

**IMPACT OF CARDIORESPIRATORY FITNESS ON SELECTED
PULMONARY CARDIOAUTONOMIC AND NEUROCHEMICAL
MARKERS**

A Thesis

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By

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*Dedicated to
My Beloved Parents
Mr. Dinesh Roy
& Smt. Drupadi Roy,
My younger Sisters
Ms. Milan Roy
& Ms. Mamani Roy
And
My respected teachers*

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Dilip Roy

(Research Scholar)

Certified that the Thesis entitled

“IMPACT OF CARDIORESPIRATORY FITNESS ON SELECTED PULMONARY CARDIOAUTONOMIC AND NEUROCHEMICAL MARKERS” submitted by me for the award of the Degree of Doctor of Philosophy in Arts at Jadavpur University is based upon my work carried out under the supervision of Dr. Sridip Chatterjee, Associate Professor and Head, Department of Physical Education, Jadavpur University. And that neither this thesis nor any part of it has been submitted before for any degree or diploma anywhere/elsewhere.


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PREFACE

Cardiorespiratory fitness (CRF) is nowadays widely recognised as a crucial measure of overall health, indicating not just physical endurance but also the flexibility of various physiological systems. In recent studies, evidence has emerged that CRF impacts more than just aerobic capacity, influencing pulmonary function, autonomic regulation, and even neurochemical balance. Grasping these various effects of CRF is important for creating comprehensive strategies aimed at improving physical performance, psychological strength, and long-term health.

Pulmonary function tests (PFTs) play a crucial role in assessing respiratory health and function. They measure factors such as vital capacity (VC), Forced Expiratory Volume in one second (FEV-1), and Forced Expiratory Volume in three seconds (FEV-3), which indicate the lungs' operational status. People with higher cardiorespiratory fitness generally show better ventilatory function and enhanced gas exchange effectiveness. Nevertheless, the exact relationship between different levels of cardiorespiratory fitness and specific pulmonary measurements is still being actively studied. Investigating this connection could provide important insights into how aerobic training aids in achieving optimal respiratory performance and in the prevention of lung dysfunction.

Heart rate variability (HRV) serves as a crucial indicator of the regulation of the autonomic nervous system. Higher HRV signifies improved parasympathetic function and increased adaptability to stress, both of which are positively affected by consistent aerobic exercise. Since CRF enhances cardiovascular efficiency and vagal tone, exploring its relationship with HRV can provide insights into how fitness influences autonomic balance and overall cardiovascular well-being. This relationship underscores the holistic role of fitness in sustaining physiological equilibrium in both resting and stressful situations.

Besides pulmonary and autonomic influences, CRF significantly impacts brain chemistry. Physical activity alters neurochemicals such as gamma-aminobutyric acid (GABA), brain-derived neurotrophic factor (BDNF), and cortisol, which are crucial for neuroplasticity, emotional regulation, and the body's response to stress. An increase in BDNF enhances cognitive abilities and promotes neural development, while balanced levels of GABA and cortisol foster relaxation and alleviate anxiety. Therefore, CRF serves as a connection between physical fitness and mental and emotional well-being through neurobiological mechanisms.

This doctoral thesis intends to explore the interconnected effects of cardiorespiratory fitness on lung function, heart rate variability, and significant neurochemicals. By combining physiological and neuroendocrine viewpoints, it aims to enhance understanding of how aerobic capacity supports overall health. The results are anticipated to emphasise the significance of preserving high levels of cardiorespiratory fitness as a basis for physical vitality, cognitive capabilities, and psychological health.

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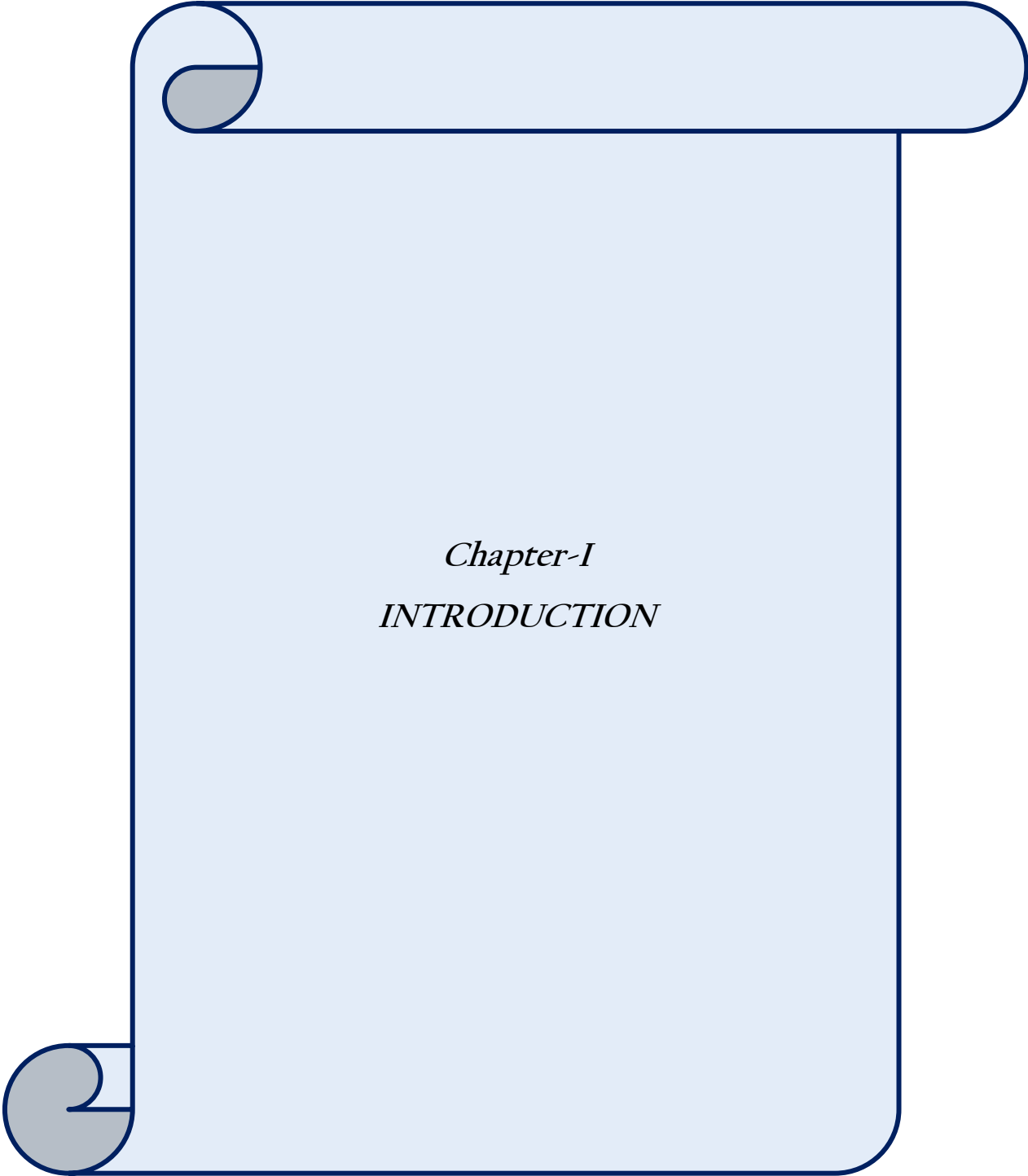
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Chapter-I
INTRODUCTION

1. Introduction

This chapter marks the beginning of the research study that aims to develop a high-quality piece of work. It includes a comprehensive depth of information. The background of the study establishes a clear justification for the ongoing research.

1.1 Background of the Study

This chapter provides a clear overview of the context and framework that influenced and guided the current research study. The study overview has systematically examined the scientific and interconnected relationships of Cardiorespiratory fitness (CRF) on pulmonary function, cardioautonomic capabilities, and neurochemical levels.

CRF is an essential measure of overall health, indicating how effectively the heart, lungs, and circulatory system deliver oxygen to the body during exercise. It has been linked to a variety of health benefits, such as improved heart health, increased physical endurance, and enhanced mental wellness. Pulmonary function, usually evaluated through assessments like forced expiratory volume (FEV) and vital capacity (VC), is crucial for CRF since proper lung function is vital for efficient oxygen exchange and cardiovascular efficiency. People with higher CRF typically show better lung function, which aids them in engaging in physical activities with less tiredness and increased endurance.

Heart rate variability (HRV) is a significant indicator associated with CRF, illustrating the adaptability of the autonomic nervous system to stress and changes in the environment. High levels of HRV are linked to better cardiovascular health, effective emotional regulation, and enhanced resilience to stress, whereas low HRV is associated with a greater risk of cardiovascular issues and unfavorable mental health outcomes. Engaging in regular physical activity and enhancing CRF has been demonstrated to support a more balanced autonomic nervous system, leading to an increase in HRV. Therefore, there is a direct connection

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between CRF and HRV through their impacts on cardiovascular and autonomic regulation, influencing both physical health and mental well-being.

Neurochemicals such as gamma-aminobutyric acid (GABA), brain-derived neurotrophic factor (BDNF), and cortisol play key roles in how the body responds to exercise and stress. GABA, which is the main inhibitory neurotransmitter, helps to manage mood, diminish anxiety, and encourage relaxation, with improved physical fitness boosting GABAergic activity. BDNF is important for brain adaptability, cognitive abilities, and the survival of nerve cells, and its levels rise with regular physical exercise. Cortisol, a hormone that is triggered by stress, is essential for metabolism and immune system function; however, prolonged stress or inadequate CRF can disrupt cortisol levels, impacting mental well-being. Exercise aids in regulating cortisol levels and enhancing neurochemical balance, indicating that CRF significantly influences both physical and mental health.

1.2 Exercise and CRF

Engaging in consistent physical exercise has been repeatedly associated with improvements in CRF, often measured by $VO_2\text{max}$. Endurance training induces both central and peripheral adaptations, including increases in stroke volume, capillary density, and the function of oxidative enzymes. Hickson, 1981 demonstrated that a six-week program of high-intensity endurance training led to significant increases in $VO_2\text{max}$, highlighting the cardiovascular system's capacity to adapt to structured aerobic exercise. Likewise, Bassett & Howley, 2000 reviewed extensive research showing that aerobic training results in measurable enhancements in oxygen transport and utilization, thereby confirming exercise as a vital factor influencing $VO_2\text{max}$.

Participating in regular aerobic activities like running, cycling, or swimming results in improvements that boost heart and lung performance, enhance mitochondrial density, and

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optimize the body's capacity to use oxygen during prolonged exercise (Bouchard et al., 2012). Collectively, these findings suggest that a well-structured exercise regimen is one of the most effective approaches in increasing VO₂max and improving overall CRF. Building on the established connection between physical activity and CRF, recent studies have further detailed how different training techniques influence VO₂max adaptations (Laursen & Jenkins, 2002; Gormley et al., 2008).

1.3 Evolution of CRF Concept

The idea of CRF originates from early physiological studies, notably those conducted by A. V. Hill and H. Lupton, who in 1923 were the first to show that oxygen consumption levels off during intense physical activity, thereby introducing the key notion of VO₂max as a cap on aerobic capacity (Hill & Lupton, 1923). This concept has since developed through enhanced experimental methodologies and standardisation, significantly propelled by researchers' like Per-Olof Åstrand and Bengt Saltin in the mid-20th century, who created reliable exercise testing methods that improved the accuracy and comparability of VO₂max measurements across different populations.

In the latter part of the 20th century and into the 21st century, CRF has been acknowledged not only as a metric of athletic capability but also as a vital sign of overall well-being. Studies conducted in both population-based and clinical environments have associated low CRF with a heightened risk of cardiovascular diseases, illness, and mortality, leading to calls for VO₂max assessments to be implemented beyond just the athletic population. Recently, there have been conversations and policy movements about the regular evaluation of CRF in medical settings, emphasizing its predictive importance and potential role in preventive healthcare. The measurement of VO₂max is increasingly being made more reliable and standardized across various demographic groups.

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In 2016, the American Heart Association (AHA) released an important scientific statement asserting that CRF should be viewed as a “clinical vital sign,” similar to blood pressure and cholesterol, because of its capacity to independently forecast cardiovascular events and overall mortality (Ross et al., 2016). Recent discoveries from genetic studies have further backed this viewpoint: for instance, genome-wide association studies done on large populations have pinpointed genetic variants linked to low CRF that also relate to risk genes for cardiovascular diseases, type 2 diabetes, and various other chronic illnesses (Wain et al., 2021). This accumulation of physiological, epidemiological, and genetic evidence highlights the growing recognition of CRF as an essential holistic measure of health.

1.4 Aerobic fitness and CRF

Aerobic fitness and CRF are interconnected concepts that both indicate the body's capability to absorb, transport, and utilize oxygen during extended physical activities. Aerobic fitness specifically pertains to how effectively the cardiovascular, respiratory, and muscular systems can perform sustained moderate to high-intensity exercises. CRF, typically assessed through VO_{2max} , is regarded as the most thorough physiological indicator of aerobic fitness because it measures the maximum amount of oxygen the body can utilize during physical exertion (Bassett & Howley, 2000). Essentially, aerobic fitness reflects the functional aspect, whereas CRF provides an objective physiological assessment of that ability.

Numerous studies support the connection between the two, showing that enhancements in aerobic exercise performance—such as running, cycling, or swimming—are linked to significant increases in CRF. Training programs aimed at improving aerobic endurance boost stroke volume, cardiac output, and mitochondrial density in skeletal muscles, all of which contribute directly to elevated VO_{2max} levels (Jones & Carter, 2000; Midgley et al., 2007).

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This physiological change clarifies why those with greater aerobic fitness typically demonstrate better cardiorespiratory efficiency and endurance performance.

In addition, both aerobic fitness and CRF serve as indicators of long-term health results. Elevated levels of either are linked to a decreased likelihood of cardiovascular disease, metabolic syndrome, and overall mortality (Blair et al., 1989). Given that aerobic fitness can be enhanced through organized exercise programs, assessing CRF offers a useful method for tracking improvement and customizing interventions. This connection emphasizes the significance of evaluating both aerobic capacity and cardiorespiratory efficiency when assessing fitness and recommending exercise for health or performance objectives.

1.5 Aerobic exercise and aerobic fitness

Aerobic exercise refers to any sustained physical activity that primarily relies on the aerobic energy system, meaning the body uses oxygen to produce energy for muscular activity. Common examples include running, cycling, swimming, and brisk walking. These exercises are characterized by moderate intensity and prolonged duration, which stimulate the cardiovascular and respiratory systems, enhance oxygen delivery to tissues, and improve energy metabolism (Kenney et al., 2012). The physiological adaptations from regular aerobic exercise include increased cardiac output, stroke volume, capillary density, and mitochondrial efficiency in skeletal muscles, all of which contribute to improved overall performance and endurance (McArdle et al., 2015).

Aerobic fitness, on the other hand, is the measurable outcome of regular aerobic exercise, often assessed via $VO_2\text{max}$ or submaximal exercise tests. It reflects the integrated efficiency of the heart, lungs, blood vessels, and muscles in supplying and utilizing oxygen during prolonged exercise (Bassett & Howley, 2000). While aerobic exercise is

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the stimulus, aerobic fitness is the physiological adaptation that results. Higher aerobic fitness is associated with enhanced endurance capacity, better metabolic health, and reduced risk of cardiovascular and metabolic diseases, making it a key indicator of both performance and long-term health (Blair et al., 1989; Jones & Carter, 2000).

1.6 Aerobic exercise and pulmonary functional ability

Aerobic exercise directly and significantly influences pulmonary functioning, which denotes the lungs' ability to ventilate properly, exchange gases effectively, and uphold optimal oxygen and carbon dioxide levels during both rest and physical activity. Consistent aerobic exercise improves the strength and endurance of the respiratory muscles, including the diaphragm and intercostal muscles, resulting in enhanced lung volumes like tidal volume (VT) and forced vital capacity (FVC). These changes enable more efficient ventilation during extended physical exertion, decreasing the perceived exertion and enhancing exercise tolerance. Beyond mechanical enhancements, aerobic exercise triggers physiological changes that optimize pulmonary gas exchange. Training boosts pulmonary blood flow and alveolar-capillary diffusion capacity, which improves oxygen uptake (VO_2) and carbon dioxide removal. This leads to increased ventilatory efficiency, assessed through the ratio of ventilation to oxygen consumption (VE/VO_2), and can raise maximal exercise capacity. Regular aerobic training significantly benefits populations with borderline or compromised pulmonary function, such as older adults or those with chronic respiratory diseases, by aiding in the preservation or even enhancement of lung function over time (Hansen et al., 2010).

Furthermore, the benefits in lung function gained from aerobic exercise work in conjunction with cardiovascular and systemic changes, improving overall CRF. Greater lung capacity and improved ventilatory efficiency enable individuals to perform at higher

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intensities during aerobic activities, which consequently fortifies the heart, enhances oxygen delivery, and boosts endurance (McArdle et al., 2010). This interconnected progression demonstrates the synergistic connection between aerobic exercise, lung function, and overall aerobic potential, highlighting the need to include regular aerobic activities in health and rehabilitation programs.

1.7 Aerobic exercise and Cardioautonomic function

Aerobic exercise is widely recognized for its beneficial effects on autonomic regulation, which is evident through Heart Rate Variability (HRV) metrics. HRV quantifies the fluctuations in time between successive heartbeats and acts as a measure of the balance within the autonomic nervous system. Engaging in regular aerobic activities—like walking, running, or cycling—boosts parasympathetic (vagal) activity and diminishes sympathetic dominance, resulting in enhanced cardiac autonomic performance. These adaptations are frequently reflected in increased high-frequency (HF) components and overall HRV, both indicating stronger vagal influence.

In both people with good health and those with cardiovascular risk factors, aerobic exercise has demonstrated an increase in time-domain HRV measures such as the root mean square of successive differences (RMSSD) and the standard deviation of normal-to-normal intervals (SDNN). These measurements have a strong connection to parasympathetic activity and overall autonomic regulation. Increases in RMSSD and SDNN after engaging in moderate-to-vigorous aerobic training programs indicate improved cardiac adaptability and decreased cardiovascular stress at rest (Riebe et al., 2018). Regular aerobic exercise also enhances baroreflex sensitivity, which further aids in achieving positive HRV results.

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Long term aerobic training leads to both structural and functional changes in the cardiovascular system, which may also affect HRV measures. An increased stroke volume, a lower resting heart rate, and enhanced endothelial function enable the autonomic nervous system to function more effectively, as shown by a higher capacity for HRV. These changes are especially advantageous for people dealing with metabolic syndrome, hypertension, and stress-related conditions, since aerobic exercise has been consistently proven to enhance HRV and lessen autonomic stiffness (Shaffer & Ginsberg, 2017). Therefore, aerobic exercise is recognized as one of the most effective non-drug approaches for improving autonomic function, as evidenced by the variations in HRV measures.

1.8 Aerobic exercise and Gamma-Aminobutyric Acid (GABA) as a neurochemical marker

Regular physical activity, including aerobic exercises, strength training, or mind-body techniques, has been demonstrated to effect levels of GABA, which is the brain's main inhibitory neurotransmitter. GABA is essential for managing mood, stress, anxiety, and overall neural excitability. Studies suggest that both short-term and long-term exercise can boost GABA levels or improve GABA signaling in different areas of the brain (Maddock et al., 2016). Aerobic activities like running or cycling have been associated with higher GABA levels in the motor cortex and reductions in anxiety symptoms, likely due to better inhibitory control and diminished stress reactions. Mind-body practices, particularly yoga, have been found to raise GABA levels in the brain, which may clarify their renowned calming and mood-stabilizing benefits (Streeter et al., 2007). Strength training might also impact GABA pathways in an indirect manner by alleviating systemic stress and enhancing overall neurochemical equilibrium. In summary, engaging in physical exercise seems to foster a healthier balance between inhibitory and excitatory

processes in the brain, which may lead to improved mental health, cognitive abilities, and emotional regulation (Streeter et al., 2007; Maddock et al., 2016).

1.9 Aerobic exercise and Brain-Derived Neurotrophic Factor (BDNF) as a neurochemical marker

Regular physical activity—whether aerobic exercise, resistance training, or high-intensity interval training—has a well-established link to BDNF, a protein essential for neuronal growth, synaptic plasticity, and cognitive function. Short sessions of aerobic exercise consistently increase circulating BDNF levels, supporting improvements in learning, memory, and mood regulation (Knaepen et al., 2010). Long-term physical training further elevates resting BDNF levels and promotes neurogenesis, especially in the hippocampus, a key brain region for memory (Cotman et al., 2007). Resistance training has also been shown to raise BDNF levels, although results are more variable compared to aerobic activity (Szuhany et al., 2015). High-intensity interval training can produce particularly substantial increases in BDNF due to its elevated metabolic and neurochemical demands (Dinoff et al., 2017). In summary, regular physical activity is strongly associated with improved brain health through increased BDNF signalling, which benefits cognitive performance, reduces the risk of neurodegenerative diseases, and enhances psychological well-being.

1.10 Aerobic exercise and Cortisol as a neurochemical marker

Regular physical activity is essential for managing cortisol levels and fostering a well-balanced stress response. Although cortisol is released due to stress and physical activity, ongoing moderate-intensity exercise helps control its release and minimizes the adverse effects of sustained high cortisol levels. During physical activity, cortisol levels incline

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naturally to meet the body's heightened energy demands, assist in tissue repair, and manage metabolic functions (Kivlighan et al., 2005). Nonetheless, with regular training, the body becomes more adept at handling these stress responses. People who participate in regular exercise typically show a more balanced cortisol profile, exhibiting lower resting cortisol levels than those who are inactive, which is advantageous for overall health (Hackney, 2006). Furthermore, consistent exercise enhances the body's capability to manage everyday stressors, helping to avoid the chronic elevation of cortisol associated with negative consequences like anxiety, disrupted sleep, and immune system issues (Kivlighan et al., 2005). Although strenuous or excessive exercise without sufficient recovery may result in heightened cortisol levels and overtraining, moderate and regular exercise boosts resilience to stress and supports both mental and physical health (Kreher & Schwartz, 2012).

1.11 Research gap

A comprehensive review of the current literature, which is included in the second chapter of this study, identified a research gap that still needs to be explored. While numerous studies have thoroughly investigated the impact of exercise on CRF, pulmonary function, HRV, and neurochemical markers such as BDNF, GABA, and cortisol, they predominantly examine these systems in isolation and primarily in the context of exercise-training interventions. The current body of literature lacks a unified analysis that connects VO_2 max with pulmonary function indices, HRV parameters, and neurochemical markers simultaneously, nor has it assessed how these physiological and neurochemical factors vary together with natural differences in fitness levels. Furthermore, studies on neurochemicals have mainly concentrated on the changes induced by exercise rather than their baseline relationship with fitness, and the

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correlations between HRV or pulmonary function with neurochemical markers have not been explored together. Therefore, a distinct research gap exists in comprehending the interconnected, cross-sectional relationships among cardiorespiratory fitness and these various physiological and neurochemical markers, particularly among healthy young adults.

1.12 Formulation of research question

Recognizing a research gap is crucial as it defines what has not yet been explored by existing studies, thereby providing a basis for the necessity of new research. In the context of investigating the relationship between CRF, pulmonary function, HRV, and neurochemicals like GABA, BDNF, and cortisol, identifying the research gap emphasizes the insufficient understanding of how these physiological and biochemical systems interact as a whole rather than individually. It ensures that the study offers fresh perspectives instead of reiterating known information, enhances the scientific justification, aids in the choice of suitable methods and variables, and ultimately underlines the significance and potential influence of the research in promoting integrative health and exercise science. The development of the research question in specific domains, along with the resulting research question, is outlined in Figure 1 below.

1.13 Addressing the research question

This study revolves around a key research question, which underpins the investigation and directs both the methodology and analysis. In this chapter, an introductory context and overview of the research question are given, while a precise discussion of the

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evidence, findings, and interpretations responding to it can be found in the Summary and Conclusion chapters, derived from the results and discussions. The final section aimed to integrate the findings, address the research question, and emphasise the study's implications.

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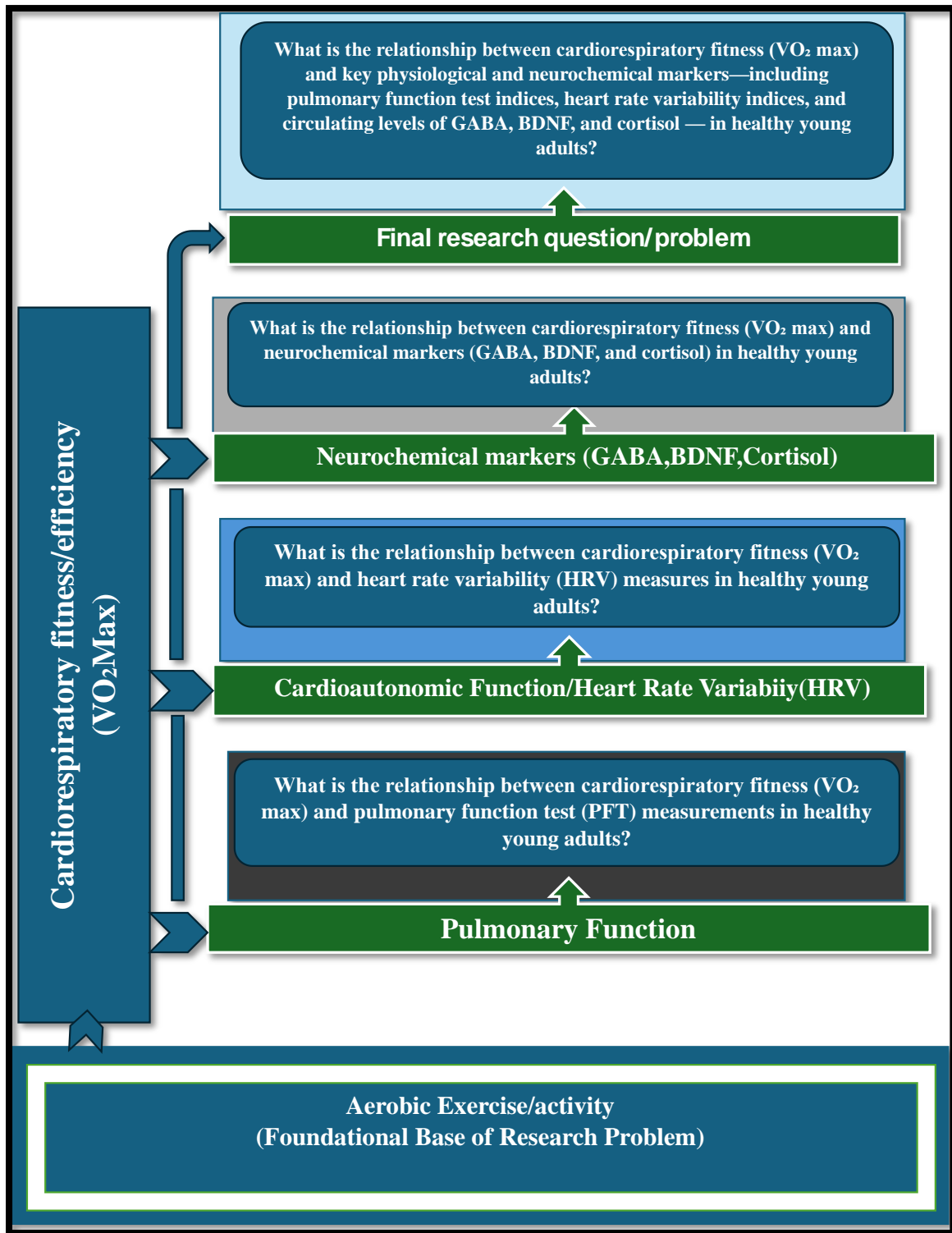


Figure 1: Schematic presentation for identifying and formulating a final research question/problem

1.14 Relevance of the study

This study's significance stems directly from the recognized research gap, emphasizing the insufficient incorporation of physiological and neurochemical elements within current literature. By filling this void, the study provides valuable insights that enhance both the scientific comprehension and practical relevance of the research.

