ≥600 (physical activity cut-off value) [19].

STATISTICAL ANALYSIS

The results of study were presented as Mean±SD. Data were compared between genders using unpaired Student's t-test. To found a correlation between VO_2 max and autonomic function test parameters, Pearson's correlation test was done. Analysis were carried out using Statistical Package for Social Sciences (SPSS) version 16.0 (Chicago, Inc., USA), and significance level for p-value was calculated ≤0.05.

RESULTS

The subjects had a mean age of 21.03±2.45 years, height of 1.64±0.08 m, and weight of 59.66±11.15 kg and BMI of 22.08±3.75 kg/m^2. Mean height was 1.69±0.06 m for male subjects and 1.58±0.06 m for female subjects; mean weight was 62.52±9.52 kg for male subjects and 56.80±11.64 kg for female subjects. The differences of mean height and weight were found to be statistically significant [Table/Fig-1].

Parameters	Male Mean±SD	Female Mean±SD	p-value (Unpaired student t-test)
Age (years)	20.82±2.46	21.2±2.43	0.219
Height (meter)	1.69±0.06	1.58±0.06	<0.00001
Weight (kg)	62.52±9.52	56.80±11.64	0.004
BMI (kg/m^2)	21.57±3.06	22.59±4.3	0.870

[Table/Fig-1]: Distribution of demographic parameters in subjects.
p-value <0.05 was considered as statistically significant

Total 100 subjects equally distributed in either gender (male and female) were included in the study and were subjected to various autonomic function test parameter. Mean±SD of Valsalva ratio was 1.43± 0.25, E/I ratio was 1.30±0.06 and blood pressure response to hand grip test was 22.22±6.39 mmHg. Distribution of different autonomic function test parameters as Valsalva ratio was 1.44±0.26 for male subjects and 1.41±0.23 for female subjects. Mean±SD of E/I ratio was 1.28±0.06 for male subjects and 1.31±0.06 for female subjects. Mean blood pressure response to hand grip test was 26.28±6.19 mmHg for male subjects and 18.16±3.25 mmHg for female subjects.The differences of mean E/I ratio and hand grip test were found to be statistically significant [Table/Fig-2].

Parameters	Male Mean±SD	Female Mean±SD	p-value (Unpaired student t-test)
Valsalva ratio	1.44±0.26	1.41±0.23	0.307
E/I ratio	1.28±0.06	1.31±0.06	0.014
Blood pressure response to hand grip test (mmHg)	26.28±6.19	18.16±3.25	0.00001

[Table/Fig-2]: Autonomic function test parameters in male and female subjects.
p-value <0.05 was considered as statistically significant

Distribution of Mean±SD of GPAQ score was 1588.6±747.10 MET per week and VO_2 max was 41.58±9.02 mL/kg/min. GPAQ Score was 1754±820.93 (MET) for male subjects and 1347.4±577.10 (MET) for female subjects. VO_2 max was 45.69±8.57 mL/kg/min for male subjects, 37.47±7.50 mL/kg/min for female subjects and this difference was statistically significant [Table/Fig-3].

Parameters	Male Mean±SD	Female Mean±SD	p-value (Unpaired student t-test)
GPAQ score (MET)	1754±820.93	1347.4±577.10	0.002
VO_2 max (mL/kg/min)	45.69±8.57	37.47±7.50	0.00001

[Table/Fig-3]: GPAQ and VO_2 max in male and female subjects.
p-value <0.05 was considered as statistically significant

According to the results, weak positive correlation of VO_2 max with Valsalva ratio for both male (r-value=0.024) and female (r-value=0.221) subjects were found. Similarly weak positive correlation of VO_2 max with hand grip BP response (mmHg) for both male (r-value=0.111) and female (r-value=0.016) subjects were found. But in case of E/I ratio weak negative correlation for both male subjects (r-value=-0.019) and female subjects (r-value=-0.016) were found. None of the associations were found to be statistically significant [Table/Fig-4].

VO_2 max autonomic function test parameters	Male		Female	
	r-value	p-value	r-value	p-value
VO_2 max and Valsalva ratio	0.024	0.868	0.221	0.122
VO_2 max and E/I ratio	-0.019	0.895	-0.079	0.585
VO_2 max and hand grip BP response	0.111	0.442	0.016	0.912

[Table/Fig-4]: Correlation of VO_2 max with autonomic function test parameters in males and females.
Pearson's correlation test; the result is significant at p<0.05

DISCUSSION

The subjects had a mean age of 21.03±2.45 years, height of 1.64±.08 m, and weight of 59.66±11.15 kg and BMI of 22.08±3.75 kg/m^2. Mean height was 1.69±0.06 m for male subjects and 1.58±0.06 m for female subjects which was found statistically significant (p-value <0.0001). Mean BMI of total subjects in the present study was found to be 22.08±3.75 kg/m^2, which is slightly higher than the BMI found in another study conducted by Chhabra P and Chhabra SK, where all subjects of same age group were under normal weight category [20]. No significant difference was found in the subjects of two studies. Similarly, mean BMI for male and female subjects was 21.57±3.06 and 22.59±4.3 kg/m^2 respectively in the present study, which is again slightly higher than the BMI of Indian healthy young male and female subjects.