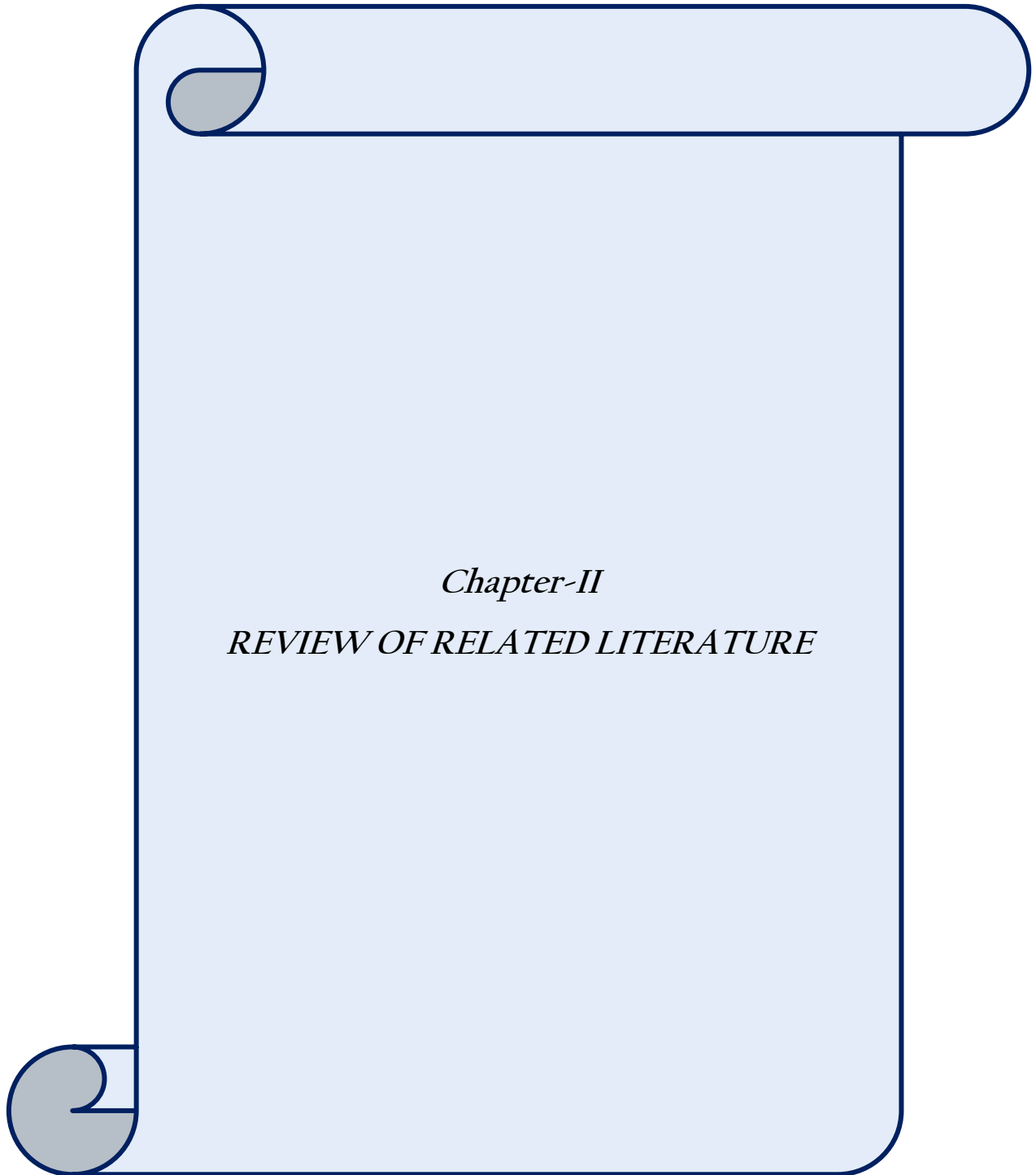
- a. The research addresses a significant void in preventive health studies by connecting fitness to the functioning of multiple systems, thereby endorsing comprehensive strategies for enhancing well-being and optimising performance.
- b. The results could aid in creating more efficient, evidence-informed exercise or rehabilitation programs aimed at achieving both physical and neurobiological results.
- c. This research focuses on the gap in integrated studies that look at CRF in conjunction with pulmonary function, HRV, and important neurochemicals (GABA, BDNF, cortisol), offering a broader insight into physiological health.
- d. The research can offer fundamental proof for upcoming interdisciplinary studies, promoting cooperation among exercise science, neurophysiology, and clinical health sectors to create more cohesive health evaluation frameworks.

1.15 Aim of the study

This research aims to investigate the relationship between CRF and different indicators from pulmonary function assessments, along with cardio autonomic and neurochemical markers.

1.16 Objectives of the study

- To assess and comprehend the impact of CRF on pulmonary function
- To evaluate and comprehend the impact of CRF on cardiac autonomic function.
- To acknowledge and comprehend how CRF influences neurochemical indicators.



2. Literature Review

After an extensive evaluation of existing literature and a careful assessment of all relevant recorded data, a thorough analysis and investigation of the pertinent studies was conducted. The researcher conducted a comprehensive review of the existing literature, which is detailed in the ensuing subsections of this chapter:

2.1 Effect of Regular Exercise on Aerobic Fitness or CRF

Lin et al., 2015 evaluate the impact of exercise on cardiorespiratory fitness and a variety of conventional and novel cardio metabolic biomarkers in individuals without cardiovascular disease, Lin et al.,2015 carried out a meta-analysis of randomized controlled trials. Between January 1965 and March 2014, the researchers used Medline, Embase, and Cochrane Central literature searches to find 160 randomized controlled trials with 7487 individuals.

They used a standardised protocol for data extraction. The findings of this meta-analysis indicated that exercise led to significant improvements in cardiorespiratory fitness and certain cardio metabolic biomarkers.

In healthy adults from Iran, **Davarzani et al.,2020** sought to investigate the association between physical activity level (PAL) and muscle strength, body composition, and cardiorespiratory fitness. 120 men and 152 women between the ages of 18 and 70 participated in this cross-sectional study. Participants underwent assessments of their physical fitness, including measurements of grip strength, maximal oxygen consumption, and body composition. The findings revealed a positive correlation between physical activity and CRF.

Yin et al.,2025 investigated the impact of high-intensity interval training (HIIT) on enhancing physical health among university students and aimed to identify factors that may affect the results of the intervention. A thorough search was performed across five electronic

databases (Web of Science, Scopus, PubMed, Sport Discus, and MEDLINE) up to December 2024, utilising Boolean operators and keywords associated with HIIT and university students. The findings indicated that HIIT leads to a significant improvement in VO₂max among university students.

Kodama et al., 2009 carried out a meta-analysis to explore the link between CRF and the likelihood of all-cause mortality as well as cardiovascular events among healthy individuals. By analysing data from 33 studies with more than 100,000 participants monitored over a median period of 11 years, the researchers discovered a robust, inverse, and graded relationship between CRF and both mortality rates and the occurrence of cardiovascular disease. In particular, a 1 metabolic equivalent (MET) rise in fitness was associated with a 13% decrease in all-cause mortality and a 15% decrease in cardiovascular events. The investigation concluded that elevated levels of CRF are strong predictors of reduced risk for death and cardiovascular disease, highlighting CRF as a significant and quantifiable indicator of health outlook.

Wenger & Bell, 1986 reviewed how the intensity, frequency, and duration of exercise training interact to affect CRF, particularly maximal aerobic capacity (VO₂max). Research shows that high-intensity workouts (90–100% VO₂max) yield the most significant improvements, while longer training sessions (approximately 35–45 minutes) allow for slightly lower intensities to achieve similar benefits. Untrained individuals can improve their fitness with just two sessions per week, while those with a higher baseline VO₂max (>50 ml·kg⁻¹·min⁻¹) need to participate in at least three sessions weekly. As fitness levels rise, the rate of improvement becomes less pronounced. These findings indicate that while very high-intensity, moderately frequent, and adequately long training sessions maximize adaptations, lower-intensity exercise still offers substantial cardiorespiratory advantages and may decrease injury risks for non-athletic individuals.

Garber et al.,2011 sought to determine the optimal amount and quality of exercise necessary for improving and sustaining cardiorespiratory, musculoskeletal, and neuromotor fitness in seemingly healthy individuals. They presented evidence-based recommendations that stress the importance of regular engagement in aerobic, resistance, flexibility, and neuromotor activities, detailing the suggested frequency, intensity, duration, and type for each aspect. Both moderate and vigorous-intensity exercises have been demonstrated to provide significant health benefits, with higher volumes or intensities resulting in greater improvements. Furthermore, the position stand emphasizes the importance of personalized exercise prescriptions and practical tactics to increase adherence, minimize injury risk, and support long-term health and functional capacity.

Review of Related Literature

Study	Population (P)	Intervention (I)	Comparison (C)	Outcomes (O)	Study Design (S)
1. Lin et al., 2015	Adults of various health statuses included in randomized controlled trials	Aerobic and mixed exercise training programs of varying duration and intensity	Non-exercise or minimal-exercise control groups	Exercise training significantly improves VO ₂ max and cardio metabolic biomarkers across adult populations.	Systematic review and meta-analysis of RCTs (85 trials analyzed; high-level evidence)
2. Davarzani et al., 2020	Children and adolescents aged 7–18 years	Habitual physical activity levels measured through questionnaires and fitness tests	Lower vs. higher physical activity groups	Higher physical activity is associated with better cardiorespiratory fitness, stronger muscles, and healthier body composition in youth.	Cross-sectional observational study (non-intervention; associations measured in 1 time point)
3. Yin et al., 2025	University students (18–25 years)	High-intensity interval training (HIIT) programs	Moderate-intensity continuous training (MICT), other training forms, or no training	HIIT is highly effective for physical fitness improvement among university students, often superior to moderate intensity exercise.	Systematic review and meta-analysis (high-level evidence pooling multiple trials involving university students)
4. Kodama et al., 2009	Healthy adult men and women from long-term cohorts	Categorized high cardiorespiratory fitness (based on VO ₂ max or MET levels)	Lower CRF categories	CRF is a powerful predictor of longevity and cardiovascular health.	Meta-analysis of prospective cohort studies (long-term follow-up; strong epidemiological evidence)
5. Wenger & Bell, 1986	Healthy adults participating in controlled exercise training	Exercise programs varying intensity, frequency, and duration	Other program variations	Intensity is the strongest determinant of VO ₂ max improvement. Frequency and duration play secondary roles. High intensity + sufficient duration = highest VO ₂ max gains. Low-intensity exercise yields small improvements even with long durations. Exercise intensity is the key driver of CRF improvement.	Narrative review of controlled training experiments (summarized data from early VO ₂ max training studies)

Review of Related Literature

Study	Population (P)	Intervention (I)	Comparison (C)	Outcomes (O)	Study Design (S)
6. Garber et al., 2011	Apparently healthy adults (18–65+)	Evidence-based aerobic, resistance, flexibility, and Neuromotor exercise prescriptions	Different types or levels of exercise; sedentary comparison	<p>Aerobic exercise improves VO₂max, body composition.</p> <p>Resistance training improves muscle mass, strength, bone density.</p> <p>Neuromotor training improves balance, gait, agility (especially for older adults). Exercise prevents chronic disease and enhances quality of life and it Provides standardized FITT-VP guidelines for developing and maintaining adult physical fitness.</p>	Evidence-based guideline / position stand (systematic evaluation of research to form exercise prescription recommendations)

Table 1: PICOS table representing characteristics of the studies on regular exercise and CRF

2.1.1 A Critical Summary of the Impact of Regular exercise on aerobic fitness or CRF

Based on the Reviewed Studies

Exercise training, including aerobic, resistance, and high-intensity interval training (HIIT), consistently improves CRF across different populations (Lin et al., 2015; Wenger & Bell, 1986; Yin et al., 2025; Garber et al., 2011). The magnitude of improvement depends on exercise intensity, frequency, and duration, with structured programs yielding the greatest benefits. Physical activity is also positively associated with muscle strength and favourable body composition, particularly in children and adolescents, supporting its multidimensional role in health (Davarzani et al., 2020). HIIT has emerged as an especially effective method for enhancing CRF and overall physical fitness in young adults, including university students (Yin et al., 2025).

Improved CRF is linked to favourable cardio metabolic biomarkers, including reductions in blood pressure, glucose levels, and lipid profiles, emphasising its role in cardiovascular health (Lin et al., 2015). CRF is also a strong predictor of all-cause mortality and cardiovascular events in healthy adults, with even moderate gains significantly lowering risk (Kodama et al., 2009). Evidence-based exercise guidelines recommend a combination of aerobic, resistance, and neuromotor training, tailored in intensity, frequency, and duration, to maximize health benefits while minimizing risk (Garber et al., 2011; Wenger & Bell, 1986). Overall, structured and regular physical activity is critical for enhancing fitness, improving cardio metabolic health, and promoting longevity.

2.2 Effect of Cardiorespiratory Fitness (VO₂Max) on Pulmonary Function Test (PFT) Indices

Rawashdeh & Alnawaiseh, 2018 investigated the effects of three weeks of continuous treadmill running, a form of aerobic exercise, on the lung function of healthy, but physically inactive, men. The study assessed forced vital capacity (FVC), forced expiratory volume in one second (FEV₁), the FEV₁/FVC ratio, and maximal voluntary ventilation (MVV). Seventy-two inactive male subjects participated in pulmonary function testing. Each exercise session consisted of three tests, starting at

five minutes and increasing by ten minutes every three sessions, culminating in a maximum of 25 minutes; the average value was used for analysis. The exercise sessions occurred three times per week for a total of three weeks. The Wilcoxon test was used to assess pre- and post-test changes. Repeated measures analysis was conducted to compare pulmonary value changes during high-intensity sessions. A Spearman correlation rho analysis was performed to examine the relationship between MVV, FVC, and FEV1. The Friedman test was used to analyse the mean ratio of FEV1/FVC before and after exercises of different intensities. There were significant improvements in FEV1, MVV, and the FEV1/FVC ratio following high-intensity aerobic exercise of different intensities. These findings indicate that high-intensity aerobic exercise on a treadmill positively influences the pulmonary function of inactive healthy individuals.

Cheng et al., 2003 sought to examine the impact of physical activity on sustaining cardiac and respiratory health in individuals without known health issues. CRF was evaluated through a maximal treadmill test (MTT), while spirometry was utilized to assess respiratory function. The longitudinal analysis included data from 5,707 healthy individuals who had an initial consultation during the same time period and a follow-up visit within the next five years, while the cross-sectional analysis included data from 24,536 healthy individuals who took part in assessments at the Cooper Clinic between 1971 and 1995. All participants, aged between 25 and 55 years, completed a medical questionnaire and a cardiorespiratory test. In the cross-sectional analysis, after adjusting for various factors, being physically active and not being a recent smoker showed a connection to improved CRF and respiratory function for both genders. In the follow-up analysis, those who either maintained or adopted an active lifestyle exhibited better MTT results than those who remained or became inactive. Compared to other groups, active males showed increased forced vital capacity (FVC) and forced expiratory volume in one second (FEV1). Smoking was found to be associated with

diminished cardiorespiratory fitness and respiratory function. The study concluded that physical activity is linked to the preservation of CRF.

Hancox & Rasmussen, 2018 used two population-based cohort studies with children and young people to investigate the relationships between lung function and fitness. A maximal cycle ergometer test was used to measure aerobic fitness at ages 9, 15, 21, and 29 in Odense, Denmark, and a submaximal cycle test was used at ages 15, 26, 32, and 38 in Dunedin, New Zealand. In both cohorts, cross-sectional analyses indicated a positive relationship between aerobic fitness and forced expiratory volume in 1 second (FEV1) as well as forced vital capacity (FVC) at all age groups. There is a positive correlation between aerobic fitness and lung volumes.

Angane & Navare, 2017 assessed the impact of aerobic exercise on pulmonary function tests involving 65 healthy adult participants aged 20 to 35 years. The same individuals were used for both the study and control groups to reduce confounding variables. The findings indicated that pulmonary functions improved following aerobic exercise training. Consistent aerobic exercise is associated with enhanced cardiorespiratory efficiency and improved pulmonary function. Aerobic trainees achieved greater lung volumes and flow rates after their training period compared to their baseline values recorded prior to training.

Soni et al., 2022 investigated the relationship between pulmonary function parameters and CRF in relation to physical activity levels. This preliminary study was carried out at the Department of Physiology, RUHS College of Medical Sciences, involving a group of 100 healthy participants (students) aged between 18 and 25 years of either gender. The findings indicate that maximum oxygen consumption (VO₂ max) showed a positive correlation with pulmonary functions, except for the FEV1/FVC ratio in males.

In a study of 896 teenagers between the ages of 12 and 19, **Chen et al., 2025** investigated the effects of varying levels of physical activity (PA) on lung function measures, namely Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 second (FEV₁), and Forced Expiratory Flow (FEF). To investigate this association, this study makes use of data from the National Health and Nutrition Examination Survey (NHANES), which was carried out from 2007 to 2012.

Seman et al., 2022 investigated the impact of aerobic exercise on lung function in healthy adults, aiming to promote aerobic activity due to its potential benefits for overall health and wellness. This study utilized a quasi-experimental design with adults selected through convenient sampling. A total of thirty healthy adults were included and subsequently separated into intervention and control groups. The intervention group engaged in treadmill running as their aerobic exercise, prescribed at a certain intensity for a duration of four weeks, performing it three times a week. Meanwhile, the control group received no exercise instructions and was advised to maintain their usual daily activities. Pulmonary function tests were conducted prior to and following the exercise intervention. The parameters assessed were FEV₁, FVC, and the FEV₁/FVC ratio. Data analysis was carried out using paired t-tests and repeated measures ANOVA. The results showed a significant enhancement in FVC, FEV₁, and FEV₁/FVC among individuals in the intervention group after the exercise period, with p-values of <0.005, specifically <0.001, 0.001, and 0.024 respectively, when compared to their baseline measurements (paired t-test).

Review of Related Literature

Study	Population (P)	Intervention / Exposure (I)	Comparison (C)	Outcomes (O)	Study Design (S)
1. Rawashdeh & Alnawaiseh, 2018	Inactive male adults (18–25 yrs.)	High-intensity aerobic exercise (8 weeks; 70–85% HRmax)	Baseline or non-exercise control	Improved FEV ₁ , FVC, Improved respiratory muscle strength. Increased lung volumes and ventilation efficiency so, HIIT significantly enhances pulmonary function in inactive males.	Experimental pre–post intervention study
2. Cheng et al., 2003	Adults 20–70 yrs	Regular physical activity (self-reported PA, frequency & intensity)	Sedentary adults	Improve VO ₂ max, endurance, ventilatory capacity. FEV ₁ , FVC in active adults. Slower age-related decline in pulmonary function so, PA improves respiratory function and exercise performance.	Large epidemiological cohort (cross-sectional + longitudinal)
3. Hancox & Rasmussen, 2018	Children, adolescents & young adults	Cardiorespiratory fitness levels (VO ₂ max test)	Lower fitness groups	Higher fitness strongly improves FEV ₁ , FVC. Predicts lung development and peak lung capacity. Effect independent of BMI or adiposity. Consequently CRF is a strong determinant of lung function across youth and early adulthood.	Longitudinal cohort study
4. Angane & Navare, 2017	Healthy adults (20–40 yrs)	Aerobic exercise program (8–12 weeks moderate–vigorous intensity)	Baseline or no-exercise group	Improves FEV ₁ , FVC, lung compliance and respiratory muscle endurance. Improved oxygen utilization and breathing efficiency. Aerobic exercises improves pulmonary function in healthy adults.	Pre–post quasi-experimental intervention study
5. Soni et al., 2022	Healthy young adults (18–25 yrs)	Pulmonary function test (PFT) + VO ₂ max testing	Correlation (no intervention)	Strong positive correlation between VO ₂ max and FEV ₁ , FVC. Higher lung function values predict higher aerobic fitness; Demonstrates	Cross-sectional correlational study

Review of Related Literature

Study	Population (P)	Intervention / Exposure (I)	Comparison (C)	Outcomes (O)	Study Design (S)
				respiratory capacity influences cardiorespiratory fitness. VO ₂ max is significantly correlated with PFT variables.	
6. Chen et al., 2025	Adolescents aged 12–19 yrs	Physical activity via accelerometer	Low vs. moderate vs. high PA	<ul style="list-style-type: none"> Higher PA improves FEV₁, FVC. Strong dose response (more PA better lung function). Effect persists after adjusting for age, BMI, smoking exposure. PA is positively associated with lung function in adolescents. 	Cross-sectional population-based study
7. Seman et al., 2022	Healthy adults (18–45 yrs)	Aerobic exercise program (6–8 weeks; moderate intensity)	Baseline or non-exercising control	Improves FEV ₁ , FVC, after aerobic training. Improved respiratory muscle performance. Enhanced ventilatory capacity and lung elasticity. Regular aerobic exercise significantly improves pulmonary function in healthy adults.	Experimental pre–post interventional study

Table 2: PICOS table representing characteristics of the studies on CRF and PFT

2.2.1 A Critical Summary of the Effect of Cardiorespiratory Fitness (VO₂Max) on PFT indices Based on the Reviewed Studies

Across the studies examined, there is strong evidence indicating that both aerobic and high-intensity exercises significantly improve lung function in both sedentary and healthy individuals. Rawashdeh & Alnawaiseh, 2018 found that high-intensity aerobic training enhanced vital respiratory measures, including forced vital capacity (FVC) and forced expiratory volume (FEV₁), in inactive males. Likewise, Angane & Navare 2017 and Seman et al., 2022 discovered that regular aerobic workouts lead to increased lung capacity, improved expiratory flow rates, and greater overall respiratory efficiency in healthy adults. These results are consistent with the findings from Soni et al., 2022, who identified a positive relationship between lung function and VO₂max, suggesting that improved aerobic capacity correlates with enhanced respiratory function.

Both longitudinal and cross-sectional research further corroborate these results by associating regular physical activity with better lung function across various age demographics. Cheng et al., 2003 demonstrated that those who are physically active show greater exercise endurance and ventilatory performance when compared to those who are sedentary. Meanwhile, Hancox & Rasmussen, 2018 concluded that increased fitness levels during youth correlate with enhanced lung development and function as individual's progress into adulthood. Recent findings by Chen et al., 2025 reinforced this connection, revealing that adolescents who regularly engage in physical activity have higher FEV₁ and FVC measurements. Overall, the collective research highlights that regular aerobic exercise, regardless of age or initial activity level, is crucial for improving lung function and respiratory health.

2.3 Effect of Cardiorespiratory Fitness (VO₂Max) on Heart Rate Variability (HRV) Indices

Yang et al., 2024 assessed the effects of high-intensity interval training (HIIT), combination training (CBT), resistance training (RT), and aerobic training (AT) on adult heart rate variability (HRV) using a network meta-analysis (NMA). They looked through a number of databases, including the China National Knowledge Infrastructure, the Web of Science, Embase, PubMed, the Cochrane Library, and Wanfang Data, to locate randomized controlled studies that looked at how exercise influenced HRV in adults. According to the NMA, HIIT had the greatest impact on the normal-normal-interval standard deviation (SDNN), the low-frequency (LF) power/high-frequency (HF) power ratio, and the root mean square of successive differences between adjacent normal-to-normal intervals (RMSSD) (surface under the cumulative ranking curve (SUCRA) = 99.75%, 98.7%, and 84.9%, respectively); CBT had the greatest impact on LF power (SUCRA = 66.3%), while RT had the greatest impact on HF power (SUCRA = 72.5%). According to the results, RT is the best exercise for increasing HF power, CBT is best for increasing LF power, and HIIT is the greatest exercise for improving SDNN, RMSSD, and the LF/HF power ratio in adults.

Graessler et al., 2021 provided a thorough analysis of the effects of different physical training techniques on cardiovascular health, resting HRV, and related risk factors (e.g., blood pressure, body fat percentage, body mass, body mass index, baroreflex sensitivity, heart rate recovery, VO₂ max, and VO₂ peak) in healthy young and middle-aged adults (average age up to 44 years). A search was conducted across five electronic databases covering the period from 2005 to September 8th, 2020. Studies were deemed eligible if the intervention spanned a minimum of 4 weeks and the participants were considered generally healthy. Twelve of the studies included endurance training (three of which included high-intensity sessions), six

looked at resistance training, four studied coordination training, two used high-intensity training, and two employed a multimodal strategy. The results showed that both improved with every type of intervention.

Mamatha et al., 2019 examined the autonomic activity of individuals engaging in aerobic exercise with those practicing yoga. The study involved ninety healthy male participants aged between 30 and 40 years. It comprised three groups, each containing 30 subjects. Group 1: Participants who consistently engaged in structured aerobic exercise for at least six months. Group 2: Individuals who regularly practiced yoga for a minimum of six months. Group 3: Healthy subjects (with normal BMI) who did not participate in yoga or any form of exercise regularly. The findings indicated a reduction in LF (Low Frequency) among both the yoga and exercise groups compared to the control group, alongside a decrease in heart rate and LF/HF (Low frequency / High Frequency) ratio, while the yoga group exhibited an increase in heart rate. This suggests that parasympathetic activity is significantly higher in yoga practitioners, followed by athletes, with the control group showing the least activity.

In a cross-sectional study, **De Meersman, 1993** evaluated the heart rate variability amplitude of 72 male runners, ages 15 to 83, by comparing them to 72 age and weight-matched inactive control volunteers. Participants were given an augmented tidal volume (tidal volume = 30% of vital capacity) and instructed to breathe at a rate of six breaths per minute while heart rate variability was recorded at rest. Online, open-circuit spirometry was used to assess fitness levels during an incremental stress test. The overall results showed that the physically active group had significantly higher levels of fitness ($p < 0.001$), which were associated with significantly higher levels of heart rate variability than the sedentary group ($p < 0.001$). According to these findings, heart rate variability may be positively impacted by frequent aerobic exercise.

Kaikkonen et al., 2014 investigated the relationship among obese people's HRV, aerobic fitness, and lifetime physical activity. With a median body mass index (BMI) of 35.7 and an average age of 44.5 years, the 107 volunteers (87 females) who participated in the study filled out questionnaires about their lifestyle and health. They also took part in tests of 24-hour HRV, maximal aerobic performance, and body measurements. Forty percent of the variation in normal R-R intervals (SDNN) in the multivariate linear regression analysis was explained by lifetime physical activity. The natural logarithmic value of ultra-low frequency power varied by 24% ($P = .050$), and each increase of one category in the activity index was linked to a 15.4 rise in SDNN ($P = .009$). A high measured $VO_2\max$ was responsible for 25% of the variance in the low frequency/high frequency ratio ($P < .001$) and 45% of the variance in the natural logarithmic value of high-frequency power ($P = .009$). In obese people of working age, lifetime physical activity and aerobic fitness have a positive correlation with HRV and have a major positive influence on cardiac autonomic function. By improving the autonomic nervous system's performance, as demonstrated by HRV measures, physical activity reduces the health risks linked to obesity.

Gallagher et al., 1992 investigated heart rate variability (HRV) among three groups of individuals matched by age, each with distinct lifestyles (smoking, inactive, and physically fit). Heart rate data were collected from regular RR intervals using a continuous electrocardiogram while participants were seated and breathing at an increased tidal volume, and also while they were standing and breathing at their normal tidal volumes. The group that was physically active showed a significant increase in HRV both at rest and during several autonomic tests compared to the inactive and smoker groups ($p < 0.05$).

Grant et al., 2013 examined the connections between an essential cardiovascular health measure like $VO_2\max$ and several factors: heart rate (HR), heart rate variability (HRV)

markers, and HRV indicators adjusted for heart rate. A cross-sectional descriptive study was conducted with 145 healthy participants aged 18 to 22 years. HRV was assessed using time domain, frequency domain, and Poincaré plot analysis methods. The indirect measurement of VO₂max was obtained through the Multistage Cooper's test. To assess the strength of the associations, the Pearson correlation coefficient was utilized. Metrics such as HR, RR interval, and pNN50 displayed significant correlations ($p < 0.01$, $p < 0.01$, and $p = 0.03$, respectively) with VO₂max. The observation that only one HRV metric (pNN50) had a significant correlation with VO₂max may suggest that the relationships between HRV measures and VO₂max primarily stem from the link between HR (regardless of variability) and VO₂max.

Gaurav & Maman, 2022 investigated the impact of a 6-week short interval running training program and Small Sided Games on Heart Rate Variability measurements, aerobic fitness, and performance among well-trained Indian elite soccer players. A pretest-post test experimental design was utilized in this study. Ninety elite male soccer players were divided into three groups using computer-generated block randomization. Group I received Short Interval Running Training (N=30), Group II engaged in Small Sided Game Training (N=30), and Group III served as the Generic Training (control) group (N=30). The results from pre-intervention and post-intervention assessments were analyzed and compared. When comparing the three groups, a significant increase in RMSSD was observed in the SIRT group (with an increase of 39.87 ± 22.95) in contrast to the SSG group (which saw a decrease of 8.28 ± 9.24) and the Generic (control) group (which experienced a decrease of 44.23 ± 24.06), both of which exhibited a decline. This change proved to be significant ($p < 0.001$). The findings of the current study indicate that intensive training phases in elite

soccer players lead to improvements, particularly in HRV, suggesting a parasympathetic adaptation.

Winsley, 2002 examined both the short-term and long-term impacts of exercise on heart rate variability in both adults and children in a review. The findings from this review suggested that aerobic training enhances HRV and revealed a positive relationship between peak oxygen uptake and a dominance of the parasympathetic nervous system.

Bhattacharya et al., 2023 examined the effects of consistent karate training on cardiac autonomic responses in karate practitioners as determined by HRV in comparison to active controls who were matched for age and sex. 30 male youths in all were evaluated for the study; 15 were controls (10.6 ± 1.57 years old) and 15 were seasoned male karate practitioners (9.5 ± 1.26 years old). Once the distribution was found to be normal, the researchers measured HRV in both the time and frequency domains. Then, they compared the Mean \pm SD results using a t-test. High frequency normalized units (HF nu) demonstrated a significant increase, suggesting enhanced parasympathetic tone, while low frequency normalized units (LF nu) and the low frequency to high frequency ratio (LF/HF ratio) significantly decreased in the karate group, suggesting an increase in sympathetic activity, according to the frequency domain metrics. Karate practitioners showed increased parasympathetic nervous system activity and higher HRV values.

Bhattacharya et al., 2025 looked into the long-term impacts of karate, a prominent but little-studied mind-body martial art, and yogasana. Ninety male school children were included in the sample: thirty karate practitioners (age: 15.23 ± 2.07 years), thirty experienced yoga practitioners (age: 15.5 ± 1.83 years), and thirty age-gender matched active controls (age: 15.46 ± 1.77 years). Compared to the active control group (32.90 ± 15.76), the results showed that the High Frequency Power Normalized Unit (HF nu) was considerably higher among

Review of Related Literature

yoga practitioners (45.18 ± 16.00 nu) and karate practitioners (43.21 ± 18.14 nu). The yoga group's Low Frequency Normalized Unit (LF nu) was 53.90 ± 18.64 nu, and its LF/HF Ratio was 1.40 ± 1.10 . These were the lowest values. The study found that although karate practitioners, who are resilient to stress, have decreased sympathetic-vagal tone and stable heart-brain wellness, yogasana promotes stable parasympathetic dominance because of its postures and regular breathing patterns.

Study	Population (P)	Intervention / Exposure (I)	Comparison (C)	Outcomes (O)	Study Design (S)
1. Yang et al., 2024	Adults aged 18–70 years	Different exercise modalities: aerobic, resistance, HIIT, yoga, combined training	Modalities compared via network-meta-analysis	Aerobic & mind–body exercises produced the largest increases in HRV (RMSSD, HF). HIIT improved HRV but slightly less than moderate aerobic exercise. Resistance training had moderate improvement. Aerobic & yoga-based exercises are most effective for increasing HRV.	Systematic review and network meta-analysis
2. Graessler et al., 2021	Young & middle-aged adults	Various training interventions (endurance, resistance, HIIT, combined)	Inactive or alternative exercise groups	Endurance & combined training improves parasympathetic HRV markers (RMSSD, HF). HIIT showed mixed effects. Positive changes in BP, lipids, and body composition in conjunction with HRV improvements. Endurance training yields strongest HRV and cardiovascular improvements.	Systematic review

Review of Related Literature

Study	Population (P)	Intervention / Exposure (I)	Comparison (C)	Outcomes (O)	Study Design (S)
3. Mamatha et al., 2019	Young adults (30–40 yrs)	Aerobic exercise vs. yoga (6–8 weeks)	Aerobic vs. yoga vs. baseline	Both yoga and aerobic exercise improve HRV. Yoga produced greater HF and lower LF/HF (stronger parasympathetic shift). Aerobic exercise improves overall HRV but less vagal dominance. Yoga more effectively improves autonomic balance than aerobic exercise.	Interventional comparative study
4. De Meersman, 1993	Healthy population (15-83 yrs)	Aerobic fitness (VO ₂ max levels)	Low vs. high aerobic fitness	Higher aerobic fitness strongly correlated with higher HRV (especially HF, RMSSD). Sedentary individuals had significantly lower vagal tone. Aerobic fitness is a major predictor of HRV.	Cross-sectional observational study
5. Kaikkonen et al., 2014	Obese adults (20–60 yrs)	Physical activity & aerobic fitness (measured)	Low vs. high PA and fitness	Higher PA & fitness improves parasympathetic HRV markers. HRV predicted cardio metabolic risks. Aerobic fitness and PA are positively associated with HRV in obese adults.	Cross-sectional study
6. Gallagher et al., 1992	Adult smokers, sedentary adults, aerobically fit adults	Smoking status & aerobic fitness	Smokers vs. sedentary vs. fit	Smokers had the lowest HRV. Fit individuals had the highest HRV, reflecting strong parasympathetic activity. Smoking reduces HRV; aerobic fitness increases HRV.	Comparative observational study

Review of Related Literature

Study	Population (P)	Intervention / Exposure (I)	Comparison (C)	Outcomes (O)	Study Design (S)
7. Grant et al., 2013	Healthy adults	Heart rate vs. heart rate variability measurements	HR vs. HRV as markers	HRV was a superior indicator of cardiac fitness & autonomic health. HR was less sensitive to autonomic changes. HRV is a better marker of cardiac fitness compared to HR.	Cross-sectional diagnostic comparison study
8. Gaurav & Maman, 2022	Indian elite soccer players	6 weeks short intermittent running vs. small-sided games	Two training interventions	Both improved HRV, aerobic and anaerobic performance. Small-sided games improve HRV more (greater parasympathetic activation). Intermittent running improve aerobic capacity more. Training type influences HRV differently.	Randomized comparative training intervention
9. Winsley, 2002	Children & adults	Acute & chronic exercise exposure	Before vs. after exercise	Acute exercise: temporary lower HRV from sympathetic activation. Long term training: improved resting HRV (parasympathetic dominance). Long-term exercise increases HRV; acute exercise temporarily decreases it.	Narrative review
10. Bhattacharya et al., 2023	Pediatric karate trainees	Karate training (regular structured practice)	Non-karate active children	Karate participants had greater HRV; indicates enhanced autonomic regulation and vagal dominance. Karate training improves neuro-autonomic function in children.	Observational pediatric study

Study	Population (P)	Intervention / Exposure (I)	Comparison (C)	Outcomes (O)	Study Design (S)
11. Puneet et al., 2025	Adolescents (13–17 yrs)	Yoga Sana vs. Karate training	Yoga vs. karate	Both improves HRV parameters. Yoga greater in parasympathetic markers (HF, RMSSD). Karate improved autonomic balance but with more sympathetic-driven adaptations. Yoga is superior to karate for improving parasympathetic HRV.	Experimental comparative study

Table 3: PICOS table representing characteristics of the studies on CRF and HRV

2.3.1 A Critical Summary of the Effect of Cardiorespiratory Fitness (VO₂Max) on Heart Rate Variability (HRV) Indices Based on the Reviewed Studies

The studies examined collectively indicate that engaging in regular physical activity—whether it is aerobic or resistance training—leads to marked enhancements in heart rate variability (HRV), which is a recognized measure of autonomic balance and cardiovascular health. Yang et al., 2024 and Graessler et al., 2021 presented systematic and meta-analytic findings suggesting that aerobic and combined training methods are the most effective in boosting parasympathetic modulation and overall HRV when compared to a sedentary lifestyle or single-mode exercises. Research by De Meersman, 1993; Kaikkonen et al., 2014, and Gallagher et al., 1992 further supports the notion that higher levels of aerobic fitness correlate positively with improved vagal tone and a decrease in cardiovascular risk factors, even among individuals with obesity or other health challenges.

Additional studies focusing on specific exercise modalities reveal more nuanced effects. Mamatha et al., 2019 and Gaurav & Maman, 2022 found that both aerobic and interval training can enhance HRV, while yoga and mind-body techniques similarly promote parasympathetic benefits through relaxation and regulated breathing. Winsley, 2002 noted both short-term and long-term adaptations, emphasizing that consistent training leads to sustained improvements in HRV. In younger groups, Bhattacharya et al., 2023 and Bhattacharya et al., 2025 indicated that engaging in karate and yogasana improves cardio-autonomic regulation, implying that different types of exercise can specifically modulate the balance between sympathetic and parasympathetic systems. Collectively, these insights highlight that regular engagement in a variety of exercise modalities fosters beneficial autonomic and cardiovascular changes, with integrated aerobic exercise forms yielding particularly significant enhancements in HRV and overall heart health.

2.4 Effect of Cardiorespiratory Fitness (VO2Max) on Neurochemical Markers (GABA, BDNF and Cortisol)

In order to ascertain the effect of exercise training on resting levels of BDNF in peripheral blood, **Dinoff et al., 2016** conducted a meta-analysis. They looked for original, peer-reviewed research on peripheral blood BDNF levels before and after two-week exercise interventions in the databases MEDLINE, Embase, PsycINFO, SPORTDiscus, Rehabilitation & Sports Medicine Source, and CINAHL. Peripheral blood BDNF resting levels were higher after the intervention in 29 trials that satisfied the inclusion criteria (SMD = 0.39, 95% CI: 0.17-0.60, $p < 0.001$). The results of subgroup analysis showed that aerobic treatments had a substantial impact (SMD = 0.66, 95% CI: 0.33-0.99, $p < 0.001$).

Ospina & Cadavid, 2024 examined how aerobic exercise affected inhibitory control and serum BDNF levels in college students with different levels of physical activity. The study included 62 college students (48.4% male) who represented different levels of activity based on their IPAQ scores: 20 were athletes, 19 were regular fitness lovers, and 23 were inactive. Before and after a 30-minute aerobic workout, serum BDNF levels and Victoria Stroop test scores were measured. Significant variations in serum BDNF levels were seen after the aerobic session between the athletic and sedentary groups ($p = 0.030$) and between the regular fitness and sedentary groups ($p = 0.031$). Nevertheless, there was no discernible difference between the athletes' and routine fitness groups ($p > 0.999$). These findings suggest that young adults who engage in physical activity, especially athletes, exhibit adaptation to exercise training, as evidenced by decreased baseline levels of BDNF in their serum.

Ashcroft et al., 2022 conducted a systematic review and meta-analysis that involved searching seven electronic databases. Studies, both experimental and observational, that assessed changes in BDNF levels following exercise in individuals who had a stroke were included. Notable enhancements in BDNF levels were identified. The study concluded that high-intensity aerobic exercise can elevate circulating BDNF concentrations.

Ceylan et al., 2024 investigated how acute and regular physical activity influences circulating BDNF in individuals who are obese. A thorough search was performed across various electronic databases, such as PubMed, Academic Search Complete, and Web of Science, in August 2022, adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Notable heterogeneity was found for both acute ($I^2 = 80.4\%$) and long-term effects ($I^2 = 88.7\%$), while a low risk of bias was noted among the included studies. When considering prolonged physical activity, there was no significant rise in circulating BDNF levels compared to the control group ($ES = 0.49$, $95\% CI = -0.08$ to

1.06, $p = 0.089$). These results emphasise the importance of accounting for the type and duration of exercise when examining neurobiological responses in obesity and exercise research.

Wang et al., 2022 examined the impact of physical exercise (PE) on brain-derived neurotrophic factor (BDNF) through randomised controlled trials (RCTs) involving healthy individuals. A total of seven databases (PubMed, Web of Science, Cochrane, Embase, PsycINFO, CINAHL, SPORT Discus) were explored for RCTs that evaluated the influence of PE on serum and/or plasma BDNF up to December 18, 2021. A meta-analysis was conducted using the random-effects approach, calculating standardised mean differences (SMD) along with 95% confidence intervals (CIs). Significant positive effects on BDNF levels were observed for both acute (5 trials, SMD: 1.20, 95% CI: 0.36 to 2.04, $p = .005$) and long-term (17 trials, SMD: 0.68, 95% CI: 0.27 to 1.08, $p = .001$) physical exercise.

Kim et al. (2022) summarised and analysed randomised controlled trials (RCTs) in a review regarding the impact of aerobic exercise on BDNF in individuals with mild cognitive impairment, both qualitatively and quantitatively, to emphasise the importance of aerobic exercise. The researchers searched for RCTs focusing on BDNF changes as a result of aerobic exercise across four international databases. Assessments of quality and quantitative analyses were carried out using RevMan 5.4. The quantitative analysis was expressed in terms of a standardised mean difference (SMD) and was illustrated as a random effects model. The synthesis of RCTs involving aerobic exercise demonstrated a significant increase in BDNF levels.

Schmolesky et al., 2013 investigated the combined influences of aerobic exercise intensity and duration on serum BDNF levels in healthy adult males aged 18-25 years. A total of 45 participants were randomly allocated to one of six exercise conditions, which varied by

intensity (either 80% or 60% of heart rate reserve, or a control group) and duration (20 or 40 minutes). The vigorous exercise (80% heart rate reserve, termed “Vig”) and moderate exercise (60% heart rate reserve, termed “Mod”) were both performed on cycle ergometers. Participants in the control group remained seated and at rest throughout the exercise duration.

Lucertini et al., 2015 investigated the impact of cardiorespiratory fitness on the activity of the hypothalamic-pituitary-adrenal (HPA) axis in healthy older men. By analysing salivary cortisol levels at various times throughout the day and in reaction to mental stress, the researchers discovered that men with higher fitness levels exhibited consistently lower baseline cortisol and a reduced overall cortisol output throughout the day compared to those who were less fit. Although the more fit participants displayed somewhat stronger cortisol reactions and quicker recovery following stress, these variations were not statistically significant. In summary, greater fitness was associated with lower daily cortisol production, indicating it may aid in better stress management and potentially shield against cognitive and physical decline related to ageing.

Roy et al., 2025 carried out a comprehensive review of research articles investigating the effects of Physical Activity (PA), Physical Exercise (PE), and Yoga asana on Gamma-aminobutyric acid (GABA) levels in the human brain. The study, following the PRISMA-P 2015 guidelines, compiled the most recent information to enhance the understanding of how physical exercise affects brain GABA levels. The use of the PRISMA 2020 flow diagram ensured a systematic approach during the screening of the literature that met the established criteria. The reviewed non-randomized controlled trials (non-RCT) and randomized controlled trials (RCT) have indicated that aerobic interventions elevate GABA levels in the human brain, leading to a beneficial effect.

Review of Related Literature

Study	Population (P)	Intervention / Exposure (I)	Comparison (C)	Detailed Outcomes (O)	Study Design (S)
1. Dinoff et al., 2016	Healthy adults, older adults, clinical populations	Chronic exercise training (aerobic, resistance, mixed)	Exercise vs. non-exercise controls	Exercise significantly increased resting peripheral BDNF. Aerobic exercise produced stronger BDNF enhancement.	Systematic review & meta-analysis
2. Ospina & Cadavid-Ruiz., 2024	College students	Structured aerobic exercise program	Baseline or non-exercise controls	Aerobic exercise increases serum BDNF levels. Improved executive function (working memory, inhibition tasks). BDNF elevation correlated with cognitive improvement so, aerobic training enhances both BDNF and executive function.	Experimental exercise intervention
3. Ashcroft et al., 2022	Stroke survivors	Exercise interventions (aerobic, mixed rehab, strength + aerobic)	Control (usual care or non-exercise rehab)	Exercise improves circulating BDNF significantly. Aerobic training showed largest effect. BDNF increases associated with cognitive & motor function recovery. Exercise enhances neuroplasticity in stroke via BDNF improvement.	Systematic review & meta-analysis
4. Ceylan et al., 2024	Individuals with obesity	Acute & regular exercise (aerobic, HIIT, resistance)	Acute vs. chronic; exercise vs. controls	Acute exercise: Large transient increase in BDNF. Chronic exercise: Moderate increase in baseline BDNF levels. HIIT and moderate-intensity aerobic exercise had	Systematic review & meta-analysis

Review of Related Literature

Study	Population (P)	Intervention / Exposure (I)	Comparison (C)	Detailed Outcomes (O)	Study Design (S)
				strongest effects. Exercise effectively enhances BDNF in obesity.	
5. Wang et al., 2022	Healthy adults (18–60 yrs)	Physical exercise (various forms; RCTs only)	Exercise vs. control groups	Exercise significantly enhance circulating BDNF. Moderate vigorous aerobic exercise most effective whereas short-term training (≤ 12 weeks) showed robust increases. Exercise elevates BDNF in healthy populations.	Meta-analysis of RCTs
6. Kim et al., 2022	Individuals with mild cognitive impairment (MCI)	Aerobic exercise programs	Non-exercise MCI control groups	Aerobic exercise increases BDNF significantly. Also improved cognitive function (memory, attention). Longer-duration programs had stronger effects. Aerobic exercise is beneficial for neurotrophic and cognitive health in MCI.	Systematic review & meta-analysis of RCTs
7. Schmolesky et al., 2013	Healthy adult men	Aerobic exercise varying in duration & intensity	Different intensity and duration conditions	High-intensity, longer-duration sessions indicated largest acute BDNF increases. Low-intensity exercise produced small/no BDNF change. BDNF response is intensity- and duration-dependent.	Controlled experimental study

Study	Population (P)	Intervention / Exposure (I)	Comparison (C)	Detailed Outcomes (O)	Study Design (S)
8. Roy et al., 2025	Adults across various populations (mixed)	Acute & chronic exercise effects on GABA pathways	Exercise vs. non-exercise	Exercise ↑ GABA concentration and improves GABAergic signaling. Moderate–vigorous intensity produces best GABA responses. Improvements linked to reductions in anxiety and improved cognition. Exercise positively influences GABA neurotransmission.	Systematic review
9. Lucertini et al., 2015	Healthy aging men (50–70 yrs)	Cardiorespiratory fitness (measured via VO ₂ max)	Low vs. high fitness groups	Higher fitness demonstrated lower daily cortisol output. Improved HPA-axis regulation. Suggests protective effect of aerobic fitness against stress-related aging.	Cross-sectional observational study

Table 3: PICOS table representing characteristics of the studies on CRF and neurochemical markers

2.4.1 A Critical Summary of the Effect of Cardiorespiratory Fitness (VO₂Max) on Neurochemical Markers Based on the Reviewed Studies

Numerous meta-analyses consistently indicate that engaging in physical exercise leads to significant increases in circulating brain-derived neurotrophic factor (BDNF) levels among various populations. **Dinoff et al., 2016** demonstrated that both one-time and ongoing exercise training raised the resting peripheral BDNF levels, suggesting a prolonged neurotrophic reaction to regular physical activity. Similarly, Wang et al., 2022 reported that both aerobic and resistance training in healthy individuals boosted BDNF levels, regardless of age or gender. In a study by Kim et al., 2022, it was found that aerobic exercise significantly elevated BDNF levels in individuals experiencing mild cognitive impairment, highlighting the potential of exercise to slow down neurodegenerative progression. Furthermore, Ceylan et al., 2024 verified that both acute and chronic exercise programs

enhanced BDNF levels in obese individuals, connecting improved neurotrophic signalling to benefits in metabolic health.

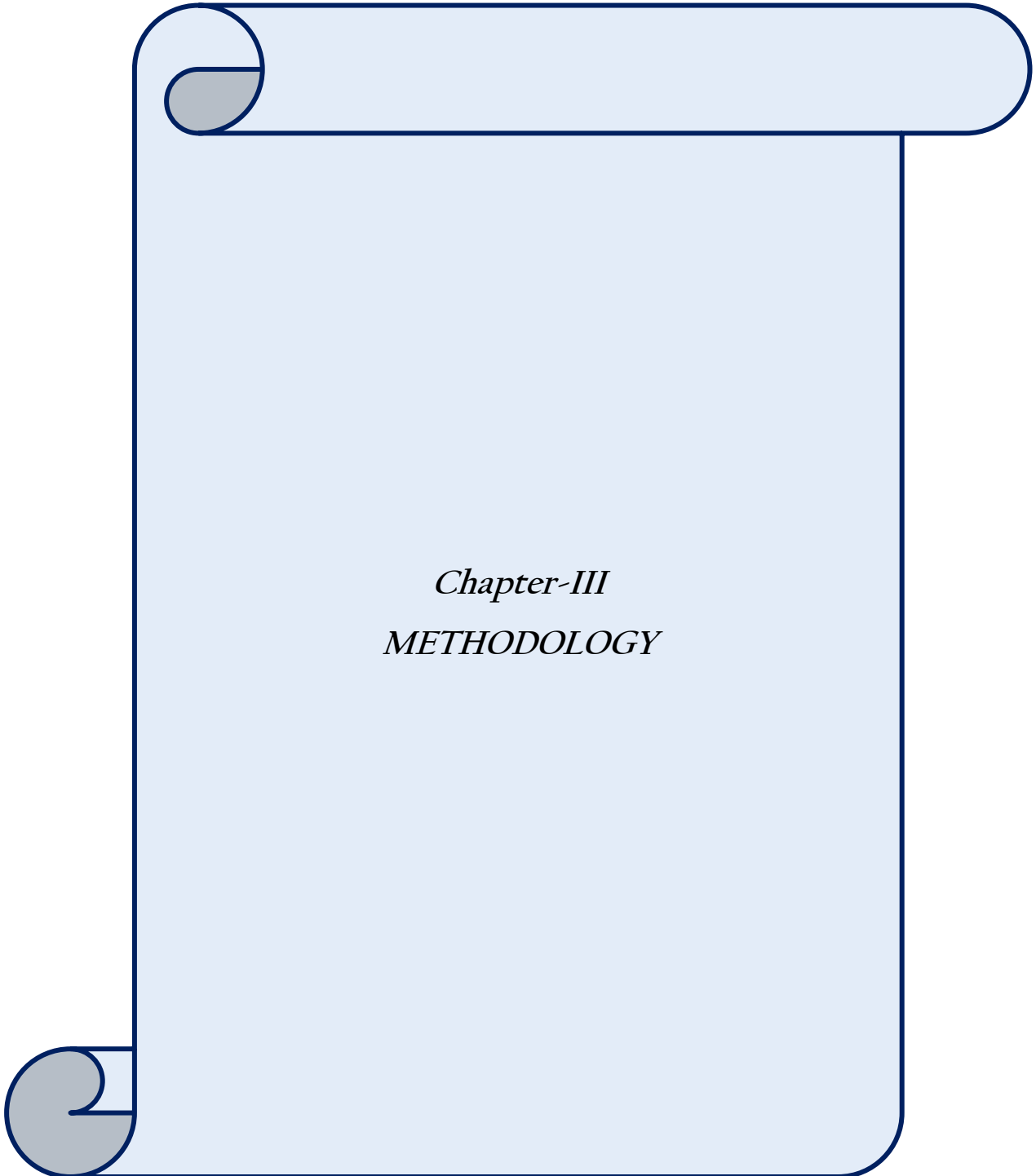
Ashcroft et al., 2022 expanded this evidence to clinical populations, demonstrating that exercise programs for stroke survivors markedly increased peripheral BDNF, potentially aiding in neural recovery and plasticity. Schmolesky et al., 2013 noted that the intensity and duration of aerobic activity influenced the extent of the BDNF response, with higher intensity and longer workouts producing greater effects. Complementary findings from Lucertini et al., 2015 associated high levels of cardiorespiratory fitness with lower cortisol levels, suggesting a wider neuroendocrine equilibrium fostered by consistent exercise. While Roy et al., 2025 explored the impact of exercise on neurotransmitters like GABA, their synthesis reinforces the broader idea that physical activity encourages neurochemical changes that support brain health. Together, these studies highlight exercise as a powerful influencer of neurotrophic and neurochemical systems, promoting cognitive and emotional resilience across various health conditions.

2.5 Concluding Summary of the Literature Review

CRF is recognized as a vital factor influencing both physiological and neurochemical health, which may influence pulmonary function, HRV, and neurochemical markers like GABA, BDNF, and cortisol. Mechanistically, heightened CRF could lead to better outcomes in PFTs by promoting improved lung ventilation and oxygen utilization, which supports systemic oxygen distribution and metabolic stability. Similarly, regular aerobic exercise contributes positively to autonomic balance, as evidenced by increased HRV, by affecting parasympathetic activity and reducing sympathetic dominance. At the neurochemical level, CRF may boost BDNF expression, fostering neuroplasticity, while simultaneously modulating GABAergic functions to sustain inhibitory signaling in the central nervous system. Furthermore, elevated CRF is associated with lower baseline cortisol levels and reduced stress responses, suggesting a link between cardiovascular fitness and the regulation

of the hypothalamic-pituitary-adrenal (HPA) axis. Collectively, these mechanisms suggest a theoretical connection where increased CRF is associated with more favorable outcomes in PFT, HRV, and neurochemical markers.

While interest in this complex relationship is growing, there remains a notable lack of research in this area. Most existing studies have focused on these variables in isolation, either examining cardiorespiratory fitness and autonomic regulation or neurochemical changes that occur post-exercise, rather than taking a holistic approach. There is a deficiency of longitudinal or interventional studies that explore the combined effects of CRF on pulmonary, autonomic, and neurochemical indicators simultaneously. Additionally, the causal mechanisms linking CRF to neurochemical changes and HRV are not fully understood, and the potential for reciprocal effects is primarily speculative. Addressing these gaps through well-designed, multimodal research could illuminate the complex interactions among fitness, autonomic function, pulmonary capacity, and neurochemical signalling, ultimately resulting in targeted approaches to improve both physical and mental health.



Chapter-III
METHODOLOGY

3. Methodology

Research methodology refers to the structured and scientific method set about to address a research question. This chapter delves into the detailed procedural decisions and research plan of the study. The methodology encompasses a comprehensive overview of the participants, the setting, the methods used for data collection and analysis, along with the ethical considerations.

3.1 Enquiry Framework

The current research is deductive in nature and employs a quantitative methodology. The investigation is centred around a research question that was formulated through a fundamental, critical, and systematic literature review. It posed the question: “what is the relationship between cardiorespiratory fitness(VO_2Max) and key physiological and neurochemical markers-including pulmonary function test indices, heart rate variability indices, and circulating levels of GABA,BDNF and Cortisol in healthy young adults?” To ensure that the study was aligned with this research question, which stemmed from the review findings, the researcher aimed to measure the impact of regular aerobic exercise on healthy young adults concerning their pulmonary, cardio autonomic, and neurochemical markers.

3.2 Study Location and Laboratory setup

The study was conducted in the Exercise and Sports Physiology Laboratory, Department of Physical Education, Jadavpur University, Kolkata, West Bengal, India. The instrumentation in laboratory was procured under Rashtriya Uchchar Shiksha Abhiyan (RUSA) 2.0 project of the Department and for the ELISA test the Department of Physical Education in guidance of Dr. Sridip Chatterjee, Associate Professor of the Department procured the necessary instrument as mentioned in Figure 1. The orientation of the research core team and the young

Methodology

adult participants and the technician set up was also planned in the same venue.



Figure 2: Laboratory Machinery Setup

3.3 Description of population

A comprehensive review conducted by the researcher highlighted that there are few studies addressing an observational approach finding out impact of cardiorespiratory fitness on pulmonary, cardio autonomic, and neurochemical markers of healthy young population. The researcher identified certain areas that have not yet been explored. As a result, a study was designed based on a review of the relevant literature concerning healthy young individuals who engage in regular exercise.

3.3.1 Sample Size

The sample size determined through G*Power software, version 3.1.9.7, resulted in 112 participants. This number was based on a power ($1-\beta = 0.90$), a significance level ($\alpha = 0.05$), and an effect size ($d = 0.3$) for the research study conducted at Jadavpur University.