In the present study, autonomic functional status was assessed by autonomic function tests. Mean Valsalva ratio for total subjects was found slightly lower to normal values mentioned by Mishra UK and Kalita J [21]. The present study results were similar with those in another study conducted by Gautschy B et al., on healthy young adults. In their study, individual values were >1.23 in 97.5% of subjects of similar age group [22]. The present study results were in contrast with those of Piha SJ, who reported higher Valsalva ratio [23]. Males had higher Valsalva ratio than females which may be due to lower heart rate in adult males than adult females. The size of the heart, which is normally smaller in females than males, accounts for the majority of the variation. Because the female heart pumps less blood with each beat, it must beat quicker to match the output of the bigger male heart. Furthermore, the pacemaker in women's hearts has a distinct inherent rhythmicity, causing them to beat quicker [24].

In the present study mean E/I ratio for total subjects was found higher than the study conducted by Ziegler D et al., [25]. In the deep breathing test females had higher E/I ratio than males and the difference was found to be statistically significant (p-value <0.05). This might be due to a developmental difference or the influence of male and female sex hormone levels [26]. Oestrogen has a calming impact on the heart and circulatory system. It raises vagal tone while decreasing sympathetic activity via increasing the density and activity of muscarinic receptors [27].

Mean Diastolic Blood Pressure (DBP) increase to hand grip test for total subjects was lower than the values observed by Piha SJ [23]. Males had significantly higher DBP responses than females (p-value <0.01) indicating that men had greater forearm muscle strength than women. This might be attributed to the hormone testosterone, which promotes an increase in muscle growth and protein synthesis in boys during puberty, resulting in a 50% increase in muscle mass on average. In comparison to males, females have a greater amount of oestrogen, which dampens the decrease of cardio vagal tone to the heart during exercise, resulting in a considerably smaller DBP response and less sympathetic activity during exercise [28]. According to the previous studies, the concentration of epinephrine is very high in men on beginning of exercise explains the significant increase in the rise of DBP response in males than females [29]. These findings are in accordance with the previous studies [30].

Mean maximal aerobic capacity (VO_2 max) for males was greater than females and the difference was found to be statistically significant (p-value <0.01). Greater muscle mass in men is partly responsible for their higher absolute VO_2 max compared to women, as muscle is the largest consumer of oxygen during exercise. These discrepancies are attributable to central oxygen delivery constraints induced by decreased cardiac outputs as a result of smaller stroke volumes and poorer oxygen carrying capabilities. Women's oxygen carrying capacity is reduced due to lower haemoglobin levels [31]. VO_2 max in the present study was found to be higher in males than females which were similar to results of a study conducted by Loe H et al., However, the mean values of VO_2 max were found to be lower for both male and female participants as compared to above mentioned study. This may be due to different age groups (20-29 years) recruited by Loe H et al., who had of high level of physical activity [32].

Regular physical activity is the most important part of physical fitness, which may be quantified using maximum aerobic capacity (VO_2 max). The GPAQ can measure moderate to vigorous physical activity. As a result, GPAQ may be used to relate subjective measurement of physical activity to physical fitness. Adult can be categorised in physically active category if MET minutes per week are ≥600. The mean GPAQ score of total subjects under

the present study was 1588.6±747.10 MET per week and that of male and female subjects was 1754±820.93 MET per week and 1347.35±577.1 MET per week, respectively and the difference was found to be statistically significant (p-value <0.05) as male subjects were more active than female subjects. Overall subjects were falling under the category of physically active individuals [33].

The authors correlated the maximum aerobic capacity (measured by VO_2 max) with autonomic function test values. VO_2 max had a weak positive association (r-value=0.024) with Valsalva ratio and hand grip blood pressure response (r-value=0.111), but a weak negative correlation (r-value=-0.019) with E/I ratio. All these were statistically non significant. Higher values of mean RR intervals are associated with high maximal aerobic capacity (VO_2 max) due to changes in the intrinsic processes operating on the sinus node, as well as changes in the autonomic nervous system's regulation of the heart [34].

Male (r-value=0.111) and female (r-value=0.016) had a weak positive association between VO_2 max with hand grip blood pressure response (mmHg). Similar weak positive association was found in the study conducted by Kilbom A and Persson J, for blood pressure response to exercise [35]. Exercise training decreases baseline muscle sympathetic nerve activity and causes parallel reductions of arterial pressure and sympathetic tone [36]. The initial response to exercise, up to a heart rate of approximately 100 beats/min, is attributable to the withdrawal of vagal tone but moderate and heavy exercise causes augmented sympathetic activity [37]. Similarly, in the present study, authors used maximal level exercise, which may be the reason for increased sympathetic activity.

Male (r-value=-0.019) and female participants (r-value=-0.079) had a weak negative association with E/I ratio. This could be due to irregular physical activity and maximal level of exercise test. In a research done by Aboudrar S et al., athletes of similar age group were observed with a greater E/I ratio which shows regular aerobic exercise appears to be associated with considerable decreases in heart rates (increased parasympathetic activity) both at rest and during submaximal activity [38].

Limitation(s)

Sample size in the study was small and included only healthy young adult population.

CONCLUSION(S)

The present study indicated the existence of gender differences in autonomic function tests in young adults. VO_2 max was found higher in males than females. Weak positive correlation was observed between VO_2 max with Valsalva ratio and hand grip BP response and weak negative correlation was seen between VO_2 max with E/I ratio. This concludes that regular aerobic exercise appears to be associated with decrease in sympathetic responses and increase in parasympathetic responses. Further research on a bigger population with a broader range of age group is recommended for external validity of the results. More research into the broader range of autonomic functions, maximal aerobic capacity and other physiological parameters including muscle mass, biological maturity is needed.

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