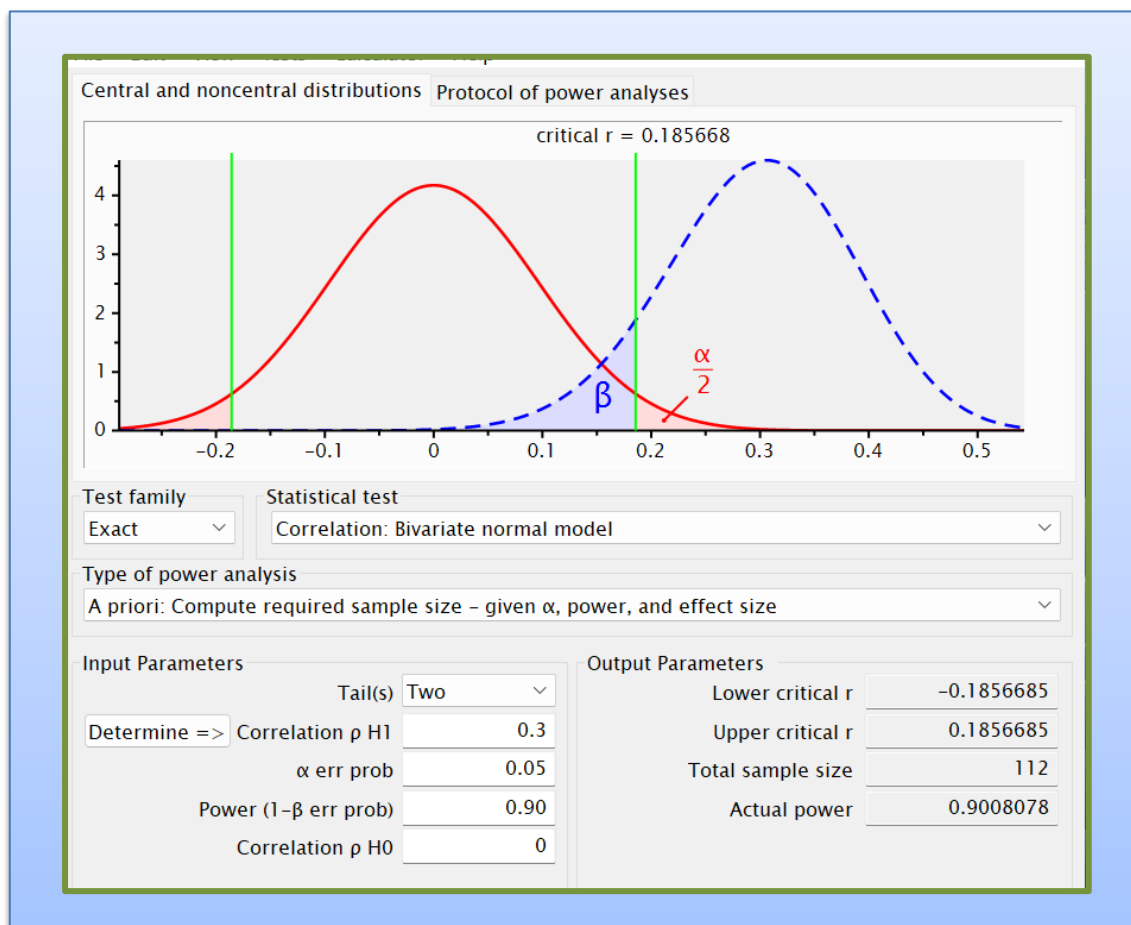


Figure 3: G Power analysis chart

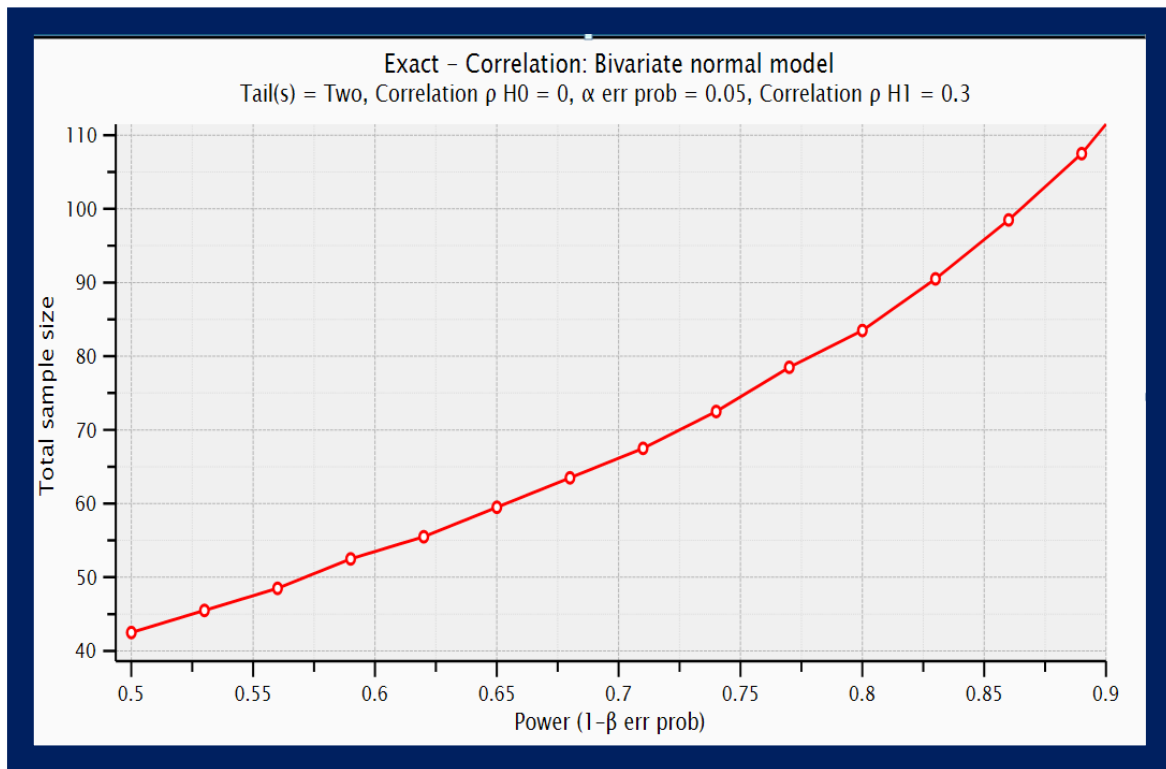


Figure 4: Plot for range of power with sample size for the study

3.3.2 Source of the Subjects

As a dedicated research scholar in the Department of Physical Education at Jadavpur University, the researcher have developed a solid relationship with the students in the department. Due to their frequent participation in exercise, the researcher arranged a meeting, with the oversight of the research guide, for the B.P. Ed and M.P. Ed students from the department.

3.3.3 Selection of Subjects

A sum of 115 students enrolled in B.P. Ed and M.P. Ed programs at Jadavpur University, Kolkata were selected for the study. The ages of the participants ranged from 20 to 25 years, in compliance with the Ethical Guidelines set forth by the Indian Council of Medical Research (ICMR) in 2017 for human subjects (Mathur, & Swaminathan., 2018).

3.3.3.1 Sampling Procedure

In this study, a convenience sampling method (Fig:5) was used, focusing on the participants' availability and their eagerness to participate. The research included only one group that engaged in regular physical activity (Male 115; age 23.40 ± 1.40).

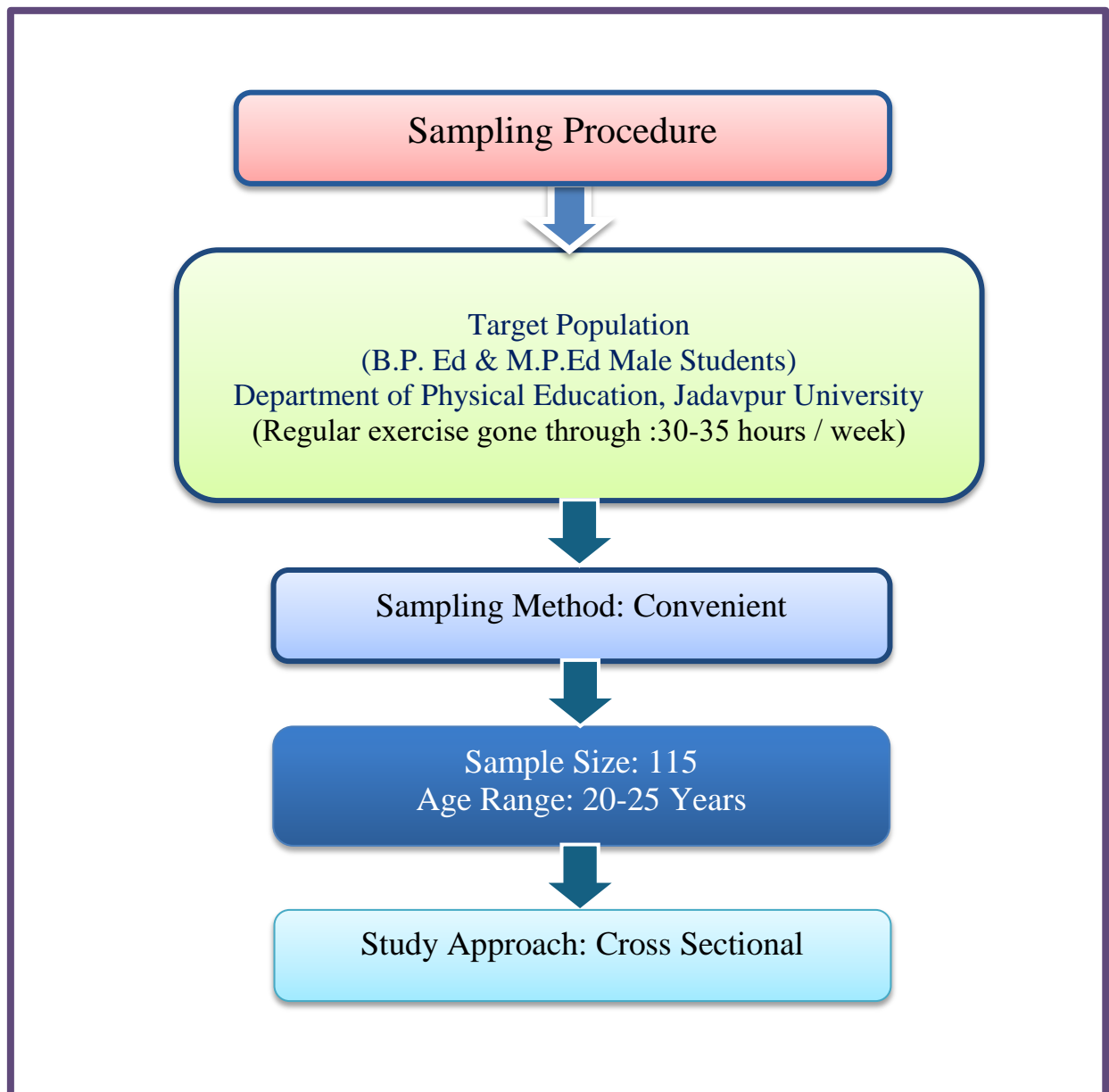


Figure 5: Layout of Sampling Procedure

3.3.3.2 Inclusion Criteria

The prospective subject population must have the attributes that will make them possible to accomplish the purpose of the research. The researcher here specifies the inclusion criteria for participation in the present study. Inclusion criteria are a set of predefined characters to match the research objectives. These are used to identify the subjects that will be included in the research study.

Sl. No	Inclusion Criteria
1	Male students enrolled in the B.P.Ed and M.P.Ed programs.
2	Aged between 20 and 25 years' male young adults.
3	Students maintained a regular exercise routine, participating in physical activities for about 30-35 hours each week.

Table 5: Inclusion Criteria

3.3.3.3 Exclusion Criteria

According to the objectives of the study, exclusion criteria were predefined and acted as a guideline for the convenient sampling subject selection process. These are a set of characteristics which identify the subjects that will not be selected for the study. The characteristics that disqualify prospective subjects from inclusion in the study fall under this category.

Sl. No	Exclusion Criteria
1	Female students enrolled in the B.P.Ed and M.P.Ed programs.
2	Experiencing any short-term or long-term injury.
3	Currently on any medication.

Table 6: Exclusion Criteria

According to the specified inclusion and exclusion criteria, the researcher selected a total of 115 participants for this study.

3.4 Ethical Guidelines

The present investigation focused on adult males between the ages of 20 and 25. This research followed the standard protocols for studies involving human participants outlined by the ICMR in 2017 (Mathur & Swaminathan, 2018), which informed the checklist used in this study; the pertinent sections are as follows:

- The research proposal was based on solid scientific principles.
- The equation between possible benefits and likely hazards was slight, as the data gathering method in this research study posed no threat.
- The research emphasizes the benefits of engaging in consistent aerobic activities and their impact on pulmonary, cardio autonomic, and neurochemical indicators, which in turn improve overall cognitive abilities in human being. Additionally, each participant will receive a personalized report after the completion and submit of the research study.
- The justification for this study was supported by a comprehensive review of existing literature, accompanied by a detailed evaluation of those references.
- The research, especially during the data collection stage, was conducted by a group of experts.

The Table 7 below outlines the ethical principles that were taken into account during the conduct of the subsequent research study.

SI No	Ethical issue	Definition
1	Voluntary participation	Participants have the option to withdraw from the study at any moment.
2	Informed consent	Participants are informed about the study's purpose, advantages, potential risks, and interpretations before they decide to accept or decline participation.
3	Anonymity	The identities of those involved are kept confidential in other locations. Any personally identifiable information is not made available to the public.
4	Confidentiality	The researcher ensured that personally identifiable information was anonymized to prevent it from being associated with other data by any external party.
5	Potential for harm	All forms of harm—be it physical, social, psychological, or otherwise—are minimized to none, with every precaution implemented regarding the subsequent concerns.
6	Results communication	Ensure that the research complies with ethical standards and that the results are presented truthfully.

Table 7: Ethical Principles of the study

3.5 Ethical Consideration

The current research was carried out on adult males enrolled in B.P.ED and M.P.ED programs, making ethical considerations a crucial element of the study. These ethical considerations were categorized into two main sections:

- Ethical Norms
- Ethical Approvals and Policies

3.5.1 Ethical Norms

All participants of the present study have attained the legal age of consent which is above 18 years. Therefore, the decision regarding their participation in the present research or withdrawal were supposed to take independently. These guidelines were completely aligned

Methodology

to the ICMR “National Ethical Guidelines for Bio-Medical Research studies involving human participants ,2017 (Mathur & Swaminathan, 2018)” and the following criteria were met.

- The chosen subjects consisted of adults who are 18 years of age or older.
- The adult participants received thorough details about the study explained in an easy-to-understand and straightforward way.
- In accordance with the standard guidelines for Informed Consent Forms (ICF), participants have provided consent for the study.
- The institutions where the students were affiliated were also consulted for approvals concerning their involvement in this study.
- The following form has been properly completed and is presented below:

❖ **Informed Consent Document (ICD)**

In the current investigation, the forms were developed in accordance with the ICMR guidelines from 2017, incorporating all pertinent information about the research study, including its aim, importance, technical aspects, and the information needed from participants, which were all detailed in the informed consent documents. Below, Figure 6 presents an example of the Informed Consent Document.

INFORMED CONSENT DOCUMENT (ICD)

Participant information sheet

INFORMATION FOR PARTICIPANTS OF THE STUDY

Instructions - This is the participant information sheet. It should address the participants of this study. Depending upon the nature of the individual project, the details provided to the participant may vary. A separate consent form should be provided for the test group and control, as applicable.

1. Title of the project:
Impact of Cardiorespiratory Fitness on Selected Pulmonary Cardioautonomic and Neurochemical Markers
2. Name of the research scholar:
Dilip Roy
3. Purpose of this project/study:
To understand the habitual and long-term effects of exercise (VO2 max) on the selected Pulmonary cardioautonomic and neurochemical markers.
4. Procedure/methods of the study:
Cross-sectional Study on cardiopulmonary and neurochemical markers

Figure 6: Informed Consent Document

Methodology

CONSENT FORM

Title of the Doctoral Programme:
Impact of Cardiorespiratory Fitness on Selected Pulmonary Cardioautonomic and Neurochemical Markers

Participant's name: _____ Address _____

The details of the study have been provided to me in writing and explained to me in my own language. I confirm that I have understood the above study and had the opportunity to ask questions. I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without the medical care that will normally be provided by the hospital. I agree not to restrict the use of any data or results that arise from this study, provided such a use is only for scientific purposes (s). I have been given an information sheet giving details of the study. I fully consent to participate in the above study.

(I also consent/do not consent to use my stored biological samples for future scientific purposes: Yes/ No – if applicable)

Signature of the participant: _____ Date: _____

Signature of the witness: _____ Date: _____

Figure 7: Participants' Consent Form

3.5.2 Ethical Approval and Policies

Considering the ethical considerations in human research, the current study received approval from two authorizing body. The Institutional Ethics Committee (IEC) of Jadavpur University (Reference No: IEC/37/C/25 dated 22.01.2025) granted approval for this study. (Annexure-II) When conducting experimental research involving human subjects, it is crucial to adhere to norms and policies to ensure that the research is both legal and ethical. The researcher and their team considered all international clinical trial guidelines (WHO) and registered their study with the Clinical Trial Registry of India, following the principles set forth by the International Committee of Medical Journal Editors (ICMJE). As this research pertains to exercise physiology within the realm of typical biomedical research, it was accepted by the

Methodology

Clinical Trial Registry of India-CTRI, and the registration number is: CTRI/2025/05/086537.

(Annexure-II)

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কলকাতা-৭০০০৩২, ভারত

*JADAVPUR UNIVERSITY
KOLKATA-700 032, INDIA

Dr.Sridip Chatterjee
Dept. of Physical Education
Jadavpur University

RefNo: IEC/37/C/25
Date: 22.01.2025

Dear Sir/ Madam,

Institutional Ethics Committee (IEC) Approval

Title of the Study: "IMPACT OF CARDIORESPIRATORY FITNESS ON SELECTED NEUROCHEMICAL AND CARDIO AUTONOMIC MARKERS"

The above application of Mr. Dilip Roy, Department of Physical Education, Jadavpur University has been considered on behalf of the Jadavpur University Institutional Ethics Committee in accordance with the procedures laid down by the University for ethical approval of all research involving human participants.

I am pleased to inform you that, on the basis of the information provided to the Jadavpur University Institutional Ethics Committee, the proposed research has been judged as per meeting appropriate ethical standards, and accordingly approval has been granted in the meeting dated 20.01.2025.

Figure 8: Institutional Ethical Permission

FULL DETAILS (Read-only) -> Click Here to Create PDF for Current Dataset of Trial															
CTRI No	CTRI/2025/05/086537 [Registered on: 07/05/2025] Trial Registered Prospectively														
Acknowledgement Number	REF/2025/04/103228														
Last Modified On:	12/05/2025														
Post Graduate Thesis	No														
Type of Trial	Observational														
Type of Study	Cross Sectional Study														
Study Design	Single Arm Study														
Public Title of Study	Relationship among Cardiorespiratory Fitness, Selected Neurochemical and Cardio Autonomic Mar														
Scientific Title of Study	Impact of Cardiorespiratory Fitness On Selected Neurochemical and Cardio Autonomic Markers														
Trial Acronym	Nil														
Secondary IDs if Any	<table border="1"> <thead> <tr> <th>Secondary ID</th> <th>Ident</th> </tr> </thead> <tbody> <tr> <td>NIL</td> <td>NIL</td> </tr> </tbody> </table>	Secondary ID	Ident	NIL	NIL										
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Details of Principal Investigator or overall Trial Coordinator (multi-center study)	<table border="1"> <tbody> <tr> <td>Name</td> <td>Dilip Roy</td> </tr> <tr> <td>Designation</td> <td>Ph.D Scholar</td> </tr> <tr> <td>Affiliation</td> <td>Jadavpur University</td> </tr> <tr> <td>Address</td> <td>Department of Physical Education, Jadavpur University, Kolkata</td> </tr> <tr> <td>Phone</td> <td>Kolkata WEST BENGAL 700032 India</td> </tr> <tr> <td>Fax</td> <td>9679157430</td> </tr> <tr> <td>Email</td> <td>dilipr.pe.rs@jadavpuruniversity.in</td> </tr> </tbody> </table>	Name	Dilip Roy	Designation	Ph.D Scholar	Affiliation	Jadavpur University	Address	Department of Physical Education, Jadavpur University, Kolkata	Phone	Kolkata WEST BENGAL 700032 India	Fax	9679157430	Email	dilipr.pe.rs@jadavpuruniversity.in
Name	Dilip Roy														
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Address	Department of Physical Education, Jadavpur University, Kolkata														
Phone	Kolkata WEST BENGAL 700032 India														
Fax	9679157430														
Email	dilipr.pe.rs@jadavpuruniversity.in														
Details Contact Person	<table border="1"> <tbody> <tr> <td>Name</td> <td>Dr. Sridip Chatterjee</td> </tr> <tr> <td>Designation</td> <td>Guide/Associate Professor</td> </tr> <tr> <td>Affiliation</td> <td>Jadavpur University</td> </tr> <tr> <td>Address</td> <td>Department of Physical Education, Jadavpur University, Kolkata</td> </tr> </tbody> </table>	Name	Dr. Sridip Chatterjee	Designation	Guide/Associate Professor	Affiliation	Jadavpur University	Address	Department of Physical Education, Jadavpur University, Kolkata						
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Designation	Guide/Associate Professor														
Affiliation	Jadavpur University														
Address	Department of Physical Education, Jadavpur University, Kolkata														

Figure 9: Ethical Permission from CTRI

3.6 Variables Studied

Variables represent a logical collection of attributes. Attributes are the features or qualities that define an object. In this study, the primary variables consist of demographic variables, while the secondary variables, referred to as pulmonary, cardio autonomic and neurochemical variables, are classified as Physiological variables based on the research question derived from the literature review.

3.6.1 Demographic variables

Demographic variables refer to the traits of the subjects that are primarily collected to characterize them to conduct a thorough analysis, and evaluate how well they represent the intended population. In this research, the demographic variables identified include age, Body Mass Index (BMI). Below, Table 8 presents the specific tools, instruments, and measurement units used for these selected variables. This provides a clearer understanding of the chosen subjects in relation to the established inclusion and exclusion criteria.

Sl. No	Demographic Variables	Measurement aids and instruments	Unit Of measurement
1	Age	Birth certificate	Years
2	Height	Stadiometer	Cms
3	Weight	Weighing Machine	Kgs
4	BMI- Body Mass Index	Formula: $\text{weight (kgs)}/[\text{height(m)}]^2$	Ratio

Table 8: Demographic Variables of the Study

3.6.2 Physiological variables

Physiological variables (Table 9) denote aspects related to the body's functioning and internal conditions, such as Aerobic fitness or Cardiorespiratory fitness (CRF) or VO₂ Max, Pulmonary Function Test (PFT) indices, Heart Rate Variability (HRV) indices, Neurochemical Markers (GABA,BDNF,Cortisol)

SI No	Physiological/observational Variables	Instrument and Software used	Outcomes
1	Cardiorespiratory Fitness	<ul style="list-style-type: none"> ➤ The iworx TA (Model IX-TA-220) ➤ iWireGA1 CO₂/O₂ Gas analyser with filter ➤ 3-liter calibration syringe ➤ Flow head tubing and A-FH -1000 flow head ➤ A-GAK-201 reusable mask ➤ 5 litre mixing chamber (Model: A-GAA-MC) ➤ PHRM-220 heart rate watch ➤ Treadmill (Nasan) ➤ Labscribe Software(4.0) 	<p>VO₂ Max (Followed by Bruce Protocol)</p>
2	PFT Indices	<ul style="list-style-type: none"> ➤ The iworx TA (Model IX-TA-220) ➤ Flow head tubing and A-FH -1000 flow head ➤ Labscribe Software(4.0) 	<p>Forced Expiratory Volume in the first second (FEV-1), Forced Expiratory Volume in 3 seconds (FEV-3), Vital capacity (VC).</p>
3	HRV Indices (Time Domain and Frequency Domain)	<ul style="list-style-type: none"> ➤ The iworx TA (Model IX-TA-220) ➤ Iwire-B3G ➤ Pulse Analyser 	<p>Mean RR, Mean HR, RMSSD, SDNN, pNN50, LF power, LF(nu), HF power, HF (nu), LF/HF ratio</p>
4	Neurochemical Markers	<p>BeneSphera™ E21 ELISA Microplate machine (Mfg. Lic.No:MFG/IVD/2023/000032) with the help of Immuno Tag's kit</p>	<p>GABA, BDNF, Cortisol</p>

Table 9: Physiological variables of the study

3.6.2.1 Selected Pulmonary Indices

Spirometry is one of the most commonly used approaches to test pulmonary function. This Pulmonary Function Test (PFT) measures the volume of air exhaled at specific time points during complete exhalation by force, which is preceded by a maximal inhalation.

Variables	Description	Units
FEV-1	Forced Expiratory Volume in 1 second. (The amount of air a person can forcefully exhale in the first second of a breath)	Litre
FEV-3	Forced Expiratory Volume in 3 seconds. (the volume of air exhaled in the first three seconds of a forced breath)	Litre
VC	Vital Capacity (The summation of Tidal Volume (TV) + Inspiratory Reserve Volume (IRV) + Expiratory Reserve Volume (ERV)).	Litre

Table 10: Details of PFT Indices of the study

3.6.2.2 Selected HRV indices

HRV is a physiological marker that measures the variation in time between successive heartbeats, derived from the R–R intervals on an ECG. It represents the dynamic interaction and balance between the sympathetic (fight or flight) and parasympathetic (rest and digest) branches of the autonomic nervous system (ANS).

	Variables	Description	Units	Dominance
TIME DOMAIN	Mean RR	Mean of all normal-to-normal (NN) intervals	ms	Reflects average cardiac cycle length (inverse of HR)
	Mean HR	Mean Heart Rate	beats per minute (bpm)	Reflects average autonomic tone (higher = more sympathetic)
	RMSSD	The Root Mean Square of Successive Differences between normal heartbeats	milli seconds (ms)	Parasympathetic dominance
	SDNN	Standard Deviation of the N-N intervals	milli seconds (ms)	Parasympathetic dominance
	pNN50	proportion of NN50 divided by the total number of NN intervals	percentage %	Parasympathetic dominance
FREQUENCY DOMAIN	LF power	Power in low frequency range	square milliseconds (ms^2)	Parasympathetic dominance
	LF (nu)	Low Frequency power in normalized units	nu	Relative sympathetic (and some parasympathetic) activity
	HF power	Power in high frequency range	square milliseconds (ms^2)	Parasympathetic dominance
	HF(nu)	High Frequency power in normalized units	nu	Relative parasympathetic (vagal) activity
	LF/HF Ratio	Ratio LF [ms^2]/HF [ms^2]	%	Sympathetic dominance

Table 11: Details of Time Domain and Frequency Domain Variables of HRV

3.6.2.3 Neurochemical markers

Neurochemical markers are substances in the nervous system, such as neurotransmitters, neuropeptides, or metabolites, that indicate neuronal activity, signaling, or pathological changes. They are used to study brain function, neurological disorders, and neurochemical balance.

Indices	Description	Unit
GABA	<p>Gamma-Aminobutyric acid</p> <p>(A protein that supports neuronal growth, survival, and synaptic plasticity, important for learning, memory, and mood regulation.)</p>	µg/dl
BDNF	<p>Brain-Derived Neurotrophic Factor</p> <p>(The main inhibitory neurotransmitter in the brain, reducing neuronal excitability and promoting calmness and relaxation.)</p>	ng/ml
Cortisol	<p>A stress hormone released by the adrenal glands, regulating metabolism, immune response, and the body's stress response.</p>	(Mcg/dl)

Table 12: Details of Neurochemical Markers (GABA, BDNF, Cortisol)

3.7 Assessment of Cardiorespiratory fitness (CRF) through VO₂ Max

Cardiorespiratory fitness (CRF) serves as an important indicator of both athletic ability and overall health (Neshitov et al., 2023). A well-established measure of an individual's CRF is the maximal oxygen uptake (VO₂ max). This concept was first introduced by Hill and Lupton in their 1923 publication (Hill et al., 1923), defining it as "the oxygen intake during an exercise intensity at which actual oxygen intake reaches a maximum beyond which no increase in effort can raise it." Methods for estimating a person's VO₂ max can be categorized into two groups: direct and indirect methods (Lima et al., 2005). Direct methods generally involve conducting a graded exercise test in a controlled lab environment that provides direct measurements of oxygen consumption and requires the person to reach their maximal physical activity level. The most common direct testing methods include treadmill tests, where individuals run on a treadmill with an increasing gradient or speed, and bicycle ergometer tests, where individuals pedal on a stationary bike with gradually increasing resistance or pedalling rates. During these assessments, oxygen consumption measurements rise with exercise intensity until a plateau is reached or the individual can no longer maintain the required level of intensity, indicating the VO₂ max level. The accuracy of these methods has been confirmed in various research studies (Hawkins et al., 2007; Beltz et al., 2016; Day et al., 2003). In the current study, a direct method was utilized.

3.7.1 Administration of Test

In this study, the assessment of VO₂ max was conducted using the NASAN TMT (Treadmill Test) system, a widely utilized computerized stress testing instrument for evaluating CRF. The system estimates VO₂ max based on established protocols such as the Bruce protocol. While the NASAN TMT provides the testing platform, iWorx software (LabScribe) was employed for data acquisition, recording, and analysis. The complete procedure for performing the treadmill test using the NASAN TMT system with the Bruce protocol, along

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with the preparatory steps undertaken in both the NASAN TMT system and iWorx (LabScribe) software, is described below.

❖ **Machine warm up and Calibration:**

Before testing, the iWorx gas analyzer and treadmill are switched on and allowed to warm up for about 20–30 minutes to ensure sensor stability. After warm-up, the LabScribe software is opened on the computer to establish communication between the gas analyzer and treadmill controller. The analyzer display is then checked to confirm that the oxygen (O₂) and carbon dioxide (CO₂) readings are stable and within the expected room-air range. For gas calibration, room air is first drawn through the analyzer, and the “Calibrate Ambient” command is selected in LabScribe to set the zero reference (O₂ ≈ 20.93 %, CO₂ ≈ 0.03 %). Next, the standard calibration gas cylinder is connected and allowed to flow for about 20 seconds, until the gas readings stabilize. Finally, the system is flushed again with room air and the calibration status is checked to confirm that both O₂ and CO₂ sensors have returned to normal baseline values, ensuring accurate measurements for subsequent VO₂ max testing.

❖ **Preparatory Steps**

➤ **Phase 1: Lead Placement and Supine**

- To ensure proper contact for the electrodes, the patient's skin is cleaned and abraded in preparation.
- Ten ECG electrodes are positioned on the patient's chest and limbs following the established clinical placement protocols (e.g., Mason-Likar setup for exercise).
- The acquisition unit is connected to the patient, and a resting electrocardiogram is obtained.

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- During the initial assessment phases, baseline measurements (ECG, HR, BP) can also be recorded with the practitioner in a supine position (lying flat on their back) to compare with values obtained while upright and during exercise.

Lead	Placement
RA (Right Arm)	Below right clavicle, on the outer edge of the chest
LA (Left Arm)	Below left clavicle, on the outer edge of the chest
RL (Right Leg, Ground)	On the lower right abdomen or right iliac crest
LL (Left Leg)	On the lower left abdomen or left iliac crest
V1	Fourth intercostal space at the right sternal border
V2	Fourth intercostal space at the left sternal border
V3	Midway between V2 and V4
V4	Fifth intercostal space at the midclavicular line
V5	At the same horizontal level as V4, at the anterior axillary line
V6	At the same horizontal level as V4 and V5, at the midaxillary line

Table 13: Placement of Leads for the Assessment of VO₂ Max

Methodology



Figure 10: Placement of Leads on a practitioner

- **Phase 2:** The standing phase (or pre-exercise standing baseline) is a short preparatory step between the resting (supine) ECG and the start of treadmill exercise.

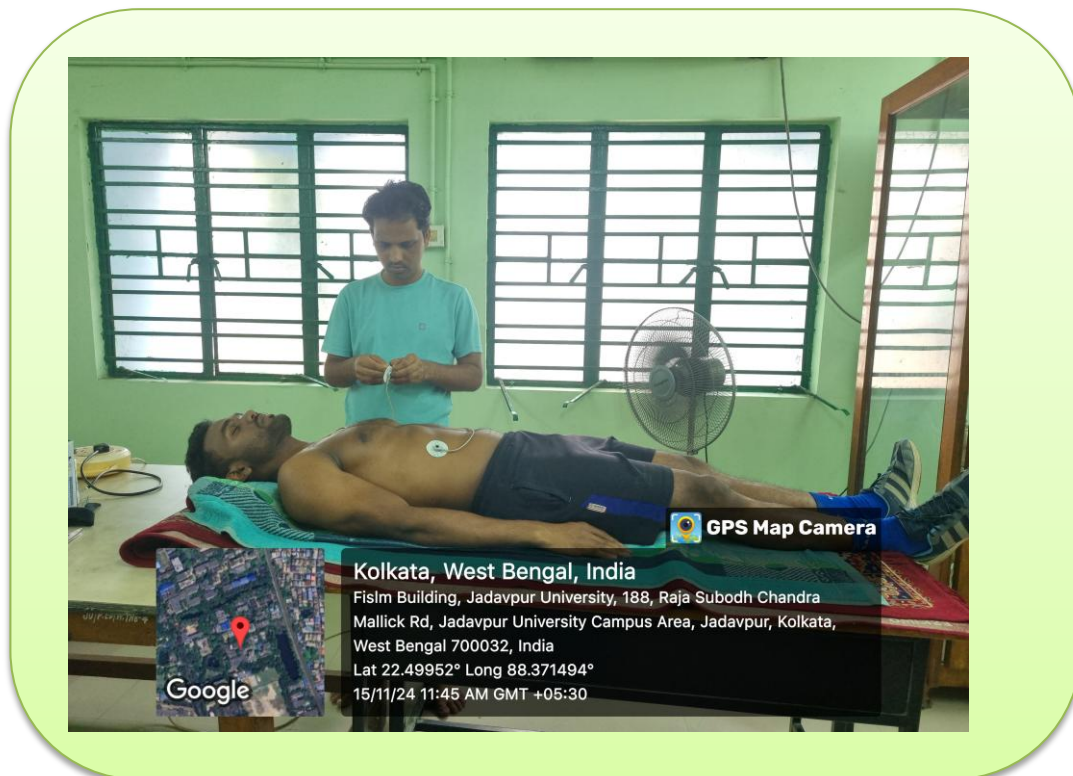


Figure 11: Standing phase after placement of leads

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➤ Phase 3: Hyperventilation

The participants might be instructed to hyperventilate while in a standing position to evaluate any ECG changes that could result from respiratory fluctuations instead of myocardial ischemia (heart problems), allowing for an accurate baseline reading.



Figure 12: Hyperventilation Phase

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➤ Phase 4: Ready for Exercise

After completing all initial baseline recordings, the subject is informed that the exercise test will begin shortly. The researcher ensures that the participant is comfortable, understands the testing procedure, and is familiar with safety measures such as the location and use of the emergency stop button. Next, the respiratory mask is carefully fitted and checked for proper sealing and comfort. Once the setup is verified, the treadmill is started, and the exercise protocol is initiated as per the selected test stages.



Figure 13: Ready phase of before exercise

Exercise Phase followed by Bruce Protocol

After turning on the treadmill, the participant begins walking on treadmill followed by the Bruce protocol, which consists of seven stages with speed and incline increasing every three minutes and this protocol is automatically controlled by the software. Details of each stage are provided in **Table 14**. The test stops when participant's heart

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rate hit 85% of maximum heart rate.

Stage	Treadmill speed (mile per hour)	Treadmill incline
1	1.70 mph	10%
2	2.50 mph	12%
3	3.40 mph	14%
4	4.20 mph	16%
5	5.00 mph	18%
6	5.50 mph	20%
7	6.00 mph	22%

Table 14: Stages, Speed and Inclines of Bruce Protocol



Figure 14: Participants during exercise

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Analysis and preparation report

After completion of test individual VO₂ Max score and report was prepared through Lab Scribe software (version 4.0).

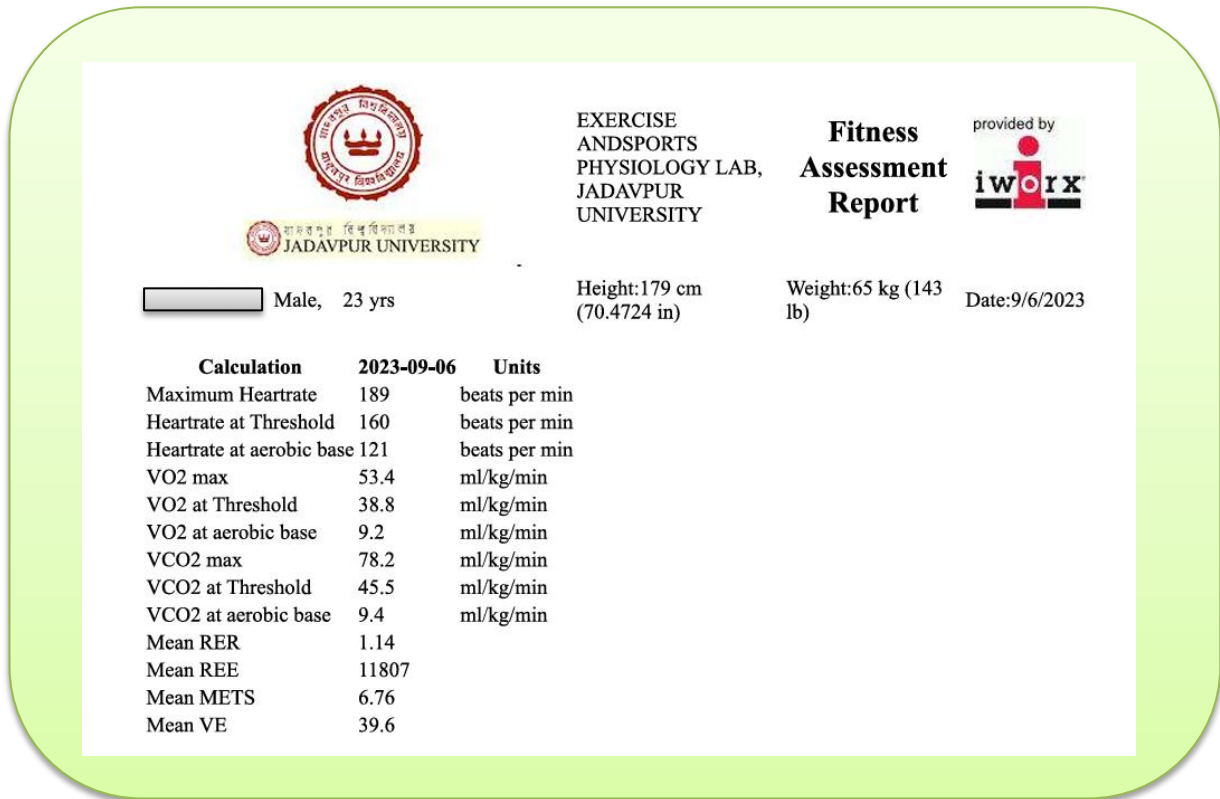


Figure 15: Representation of VO₂ Max Assessment Report

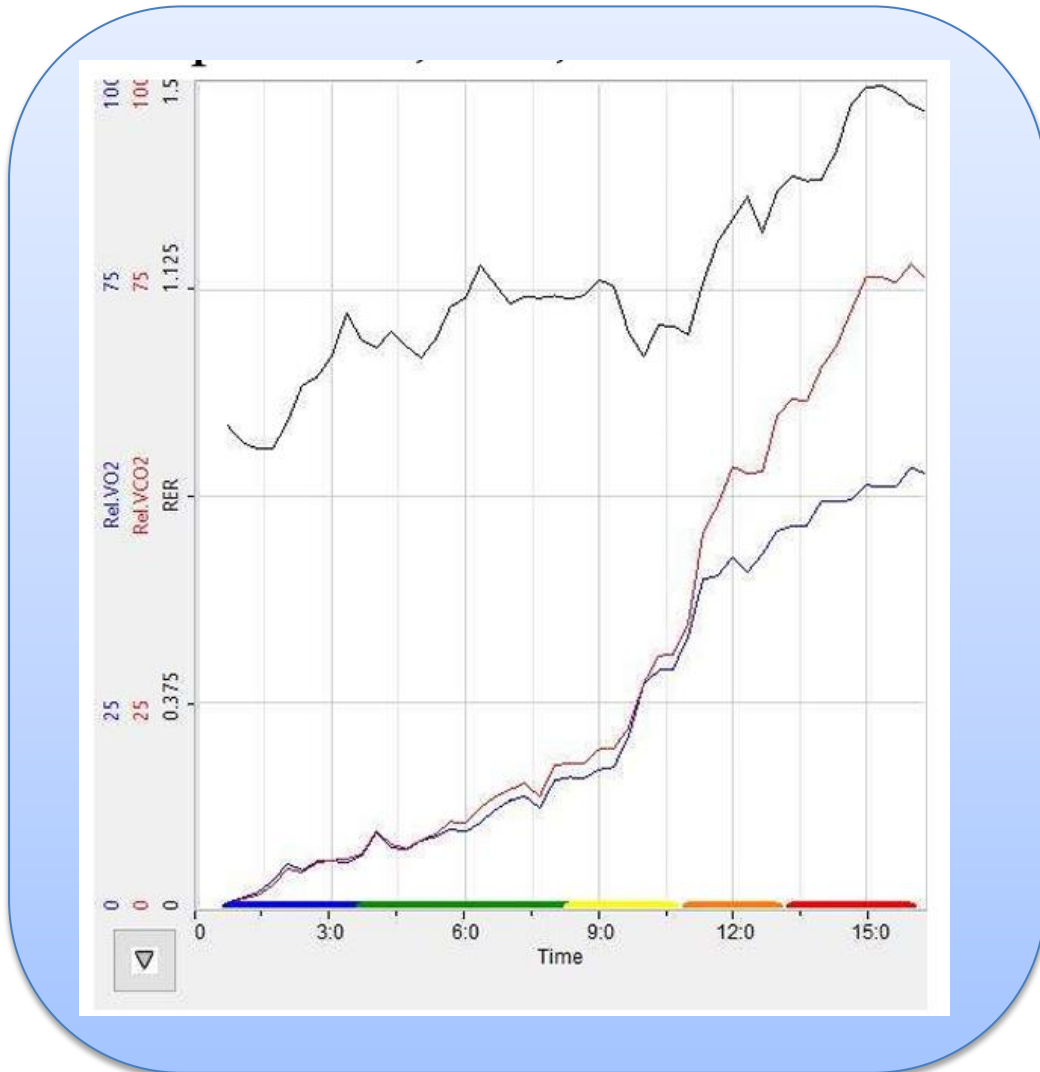


Figure 16: Graphical representation of VO₂ Max

3.8 Assessment of Selected Pulmonary Function Test Indices

The Iworx TA system and Lab Scribe (version-4.0) software were used to record selected spirometry measurements. Prior to the experimental session, all equipment was carefully calibrated to ensure accuracy. Participants were seated comfortably on a chair with their upper body kept straight and were provided with clear verbal instructions and demonstrations to ensure correct technique. Each participant performed maximal inhalation followed by maximal exhalation through the spirometer mouthpiece, according to standardized spirometry

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procedures. Two trials were conducted for each participant, and the highest reproducible value was recorded as the final measurement of an individual participant.



Figure 17: Assessment of Spirometry indices of the participants

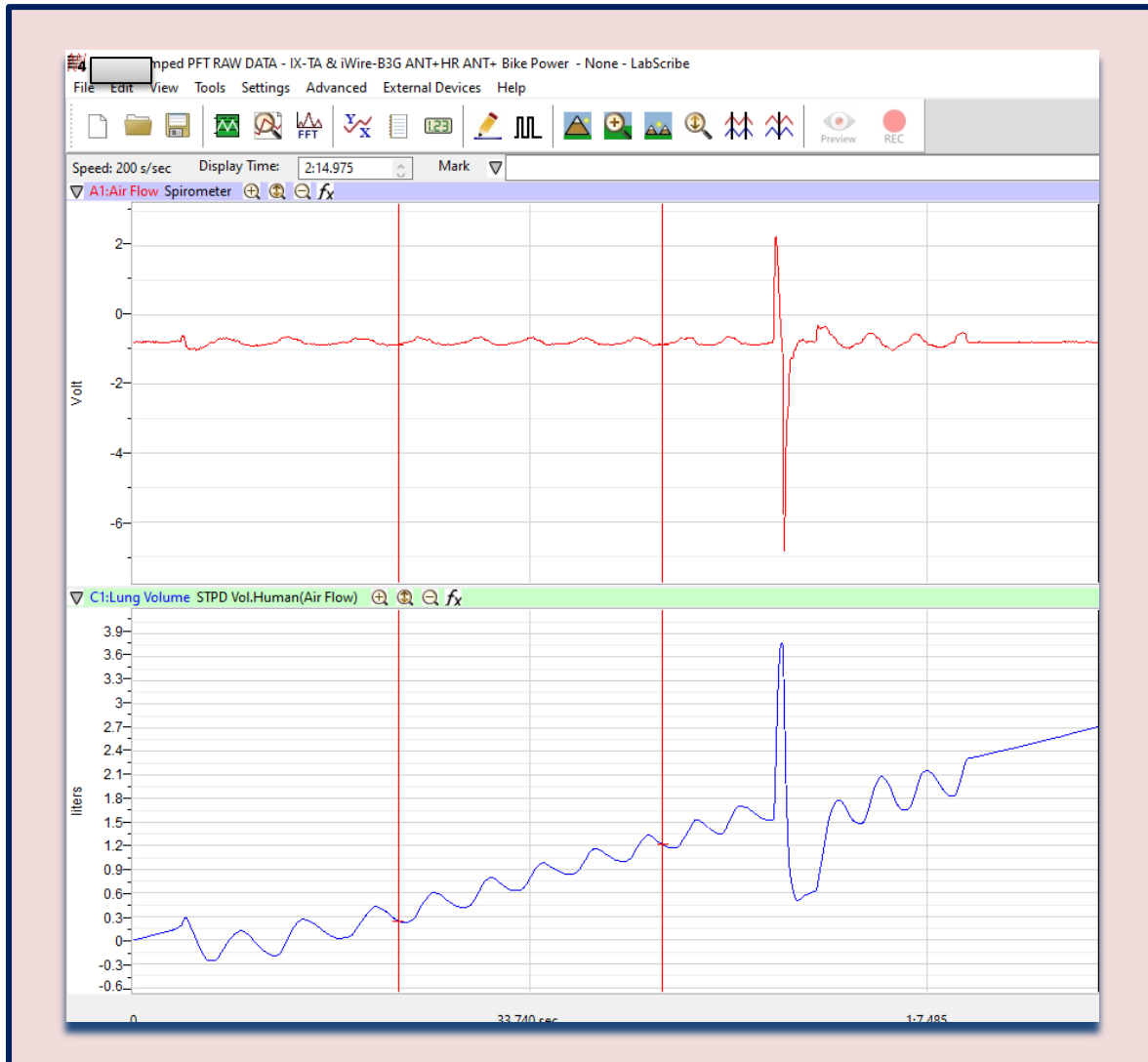


Figure 18: Graphical representation of Spirometry

3.9 Heart Rate Variability Test

To assess heart rate variability (HRV) from electrocardiogram (ECG), the researchers utilized the iwire-B3G device, Iworx TA system in conjunction with LabScribe software (version 4.0). Prior to the assessment, participants were allowed to relax for approximately thirty minutes in a quiet environment with a stable temperature. They were then positioned comfortably in an armchair with their legs resting on a wooden cube, and three disposable ECG electrodes were placed on the underside of the right wrist, the underside of the left wrist, and the right ankle.

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All electronic and metallic items were removed from the vicinity of the participants, and recordings were made for a duration of 25 minutes before extracting the R-R interval from the ECG data. When extracting the R-R interval, the researchers focused on values within the range of 500–1000 Hz from the ECG (Electrophysiology 1996). Finally, the R-R interval data was entered into the Kubios HRV standard 3.5.0 software, which generated an analysis report covering both time and frequency domains of HRV.

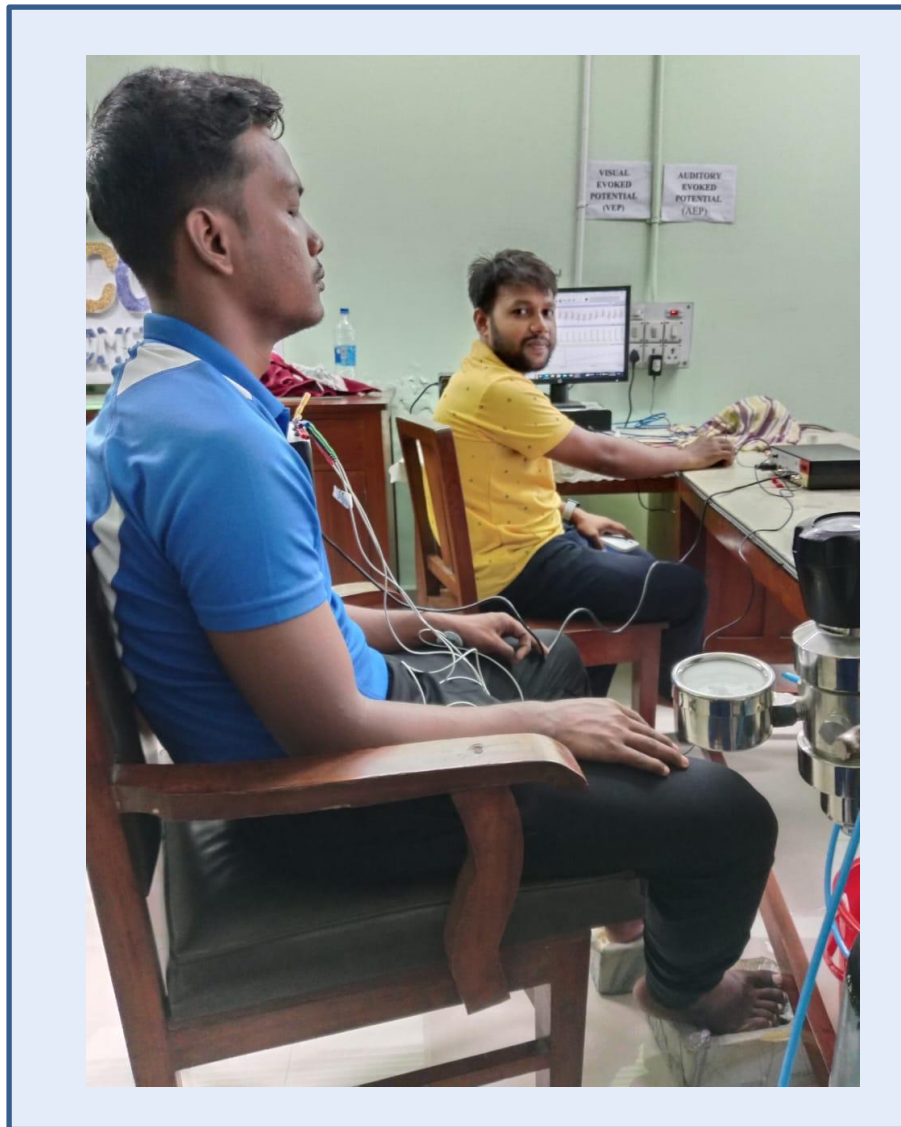


Figure 19: Measurement of ECG of participant

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Figure 20: Graphical representation of ECG recording

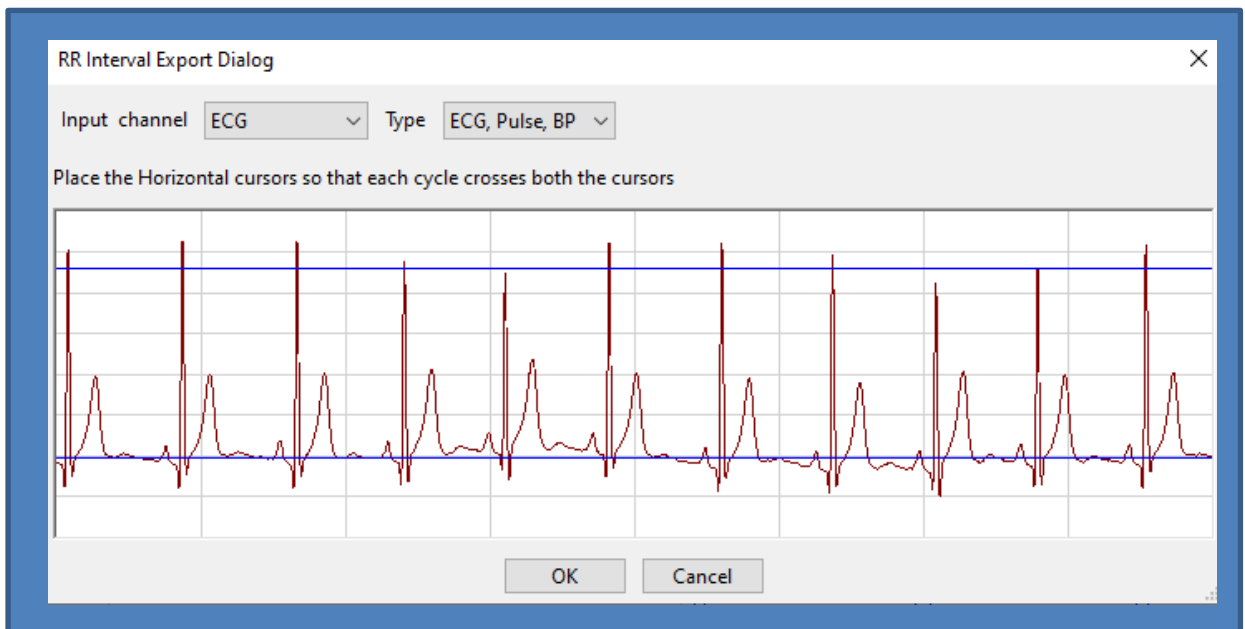


Figure 21: Graphical representation reflecting extraction of RR interval from ECG

3.10 Blood Sampling and assay for GABA and BDNF

Blood collection of all sampled subjects were drawn from the forearm vein after 12 hour fasting with 5 ml disposable syringe by trained professionals. Blood samples were centrifuged upto 20 minutes with 3000 RPM for the collection of supernatant serum without sediment and the serum samples were stored in aliquots at -20°C until analysis. BDNF and GABA quantification was performed by BeneSphera™ E21 ELISA Micro plate reader machine (Mfg.Lic.No:MFG/IVD/2023/000032) designed by Avantor Performance Materials India Private Limited (Pharma city, Selaqui, Dehradun, Uttarakhand, India) with the help of ImmunoTag's BDNF ELISA ITEH01302 & GABAITEH01526 kit containing 'Standard Solution 0.5ml', 'Biotinylated Antibody 1ml', 'Streptavidin-HRP 6ml', 'Standard Diluent 3ml', 'Substrate Solution A 6ml', 'Substrate Solution B 6ml', 'Wash Buffer 25X 20ml & Stop Solution 6ml'. All reagents and serum samples were kept to room temperature before use. After that 50 μl standard was added to standard wells and 40 μl sample to sample wells accordingly. In these sample wells 10 μl BDNF antibody was added while 50 μl 'streptavidin-HRP' added to both sample wells and standard wells and mix them properly. The micro plate was then covered with a sealer followed by one hour incubation at 37°C . Removing the sealer after one hour, the micro plate was washed 5 times with wash buffer. Then 50 μl 'substrate Solution A' and 'Substrate Solution B' was added to each wells and covered with a new sealer for 10 minutes at 37°C in the dark mode. Removing the sealer again after 10 minutes, 50 μl 'stop solution' was added into each wells and finally put the micro plate into the ELISA machine for optimal density (OD) value of each wells.

3.11 Assessment of cortisol

For cortisol level assessment, blood samples were collected at 6:30 AM after awakening, centrifuged at 3000 RPM for 20 minutes to obtain clear serum, which was aliquoted and stored at -20°C until analysis. Prior to assay, all reagents, serum reference calibrators, and controls were brought to room temperature ($20-27^{\circ}\text{C}$), and the procedure was performed by trained personnel. Quantification of Cortisol levels was carried out using the BeneSphera™ E21 ELISA microplate reader (Manufacturing License No. MFG/IVD/2023/000032), developed by Avantor Performance Materials India Pvt. Ltd., Pharma City, Selaqui, Dehradun, Uttarakhand, India. The analysis was performed using Accubind kit (License no NCD-83/16). In the assay, 25 μL of serum reference, control, or sample was pipetted into assigned wells, followed by 50 μL of Cortisol Enzyme Reagent. After gentle swirling (20–30 sec), 50 μL of Cortisol Biotin Reagent was added and mixed similarly. Plates were

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covered and incubated at room temperature for 60 min. After incubation, wells were emptied by decantation or aspiration and washed three times with 350 μ L wash buffer. Next, 100 μ L of substrate solution was added to each well (without shaking), and the plate was incubated for 15 min. Then, 50 μ L of stop solution was added and mixed gently for 15–20 sec. Absorbance was measured at 450 nm (reference 620–630 nm) using a microplate reader within 30 min of adding the stop solution.



Figure 22: Blood sample collection of the participants for BDNF, GABA and Cortisol

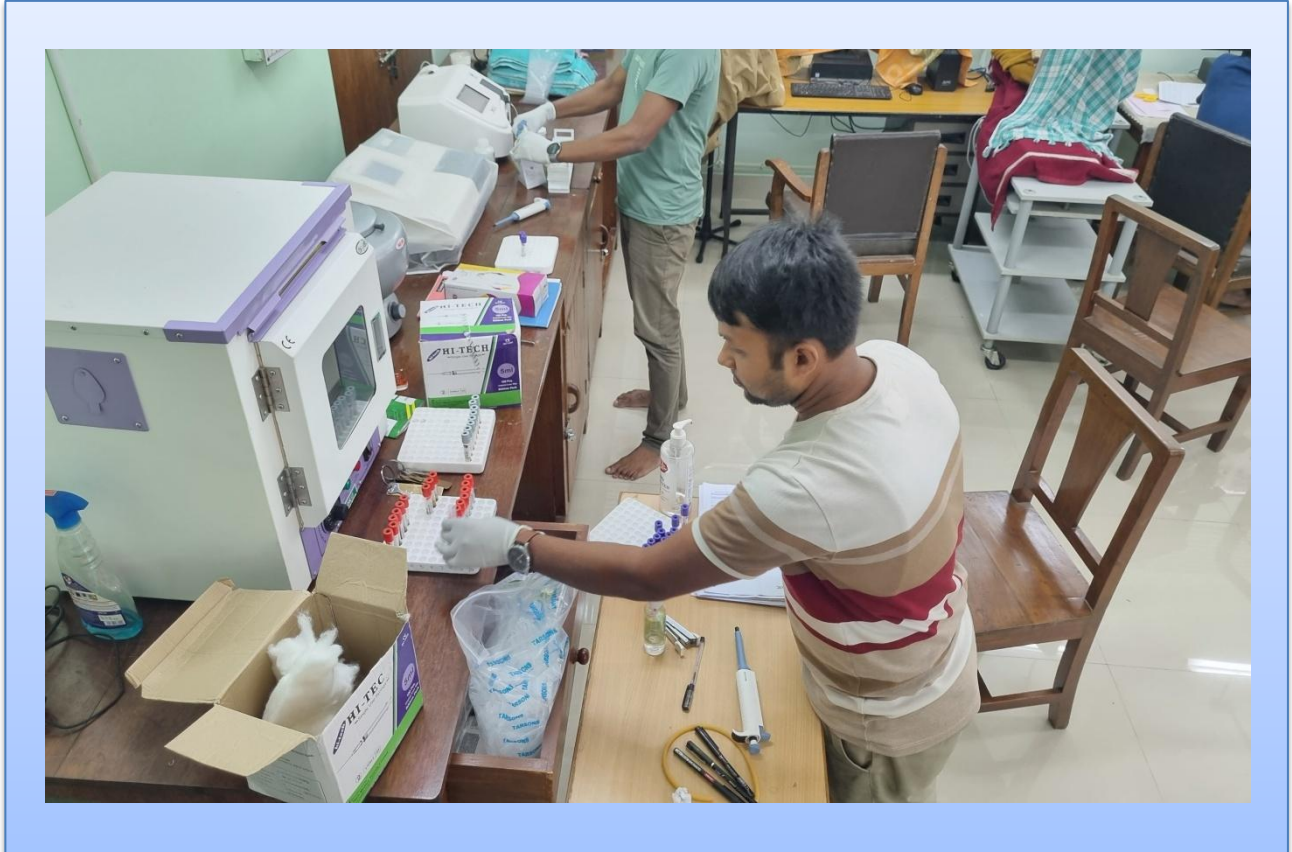


Figure 23: Preparation of samples for neurochemical markers assessment

3.12 Study Design

In the field of research methodology, study design refers to the strategy or approach used to collect and assess data in order to answer a specific research question. It includes a strategy that defines the processes and strategies for conducting a study, such as data collection and analysis, to ensure exact and dependable results. The researcher investigated the relationship between these variables. The set of variables were given in Tables no:9, and the researcher collected data from a population at a specific moment in time to look for associations that fit with the research question, whether there is any relationship among the selected variables.

This study followed published guidelines. The subjects of the present study were regularly engaged in aerobic exercise and the research design were cross-sectional. The sample size was determined scientifically, and the sampling method was convenient in

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nature. The trial profile clearly shows that the entire investigation was properly planned; this consideration is critical and raises the standard of the research study. Figure 24 shows the trial profile for the research study.

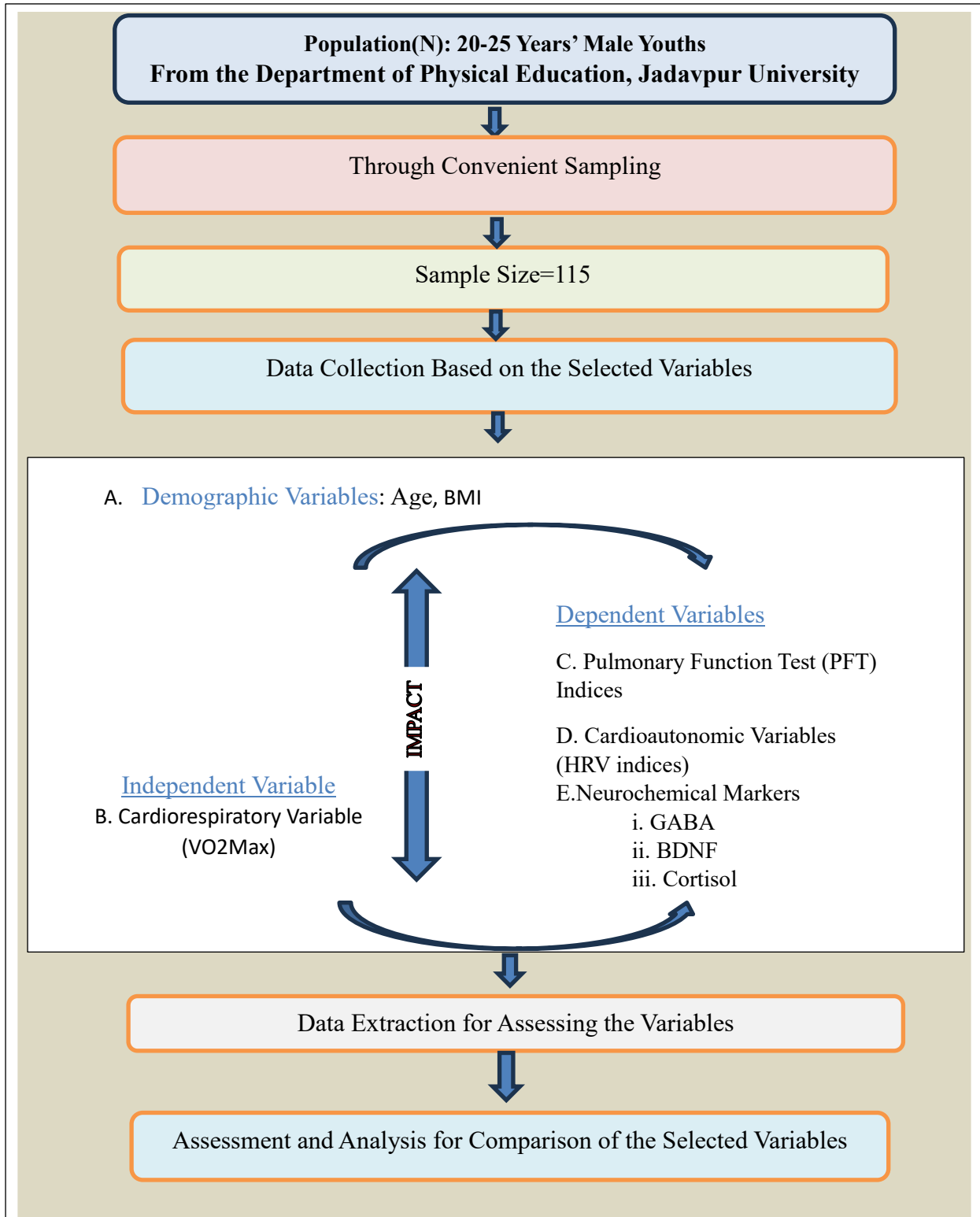


Figure 24: Cross- Sectional Study Design

3.13 Statistical Analysis

In this study, the sample size was determined using G*Power software, followed by an evaluation of normality for the participant population. Assessing normality ensures that the data is representative and provides more accurate comparative results (Mishra et al., 2019). The Kolmogorov-Smirnov normality test was employed to identify the inherent distribution of the sample population; this test is applicable for sample sizes exceeding 50 (Altman & Bland, 1995). If the test indicates insignificant results regarding the variables, the data can be considered normally distributed, allowing progression to parametric tests for comparison. Descriptive statistics, including mean and standard deviation, provided a summary of the basic characteristics of the subjects. For inferential statistics, a bivariate normal model was utilized to assess the relationship between the dependent variables and the single independent variable. The significance level was established at 0.05 ($P < 0.05$). The analysis was conducted using SPSS for Windows version 19.5.

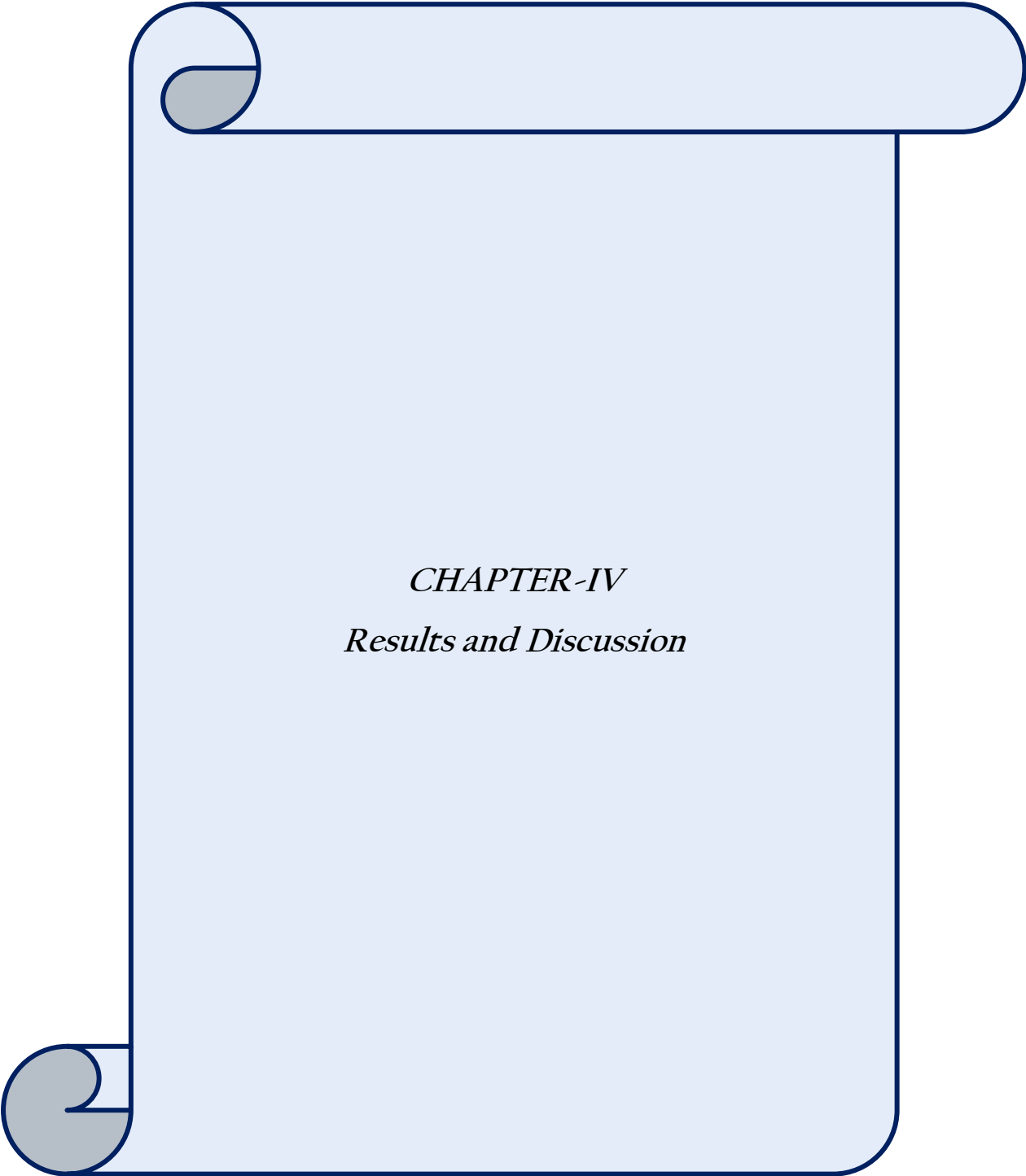
Sl. No	Type of Test	Description
1	G*Power Analysis	Determination of Sample Size
2	Kolmogorov-Smirnov test (n=115) Shapiro-Wilk test (n=35)	Determination of Normality Distribution
3	Mean±SD	Descriptive Statistics
4	Correlation: Bivariate normal model	Inferential Statistics

Table 15: Details of the Statistical Procedures

3.14 Limitations of the Study

Every research endeavour has its boundaries, and these limits emerge from constraints in different aspects of the research field. The recent research study similarly faced limitations; the points outlined below highlight the limitations of the study.

- The current research was not conducted as a randomized controlled trial.
- The participants who engaged in regular aerobic exercises were not supervised by us.
- The psychological states of the participants were not factored into the study
- We did not have full control over the consistency of the training or exercises.
- The researcher was unable to ensure that the exercisers were performing uniform aerobic exercises.
- Female subjects were not included in the study.



CHAPTER-IV
Results and Discussion

4. Results and Discussion

This segment of the research is the most crucial and influential, as it showcases the findings obtained from the implemented methodology. The results have been communicated clearly, arranged in a coherent sequence without prejudice, and accompanied by an in-depth discussion of each component.

4.1 Study Profile

The current research was a non-randomised observational study adopting a cross-sectional design, which gathered data from a specific population at a single time to explore the relationships between various variables. The objective of the study was to assess the impact of regular aerobic exercise on pulmonary function test parameters, Heart Rate Variability metrics and neurochemical markers.

According to the pre-defined inclusion and exclusion criteria based on the review study, a total of 120 samples were selected for the research. However, complete data for the group of “Pulmonary Function Test Variables and Heart Rate Variability” were provided by 115 samples, while sample size were calculating by G-Power software for 112 samples. For the neurochemical variables, only 35 samples were accessible due to the invasive nature of the technique and the expensive reagent required for the ELISA test. While comparisons were made between VO₂Max and PFT variables as well as HRV variables, the data utilized were from all 115 available samples; in contrast, for the comparison between VO₂Max and neurochemical variables, the data came from the 35 available samples.

4.2 Results of Normality Test

Evaluating normality is crucial in research as it validates the assumptions needed for different statistical methods, thereby aiding in the selection of an appropriate test and leading to more dependable conclusions. These assessments are key when deciding between parametric and nonparametric approaches, as parametric tests require the data to follow a normal distribution, while nonparametric tests do not have this requirement.

There are various approaches for assessing the normality of continuous datasets. The Kolmogorov-Smirnov test and the Shapiro-Wilk test are among the most well-known of these methods. The Kolmogorov-Smirnov test is especially preferred for larger sample sizes (more than 50), whereas the Shapiro-Wilk test is for smaller sample sizes (<50). The results indicated that there was no significant deviation from normality in the distribution of almost all variables ($p > 0.05$), suggesting that the data follow a normal distribution. In this research, the investigator utilised the Kolmogorov-Smirnov test to analyse the data (table: 16&17) and Shapiro-Wilk test (table:18) for all variables across the entire group.

Kolmogorov-Smirnov test			
Variables	Statistic	df	Sig.
VO ₂ Max	.071	115	.200*
FEV1	.076	115	.099
FEV3	.077	115	.087
VC	.078	115	.081
Since $p > 0.05$, the data are normally distributed.			

Table 16: Normality Test for VO₂ Max and Spirometry Indices

Results and Discussion

Kolmogorov-Smirnov test			
Variables	Statistic	df	Sig.
VO₂ Max	.071	115	.200*
RMSSD	.077	115	.090
MEAN HR	.076	115	.096
SDNN	.079	115	.073
MEAN RR	.076	115	.110
pNN50	.078	115	.084
LF(nu)	.081	115	.060
HF (nu)	.065	115	.200*
LF power	.055	115	.200*
HF power	.054	115	.200*
LF/HF Ratio	.072	115	.196
Since p > 0.05, the data are normally distributed.			

Table 17: Normality Test for VO₂ Max and HRV Indices

Shapiro-Wilk test			
Variables	Statistic	df	Sig.
VO₂ Max	.972	35	.488
GABA(μg/dl)	.981	35	.788
BDNF(ng/ml)	.946	35	.088
Cortisol	.964	35	.303
Since p > 0.05, the data are normally distributed.			

Table 18: Normality Test for VO₂ Max and Neurochemical Markers

4.3 Results and Discussion of Demographic Variables

The characteristics of the participants are essential for understanding the study group and assessing trends and variations among the respondents. To gain a clearer understanding of the sample's composition, these factors were examined to yield valuable insights about the participants' diversity and representativeness.

Demographic factors such as age and body mass index (BMI) were evaluated as personal data where the BMI was calculated from the data of height and weight for the identical cohort in this study. Descriptive statistics for all these variables were calculated using the Mean \pm SD method. Table 19 and 20 outlines the details of the demographic variables included in this research.

As there is no comparison group in this study, the researcher did not attempt any correlational approaches solely among the personal variables.

Demographic Variables	Measuring Unit	N	Mean	Std. Deviation
Age	Years	115	23.530	1.435
BMI	Kg/m ²	115	21.115	1.609

Table 19: Details of Demographic Variables, while the sample size=115

Demographic Variables	Measuring Unit	N	Mean	Std. Deviation
Age	Years	115	23.171	1.248
BMI	Kg/m ²	115	21.525	2.256

Table 20: Details of Demographic Variables, while the sample size=35

4.4 Results and Discussion on the VO₂ Max and Pulmonary Function Test Variables

The VO₂ Max variable related to cardiorespiratory fitness was evaluated alongside the Pulmonary Function Test variables, which included FEV-1, FEV-3, and VC. Descriptive statistics revealed the mean and standard deviation of these PFT indices, as presented in Table 21.

Variables		Mean±SD
Aerobic fitness	VO ₂ Max(ml/kg/min)	44.067 ±4.575
	PFT indices	
	FEV-1 (L)	3.893 ±0.809
	FEV-3 (L)	2.231 ±0.489
	VC(L)	5.920 ±0.668

Table 21: Descriptive statistics of Aerobic Fitness and PFT Indices' group

The correlational analysis presented in Table 22 revealed that VO₂max demonstrated a significant positive correlation with all selected pulmonary function test (PFT) indices, specifically Forced Expiratory Volume in one second (FEV-1) ($r = .219^*$, $p = .019$), Forced Expiratory Volume in three seconds (FEV-3) ($r = .192^*$, $p = .040$), and Vital Capacity (VC) ($r = .399^{**}$, $p = .000$).

Aerobic Fitness Variables	PFT Indices/Variables	N	df	(r) value	p value
VO ₂ Max (ml/kg/min)	FEV-1 (L)	115	113	.219*	.019
	FEV-3 (L)	115	113	.192*	.040
	VC(L)	115	113	.399**	.000
Correlation is significant at the 0.05* and 0.01** level(2-tailed).					

Table 22: Bivariate correlation between aerobic fitness and PFT Indices

Results and Discussion

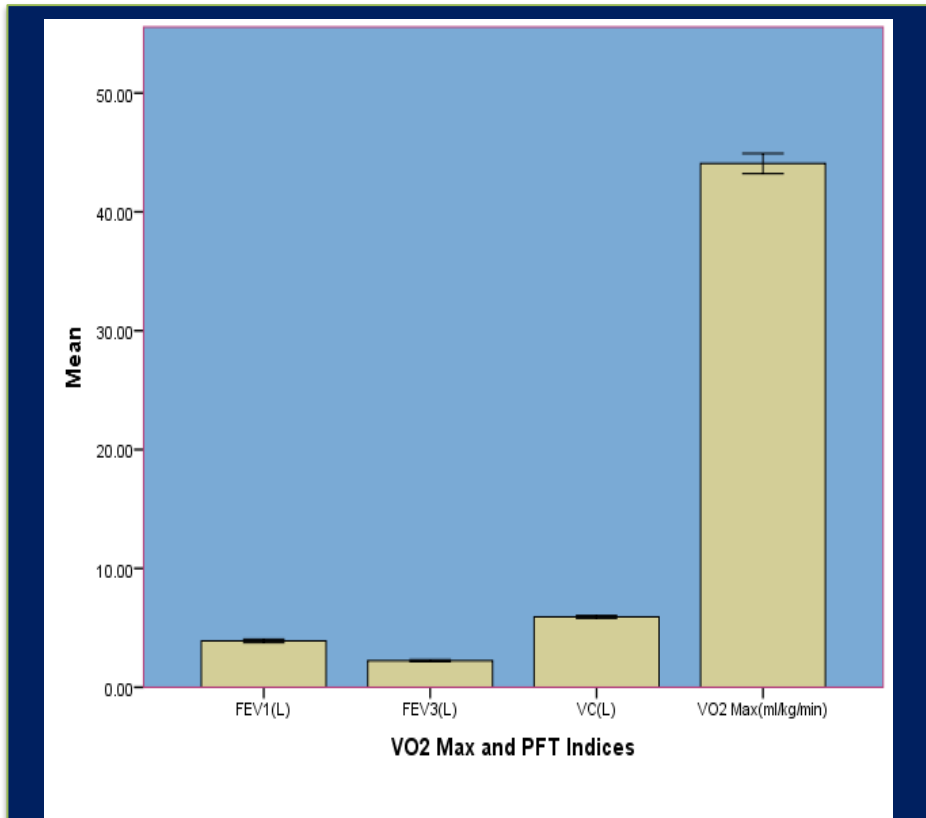


Figure 25: Graphical representation of mean of VO2 Max and PFT indices

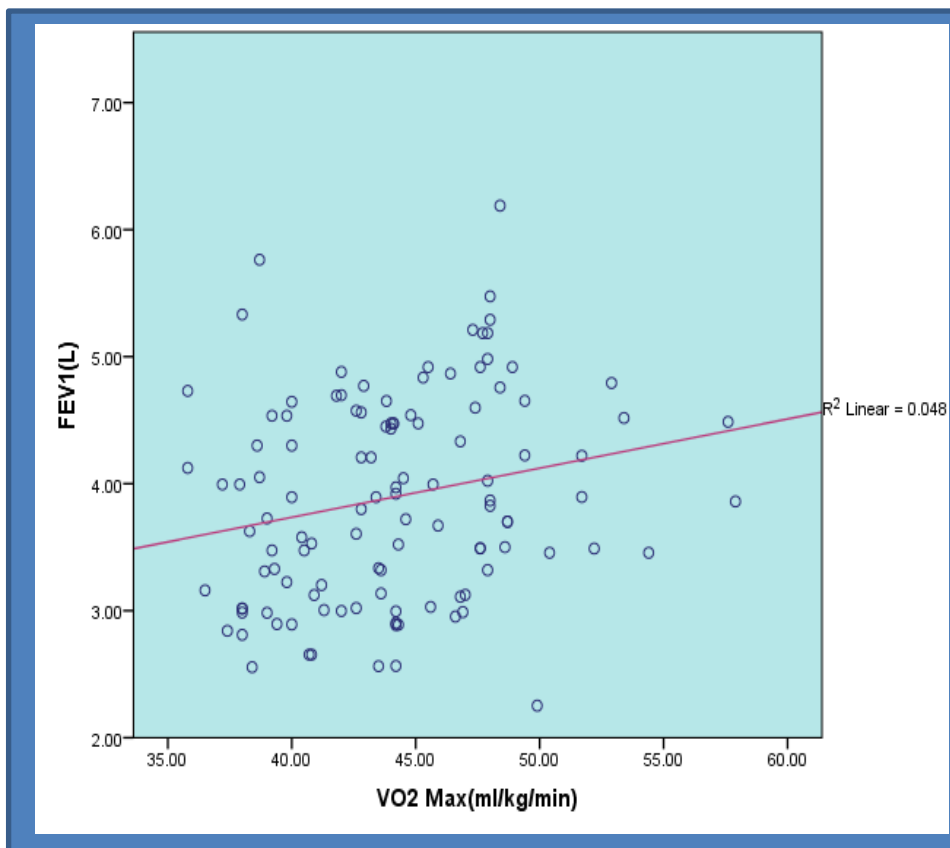


Figure 26: Scatter plot demonstrating the linear relationship ($r = .219^*$; $R^2 = 0.048$) between VO2 Max and FEV-1.

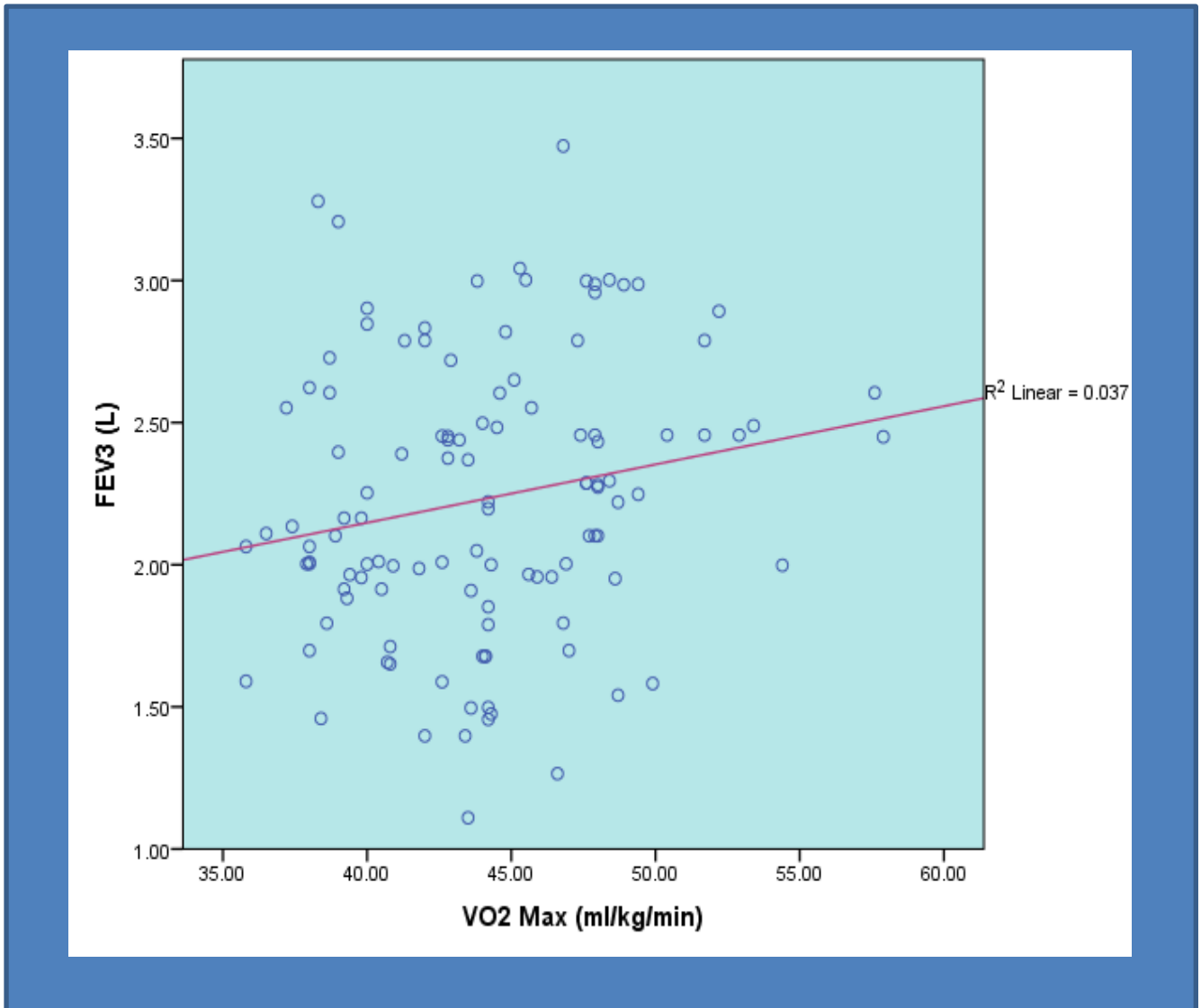


Figure 27: Scatter plot demonstrating the linear relationship ($r = .192^*$; $R^2 = 0.037$) between VO_2 Max and FEV-3.

Numerous studies have investigated the connection between cardiorespiratory fitness and indices of pulmonary function tests (PFTs). However, there is a scarcity of research on the effects of aerobic exercise or cardiorespiratory fitness within the general population (Twisk et al., 1998). Most of these studies focused on populations that did not include healthy young adults and utilized different sets of PFT indices, in contrast to the current study. Findings from prior research by Kriemler et al., 2013 and İşleyen and Dağlıoğlu., 2020 indicated that regular aerobic exercise positively influences respiratory functions and enhances aerobic

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capacity values. A study was conducted to investigate the impact of aerobic exercise on pulmonary function tests involving 65 healthy adult participants aged 20 to 35 years. According to Angane & Navare.,(2017), engaging in aerobic exercise enhances lung function. The findings of our current study regarding FEV-3 also contributed meaningful insights, despite existing literature already supporting our results related to FEV-1 and VC. FEV-3 refers to the volume of air a person can forcibly exhale during the first three seconds of a single breath. The substantial link observed between VO₂ max and FEV-3 in this study indicates that a higher FEV-3 score is associated with healthy small airways and overall strong lung function.

A high VO₂max paired with outstanding results in pulmonary function tests (such as FEV₁, FEV-3, and VC) are essential indicators of better cardiorespiratory health, a reduced likelihood of chronic diseases, and greater longevity. These fundamental mechanisms arise from a range of significant physiological changes, mainly prompted by consistent physical activity and intensive training. The most plausible explanation for this observation is that regular engagement in physical activity or sports boosts the oxygen needs of the active muscles, which subsequently activates the respiratory centers in the brain stem. This activation sends strong signals to the muscles responsible for inspiration, leading to more forceful breathing. Consistent and vigorous breathing enhances surfactant secretion, which decreases physiological dead space and reduces alveolar surface tension. Frequent participation in physical activities enhances lung function (Akhade & Muniyappanavar., 2013). Genetic, environmental, and nutritional factors somewhat regulate lung size. Variances in certain studies may be attributed to genetic and ethnic differences affecting lung size (Sc et al., 1984b). It is recognized that age, height, weight, gender, and ethnicity all influence respiratory function metrics (Quanjer et al., 2012). Recent studies suggest that the type, intensity, duration, and frequency of exercise significantly affect respiratory volumes

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(Meylan et al., 2013; Losnegard & Hallén, 2014). Another study reported a significant impact of sport type on the adaptations of the respiratory system (Durmic et al., 2015). Athletes focused on explosive power development tend to have lower respiratory function values compared to those participating in endurance sports (such as rowing, canoeing, swimming, long-distance running and marathons, cycling, and triathlons) (Lazovic et al., 2015). Several studies support our findings to some degree regarding the positive effect of exercise on pulmonary functions (Chandran et al., 2004; Nourry et al., 2005). This indicates that people who have higher cardiorespiratory fitness are more likely to demonstrate better lung volumes and expiratory performance. The ways in which physical activity affects lung function are complex. Engaging in physical activity boosts the strength of the respiratory muscles and increases lung ventilation capacity (Abdelbasset et al., 2018).

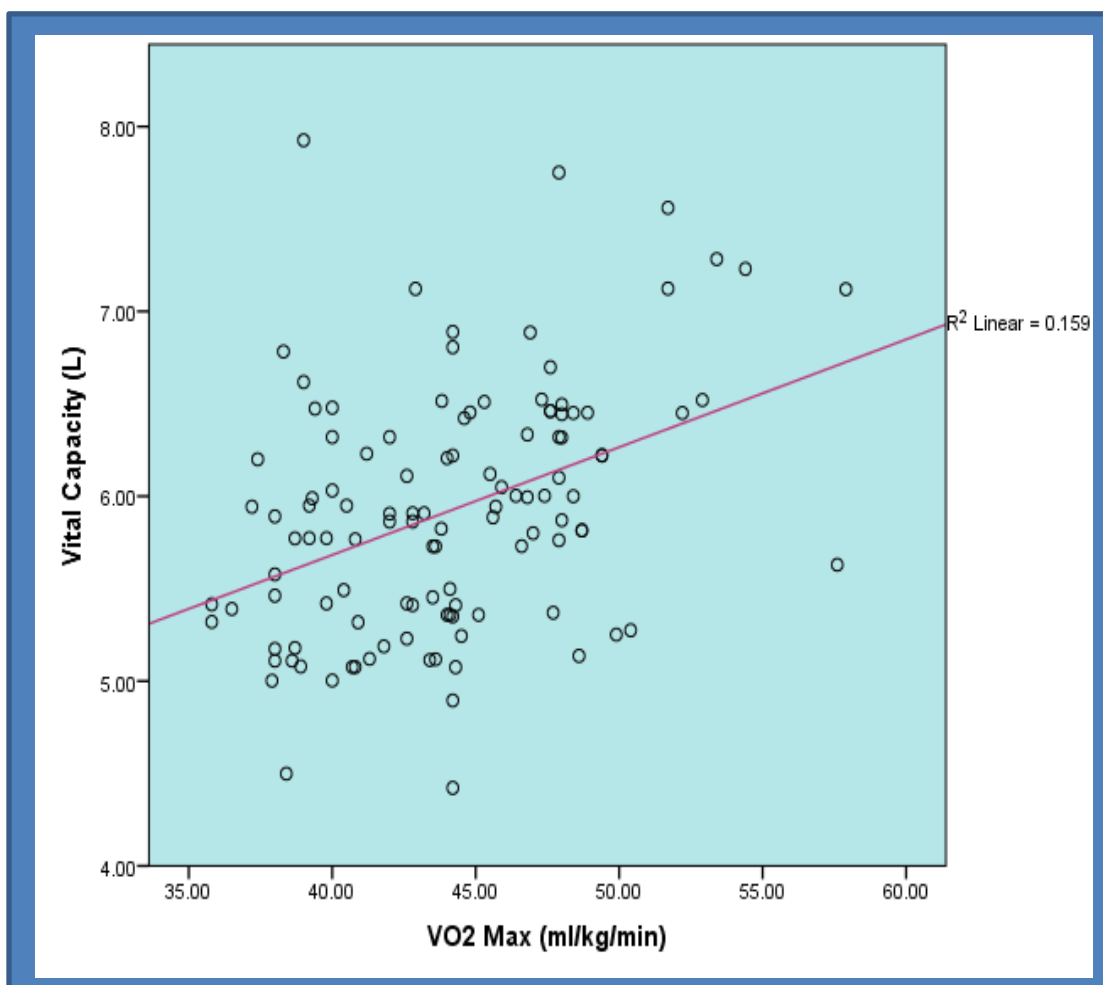


Figure 28: Scatter plot demonstrating the linear relationship ($r = .399^{}$; $R^2 = 0.159$) between $VO_2\text{Max}$ and VC.**

4.5 Results and Discussion on the VO₂ Max and Heart Rate Variability(HRV) Test Variables

The descriptive and inferential statistics related to VO₂max and specific HRV indices are outlined in Tables 23 and 24, respectively. The time-domain metrics comprised Mean HR, SDNN, Mean RR, and pNN50, whereas the frequency domain metrics included LH(nu), HF(nu), LF power, HF power, and the LF/HF Ratio.

Statistical analysis indicated the relationships between VO₂max and the chosen HRV indices. Among the time-domain metrics, VO₂max showed notable positive correlations with RMSSD ($r=.196^*$, $p=.036$) and Mean RR ($r=.219^*$, $p=.019$), while Mean HR ($r=-.003$, $p=.975$) did not present a similar association with VO₂max, as the correlation coefficient ($-.003$) is nearly zero (0). Thus, it represents a very weak negative relationship. Regarding the other two variables, pNN50 ($r=.180$, $p=.055$) and SDNN ($r=.159$, $p=.090$), neither yielded significant results, but both exhibited a positive relationship with VO₂max. Here, $p = .055$ related to VO₂max and pNN50 is slightly above the 0.05 threshold, indicating the correlation is not statistically significant at the 0.05 level, although it is on the cusp.

On the other hand, the frequency domain measures chosen for this analysis revealed both positive and negative associations with VO₂max. The aerobic fitness indicator, VO₂max, showed substantial positive correlations with HF (nu) ($r=.335^{**}$, $p=.000$) and HF power ($r=.343^{**}$, $p=.000$), whereas LF (nu) demonstrated a significant strong negative correlation ($r=-.265^{**}$, $p=.004$) and LF power also showed a strong negative correlation ($r=-.338^{**}$, $p=.000$). Additionally, the LF/HF Ratio ($r=.203^*$, $p=.030$) exhibited a noteworthy positive relationship. Notably, LF (nu) and HF (nu) displayed opposing directional relationships with VO₂max independently, while LF power and HF power exhibited similar independent relationships with VO₂max.

Variables		Mean±SD	
Aerobic fitness	VO ₂ Max(ml/kg/min)	44.067 ±4.575	
HRV indices	Time Domain	MEAN RR	834.261 ±81.905
		MEAN HR	64.104 ±4.447
		SDNN	54.657 ±12.612
		pNN50	32.249 ±15.401
		RMSSD	51.264 ±11.417
	Frequency Domain	LF (Power)%	43.257 ±14.482
		HF (power)%	51.675 ±16.377
		LF(nu)	48.246 ±10.884
		HF (nu)	54.101 ±16.203
		LF/HF Ratio	0.532 ±0.124

Table 23: Descriptive statistics of Aerobic Fitness and HRV Indices' group

Indices of heart rate variability (HRV) in both time domain and frequency domain are connected to cardiac electrophysiology and autonomic regulation, signalling healthier responses. Existing literature suggests that consistent physical activity correlates with enhanced vagal modulation and decreased sympathetic activity (Swain & Franklin, 2006).

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This vagal modulation contributes to improved exercise capacity through training, typically characterized by a lower resting heart rate.

HRV in the time domain is illustrated as the fluctuations in normal R wave to R wave (N-N) intervals over a period of time (Electrophysiology, T. F. O. T. E. S. O. C. T. N. A. S. O. P. 1996). The most commonly utilized metrics among the time domain variables include SDNN, which indicates the overall HRV, as well as RMSSD and pNN50, which are calculated over the entire duration of the recording and reflect pure vagal effects on HRV (Kumar et al., 2023). MeanRR signifies the average duration of the intervals between successive heartbeats, while MeanHR is generally obtained by taking the total recording time and dividing it by the number of heartbeats; this measure is frequently assessed alongside other time-domain indicators to give a more comprehensive understanding of heart rate variability (Electrophysiology, T. F. O. T. E. S. O. C. T. N. A. S. O. P., 1996).

High frequency (HF) and low frequency (LF) are the two main sub-bands within the HRV frequency spectrum. HF power is indicative of parasympathetic activity, while LF power can suggest both sympathetic and parasympathetic activities. The LF/HF power ratio is frequently used to assess sympathovagal balance (Wilmore & Knuttgen, 2003). LFnu and HFnu are indicators of normalized heart rate variability. LFnu serves as a measure of sympathetic modulation in the autonomic nervous system, contrasting with HFnu, which reflects parasympathetic modulation of the autonomic nervous system.

The current research aimed to determine if there is any relationship between aerobic fitness and HRV indices, as previous studies have reported a favorable correlation between enhanced exercise and training regimens with improved aerobic fitness (Zaki et al., 2024). This study identified a significant positive correlation between VO₂Max and MeanRR, as well as RMSSD. The positive relationship between MeanRR and VO₂max indicates that training

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leads to increased cardiac efficiency and vagal tone, which results in a decreased resting heart rate and more adaptable autonomic regulation (Cabral et al., 2019). A favorable relationship exists between RMSSD and VO₂ max, as both indicate how well the cardiovascular system functions and adapts. The efficiency of the heart allows for a more adaptable response to varying demands, which enhances parasympathetic control and results in an increased RMSSD (Shaffer & Ginsberg, 2017; Picard et al., 2021). However, the other time domain measures, SDNN and pNN50, showed only a weak relationship with aerobic fitness. Moreover, the moderate positive correlation found between SDNN and VO₂max suggests that those with higher cardiorespiratory fitness display increased overall heart rate variability, which indicates a healthier autonomic nervous system and a reduced risk of heart issues (Masroor et al., 2018). Likewise, the marginal positive relationship between pNN50% and VO₂max, although not statistically significant, underscores the influence of acute changes in heart rate variability in response to stressors, further demonstrating the advantages of improved parasympathetic activity (11). This study revealed a weak yet negative correlation between Mean Heart Rate (HR) and VO₂Max. This may indicate that training can lead to favorable changes in cardiac autonomic regulation, mainly shown by an increase in the influence of the parasympathetic (vagal) nervous system on the heart. A more effective heart muscle has the capability to pump a greater volume of blood with each beat, thereby necessitating fewer beats per minute to sustain adequate circulation while at rest.

In the frequency domains of HRV, the current study found a significant positive correlation between VO₂Max and both HF (power)% and HF (nu), as well as the LF/HF ratio, whereas a significant negative correlation was observed with LF (power)% and LF (nu) in relation to VO₂ Max. A prior investigation by Masroor et al., 2018 reported findings that indicated an increase in HFnu, along with a notable decrease in LFnu and the LF/HF ratio. The current research differs from the Masroor et al., 2018 study regarding the LF/HF ratio. This discrepancy may stem from the differing effects of training on HRV. A comprehensive meta-analysis conducted by Yang et al., 2024 revealed that high-intensity interval training (HIIT)

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may have the most significant impact on the LF/HF ratio, while resistance training (RT) is most effective for enhancing HF (power)%, and combined training (CT) provides the greatest benefit for LF (power)%.

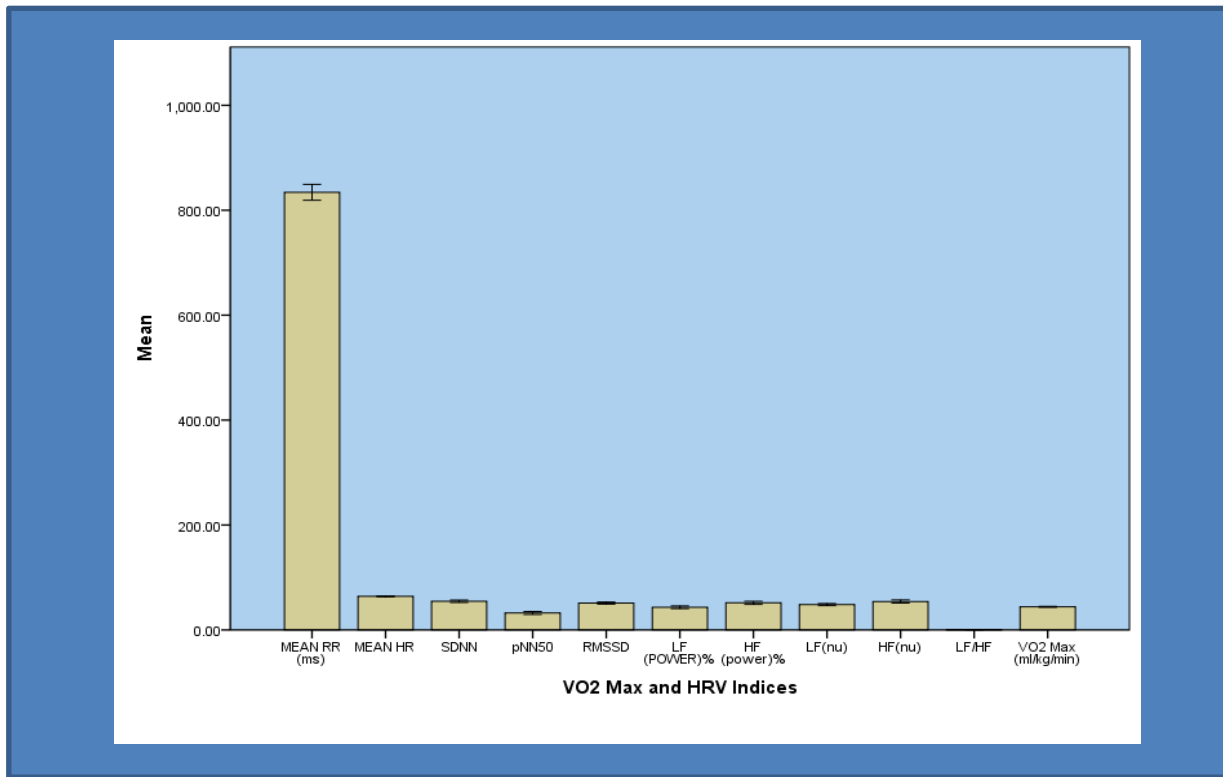


Figure 29: Graphical representation of the mean of VO₂ Max and HRV indices

Aerobic Fitness Variable	HRV Indices/Variables	N	df	(r) value	p value	
VO ₂ Max (ml/kg/min)	Time Domain	MEAN RR	115	113	.219*	.019
		MEAN HR	115	113	-.003	.975
		SDNN	115	113	.159	.090
		pNN50	115	113	.180	.055
		RMSSD	115	113	.196*	.036
	Frequency Domain	LF (Power)%	115	113	-.338**	.000
		HF (power)%	115	113	.343**	.000
		LF(nu)	115	113	-.265**	.004
		HF (nu)	115	113	.335**	.000
		LF/HF Ratio	115	113	.203*	.030

Correlation is significant at the 0.05* and 0.01 level(2-tailed).**

Table 24: Bivariate correlation between aerobic fitness and HRV Indices

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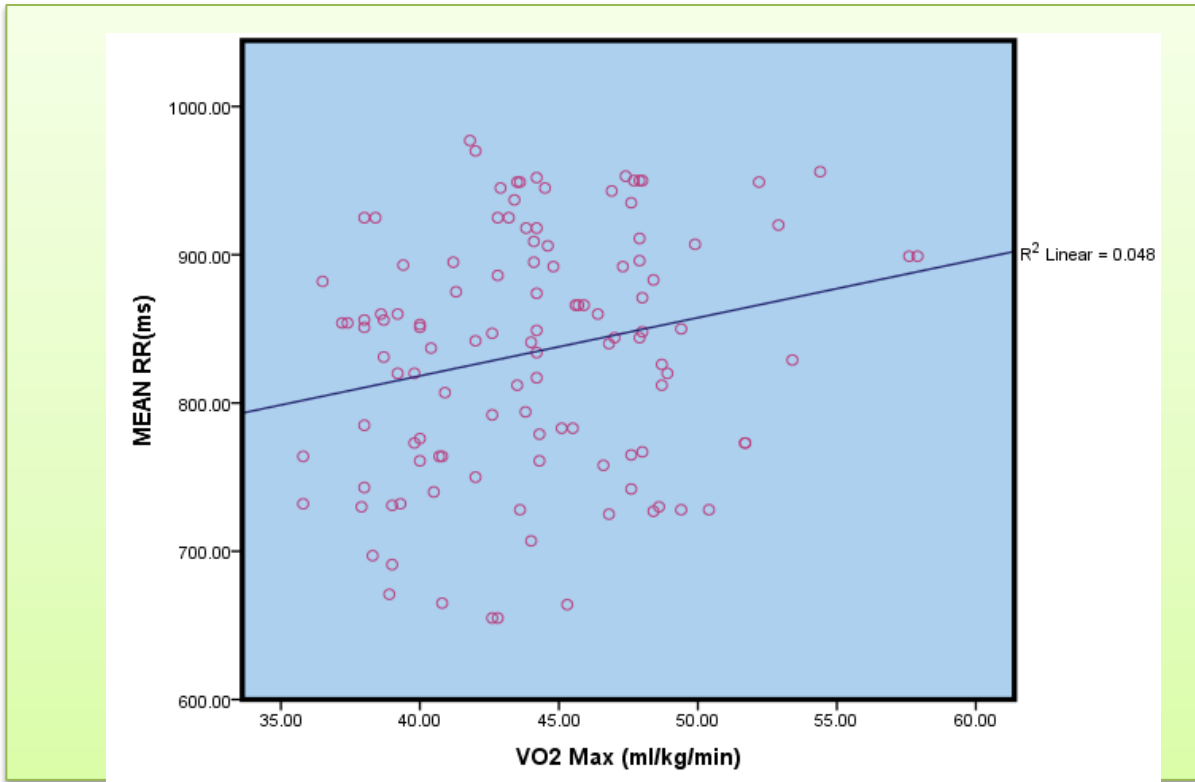


Figure 30: Scatter plot demonstrating the linear relationship ($r=0.219^*$; $R^2=0.048$) between VO₂ Max and Mean RR(ms).

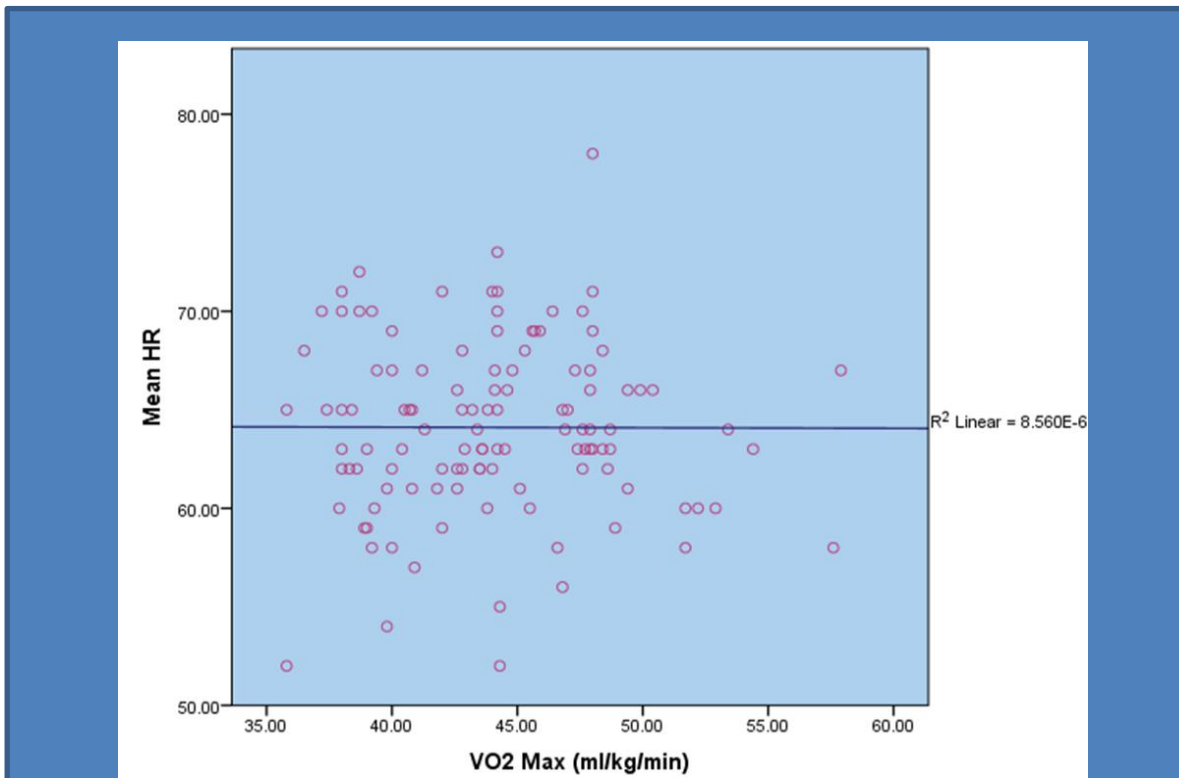


Figure 31: Scatter plot demonstrating the linear relationship ($r=-.003$; $R^2=8.560E-6$) between VO₂ Max and Mean HR

Results and Discussion

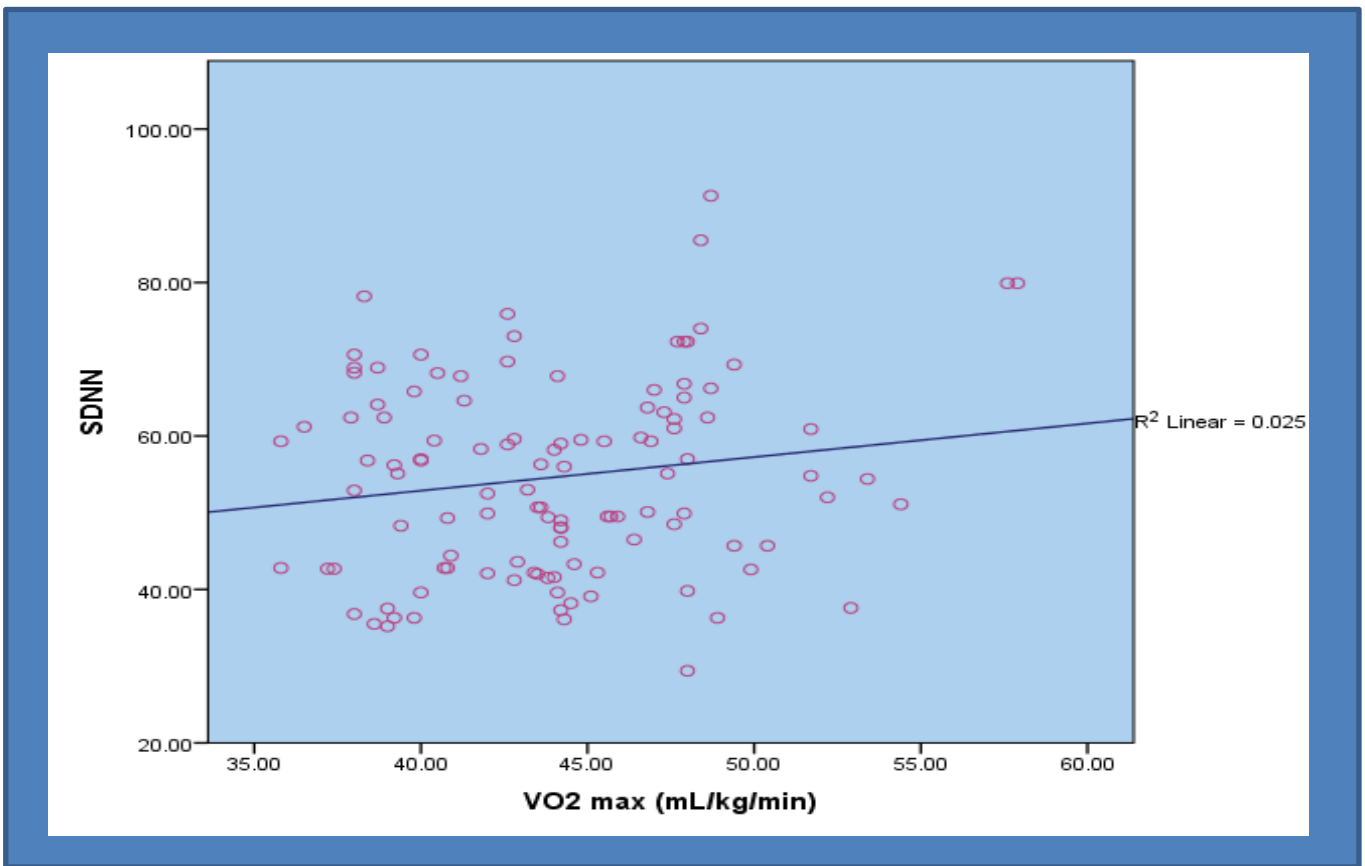


Figure 32: Scatter plot demonstrating the linear relationship ($r=.159$; $R^2=0.025$) between VO₂ Max and SDNN.

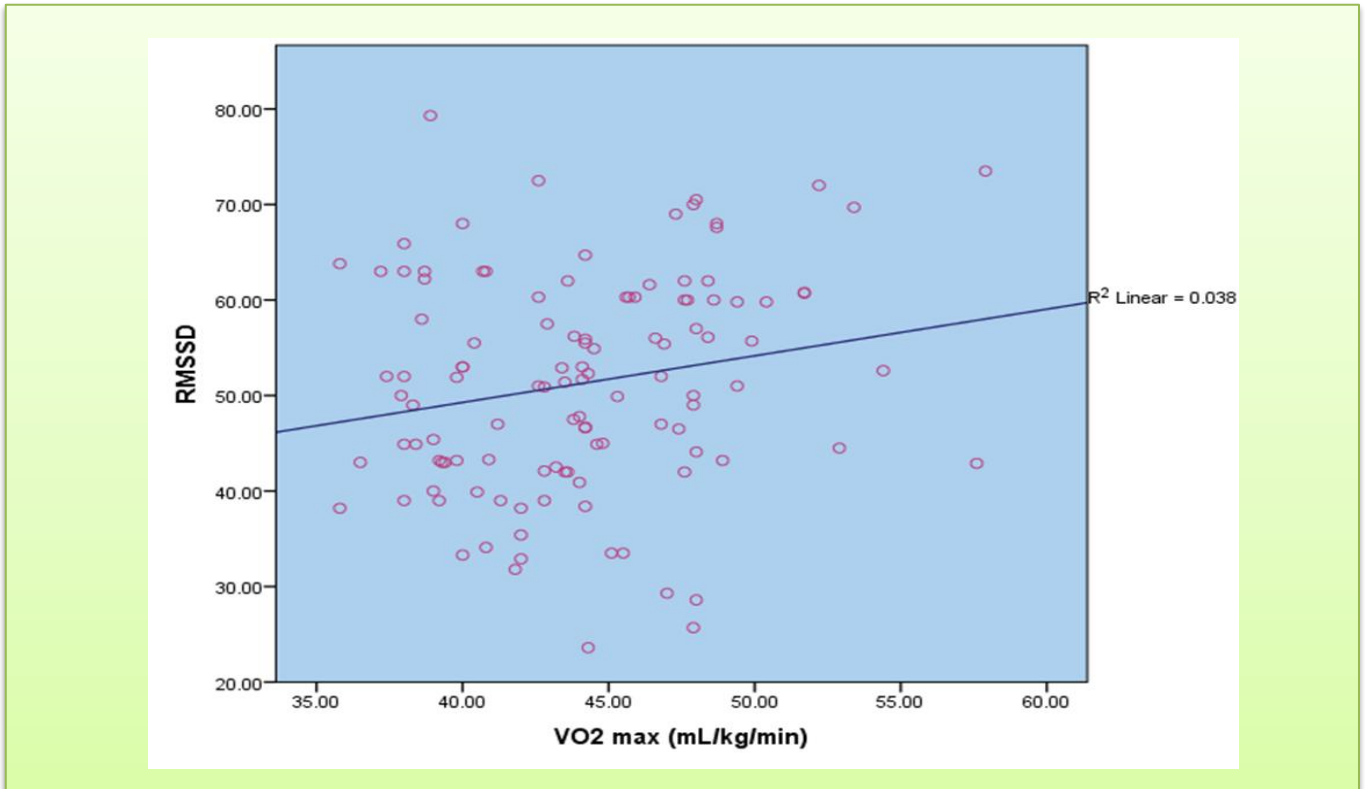


Figure 33: Scatter plot demonstrating the linear relationship ($r=.196^*$; $R^2=0.038$) between VO₂ Max and RMSSD

Results and Discussion

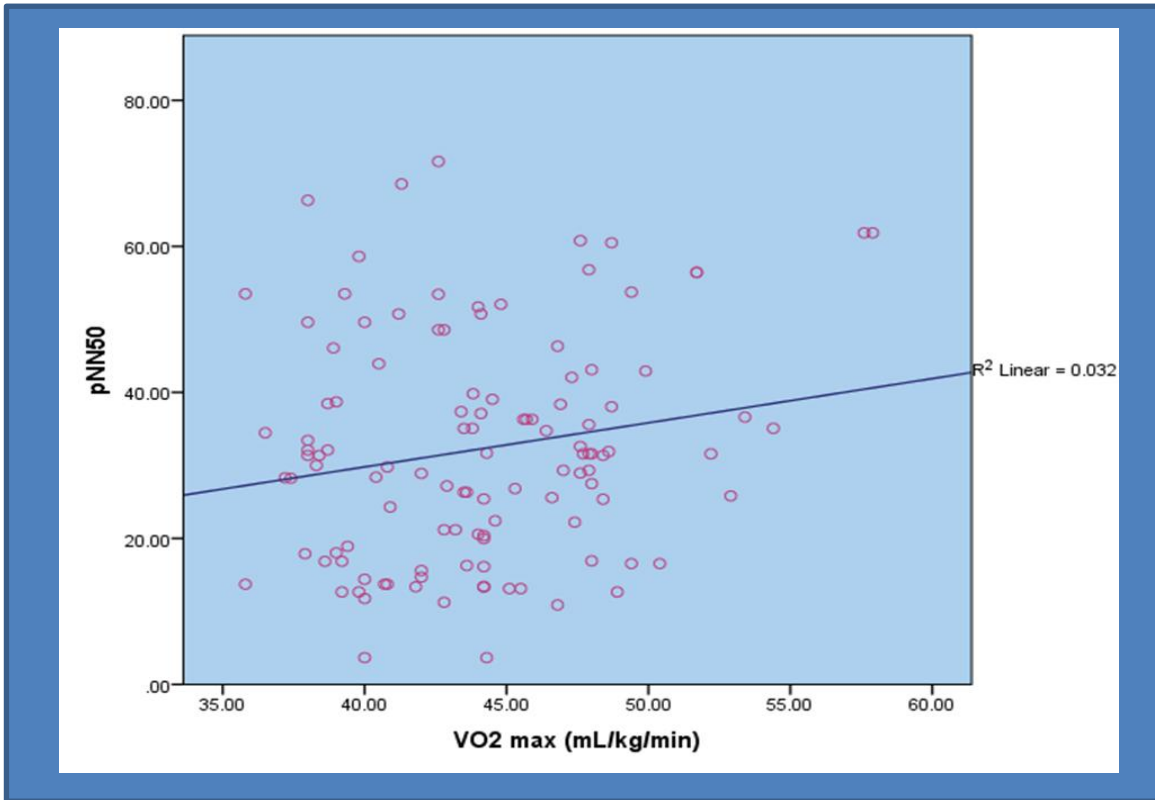


Figure 34: Scatter plot demonstrating the linear relationship ($r=.180$; $R^2=0.032$) between VO₂ Max and pNN50

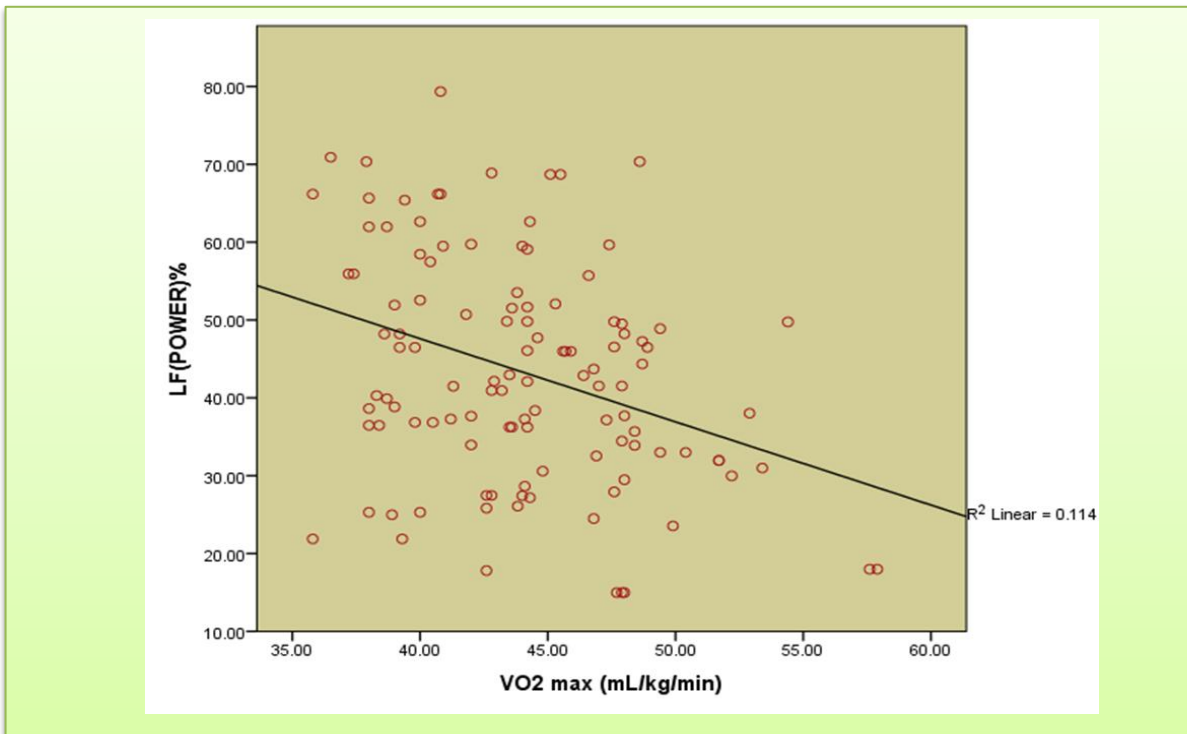


Figure 35: Scatter plot demonstrating the linear relationship ($r=-.338^{**}$; $R^2=0.114$) between VO₂ Max and LF (Power)%.

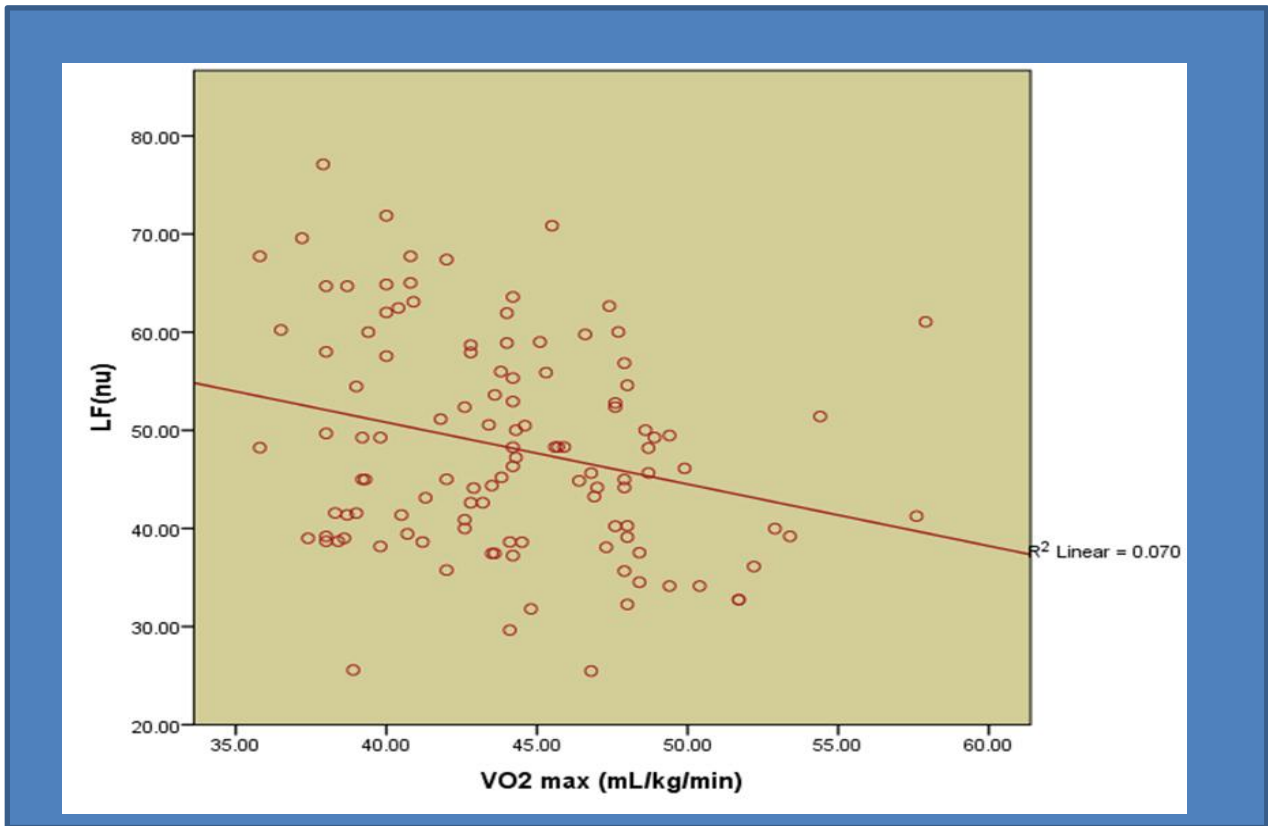


Figure 36: Scatter plot demonstrating the linear relationship ($r=-.265^{**}$; $R^2=0.070$) between VO₂ Max and LF (nu).

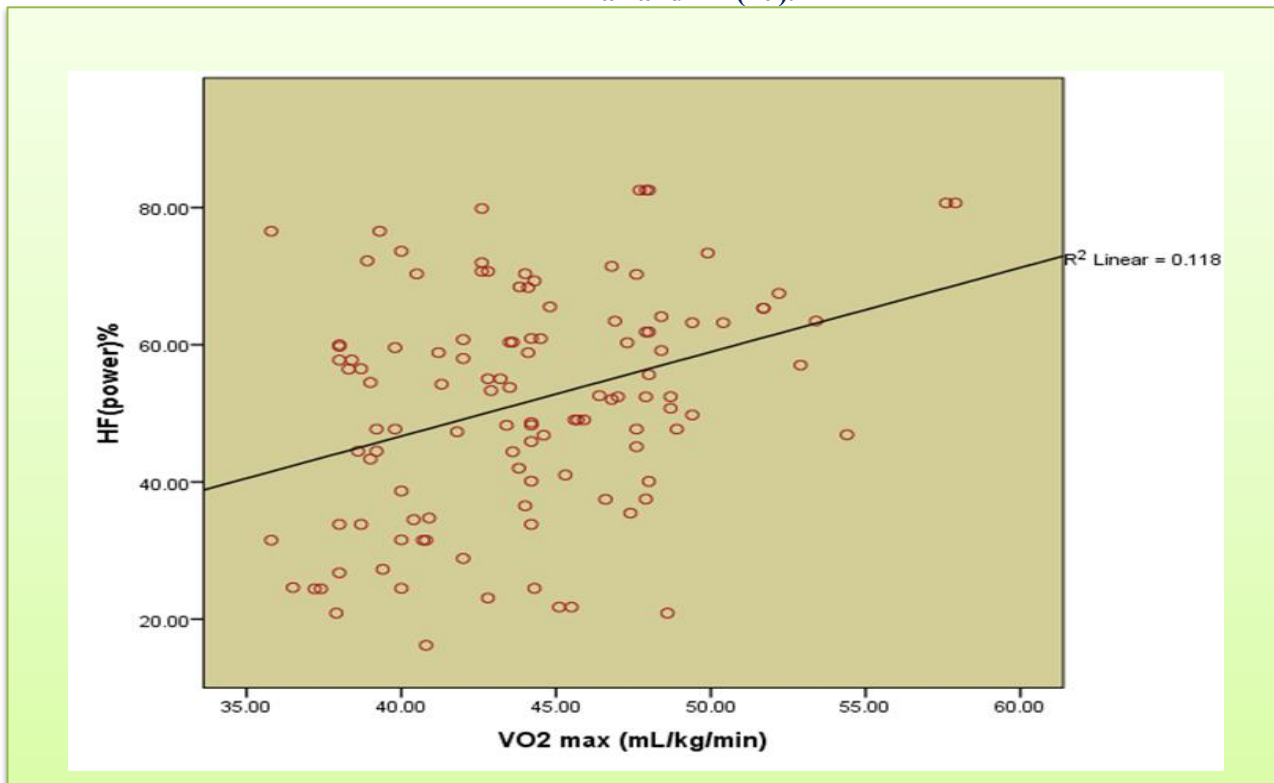


Figure 37: Scatter plot demonstrating the linear relationship ($r=.343^{**}$; $R^2=0.118$) between VO₂ Max and HF(power)%.

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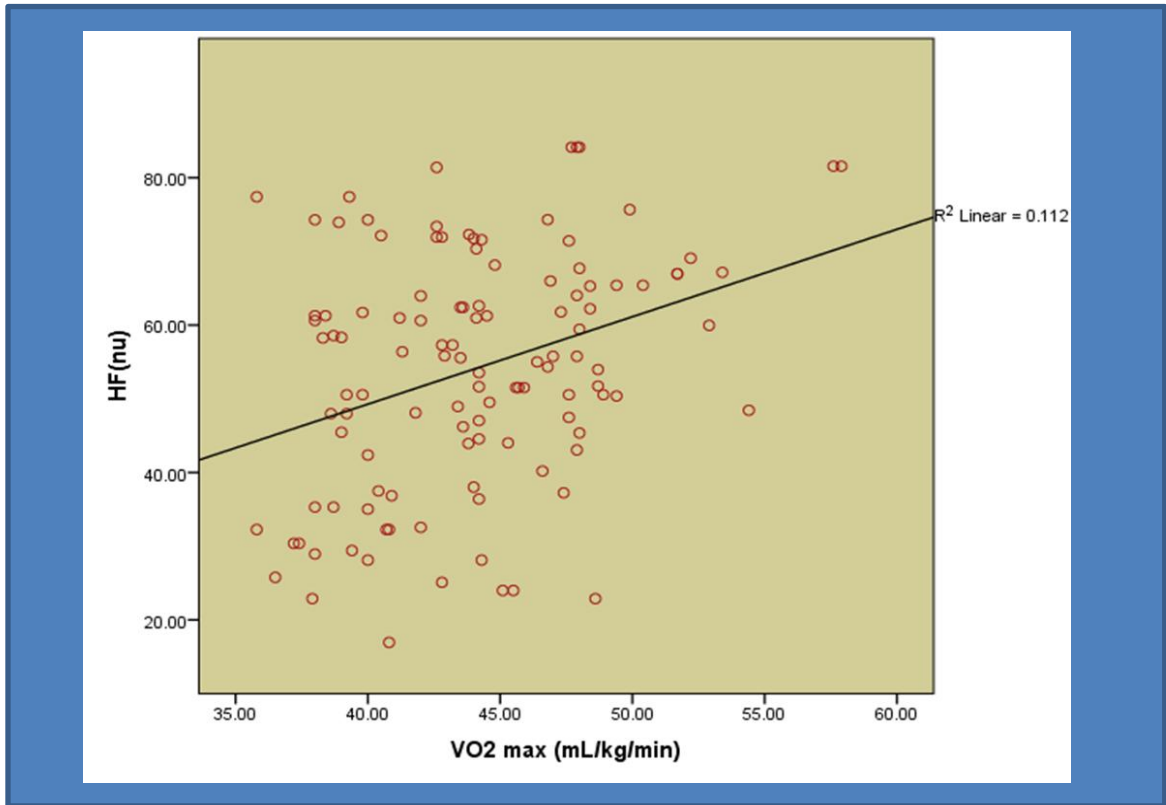


Figure 38: Scatter plot demonstrating the linear relationship ($r=.335^{**}$; $R^2 = 0.112$) between VO₂ Max and HF(nu).

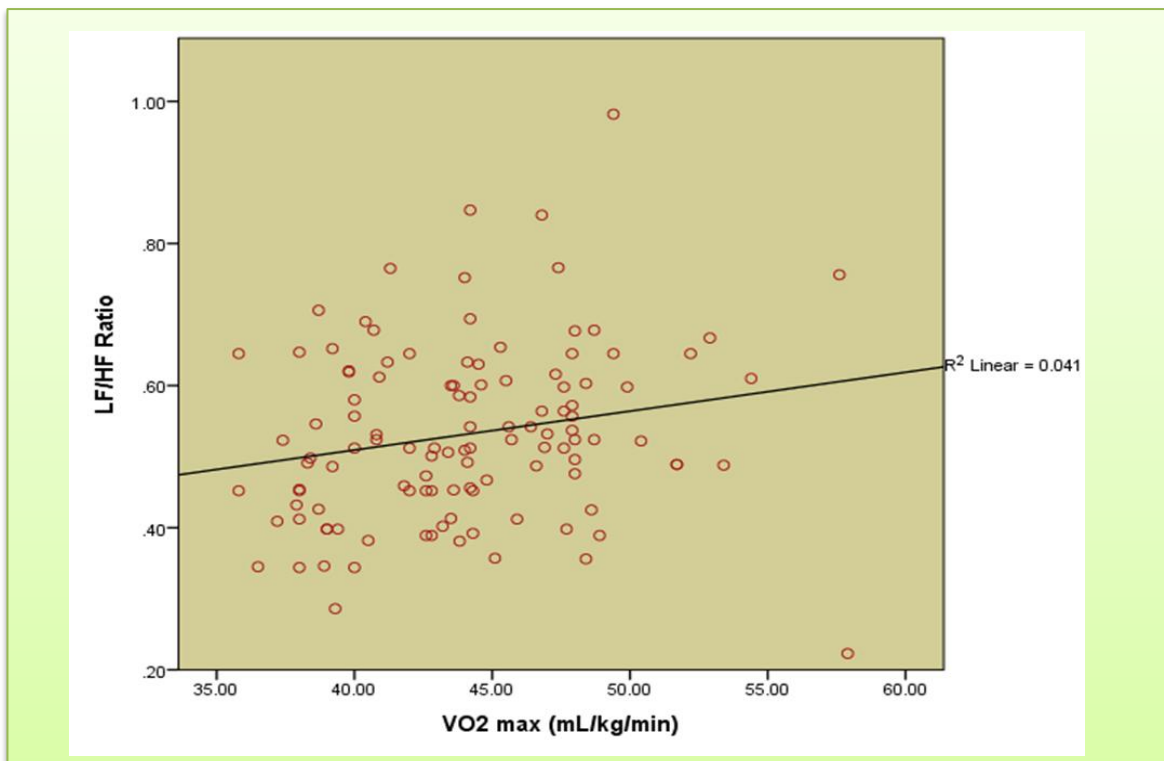


Figure 39: Scatter plot demonstrating the linear relationship ($r=.203^{\dagger}$; $R^2 = 0.041$) between VO₂ Max and LF/HF Ratio.

4.6 Results and Discussion on the VO₂ Max and Neurochemical Markers or Variables

Descriptive statistics revealed the mean and standard deviation of Aerobic Fitness along with specific Neurochemical variables, namely GABA, the main inhibitory neurotransmitter in the brain and a significant inhibitory neurotransmitter in the spinal cord; BDNF, a neurotrophin that can act as a neuromodulator; and Cortisol, a glucocorticoid, as presented in table 25.

The correlation analysis displayed in Table 26 indicated that VO₂max exhibited a significant positive correlation with the chosen neurochemical marker, GABA ($r = .393^*$, $p = .020$), whereas BDNF ($r = .241$, $p = .164$) showed an insignificant but positive relationship, and Cortisol ($r = -.075$, $p = .667$) demonstrated an insignificant but negative correlation.

The findings of this study indicated that VO₂Max significantly impacts GABA levels. Previous studies have shown that consistent and ongoing aerobic activities are crucial for achieving higher VO₂Max, which reflects cardiorespiratory fitness. Enhancements in VO₂Max are typically influenced by the frequency, intensity, and duration of exercise (Milanović et al., 2015). Recent studies suggest that engaging in various forms of aerobic exercise may positively influence brain health by maintaining a balance between excitatory and inhibitory functions. The balance of cortical excitability, or the strength of the neuronal reaction to stimuli, must be carefully maintained between excitatory and inhibitory activities to support normal brain function (Rowley et al., 2012).

Inhibitory and excitatory neurotransmitters play a crucial role in maintaining this precise equilibrium, particularly gamma-aminobutyric acid (GABA) and glutamate (Glx). Recent studies corroborate the findings of the current research and indicate that physical activity can influence GABA levels, thereby impacting cortical excitability (Maddock et al., 2016). A review article (Roy et al., 2025) showed that only a few studies have investigated the influence of exercise on GABA levels, with most of the interventions being either yoga-based

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or involving immediate exercise modules. Exploring the connection between changes in GABA levels and the benefits of exercise, as well as the mechanisms through which exercise supports GABA, is crucial. One potential relationship between exercise and variations in GABA concentration may arise from the metabolic demands that exercise places on the brain (Dalsgaard, 2016). GABA and BDNF are linked in their role in brain function, as BDNF can enhance GABAergic signalling by facilitating the production and release of GABA, along with increasing the presence of GABA transporters on the cell membrane.

Unlike GABA, the findings of the current study indicated a moderate positive connection, though not significant, between BDNF and VO2Max. A prior study found that subjects engaged in long-term sports activities exhibited lower resting serum BDNF levels (Babaei et al., 2014). However, numerous studies have demonstrated that exercise is a crucial factor in enhancing serum BDNF levels (Cotman & Berchtold, 2002; Ferris et al., 2007; Lemos et al., 2016) and that an increase in BDNF levels is a vital component linking exercise to cognitive improvements (Seifert et al., 2010). In a recent review encompassing 29 studies, the authors (Dinoff et al., 2016) noted similar findings.

A summary of the research on physical exercise and peripheral BDNF levels in human's reveals that only 31% of studies reported a significant rise in resting BDNF levels after several weeks of exercise, despite several studies suggesting otherwise. Increased BDNF levels are associated with enhanced resilience to stress, while lower levels correlate with a heightened risk of stress-related conditions like depression and anxiety. This modulation influences mood, motivation, and cognitive abilities (Miao et al., 2020). Through these mechanisms, BDNF plays a crucial role in maintaining and enhancing cognitive and behavioural performance, highlighting its potential as a target for treating cognitive impairments and neuropsychiatric disorders. Exercise-induced increases in BDNF contribute to the reduction of oxidative damage to brain cells (Cefis et al., 2023) and promote

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mitochondrial biogenesis, thereby expanding the energy capacity of neurons and supporting more advanced cognitive functions (Burtscher et al., 2021). Physical activity influences BDNF through a sophisticated interplay of genetic, molecular, and cellular processes, all of which enhance brain function and resilience. Exercise promotes neurogenesis, synaptic plasticity, and the survival of neurons by boosting the production and signaling of BDNF, in addition to offering anti-inflammatory and antioxidant effects. These mechanisms highlight BDNF's essential role in facilitating the cognitive benefits and neuroprotective effects of physical activity, underscoring the importance of regular exercise for maintaining brain health and warding off neurodegenerative diseases. In summary, exercise enhances brain functionality through a complex interaction of genetic, molecular, and cellular mechanisms, emphasizing its significance in neurogenesis, synaptic plasticity, and overall cognitive wellness (Sanaeifar et al., 2024).

Both extremely high and very low levels of resting cortisol negatively impact overall cognitive health, whereas maintaining moderate levels that follow a healthy diurnal pattern is crucial for optimal cognitive performance (Souza-Talarico et al., 2011). In this study, the relationship between normal resting (basal) cortisol levels and VO₂Max was identified as negative but not statistically significant. A prior investigation (Lucertini et al., 2015) revealed that basal cortisol levels were lower in individuals with high fitness (HF) compared to those with low fitness (LF). This finding suggests that cardiorespiratory fitness is a factor that is independently linked to improved hypothalamic-pituitary-adrenal (HPA) regulation and reduced basal cortisol levels, thereby mitigating the gradual HPA dysregulation typically associated with aging. Cardiorespiratory fitness is connected to neurobiological alterations, especially in the hippocampus and prefrontal cortex, which are brain regions that manage the HPA axis by sending inhibitory signals to the hypothalamus. Engaging in regular exercise can safeguard these regions from damage due to stress (such as dendritic retraction resulting from

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chronically elevated cortisol) and may enhance their function, thereby boosting the brain's capacity to control HPA axis activation during resting states.

	Variables	Mean±SD
Aerobic fitness	VO ₂ Max (ml/kg/min)	45.831 ±4.098
Neurochemical Variables	GABA(µg/dl)	0.640 ±0.146
	BDNF(ng/ml)	37.176 ±4.121
	Cortisol (Mcg/dl)	17.901 ±2.949

Table 25: Descriptive statistics of Aerobic Fitness and neurochemical markers' group

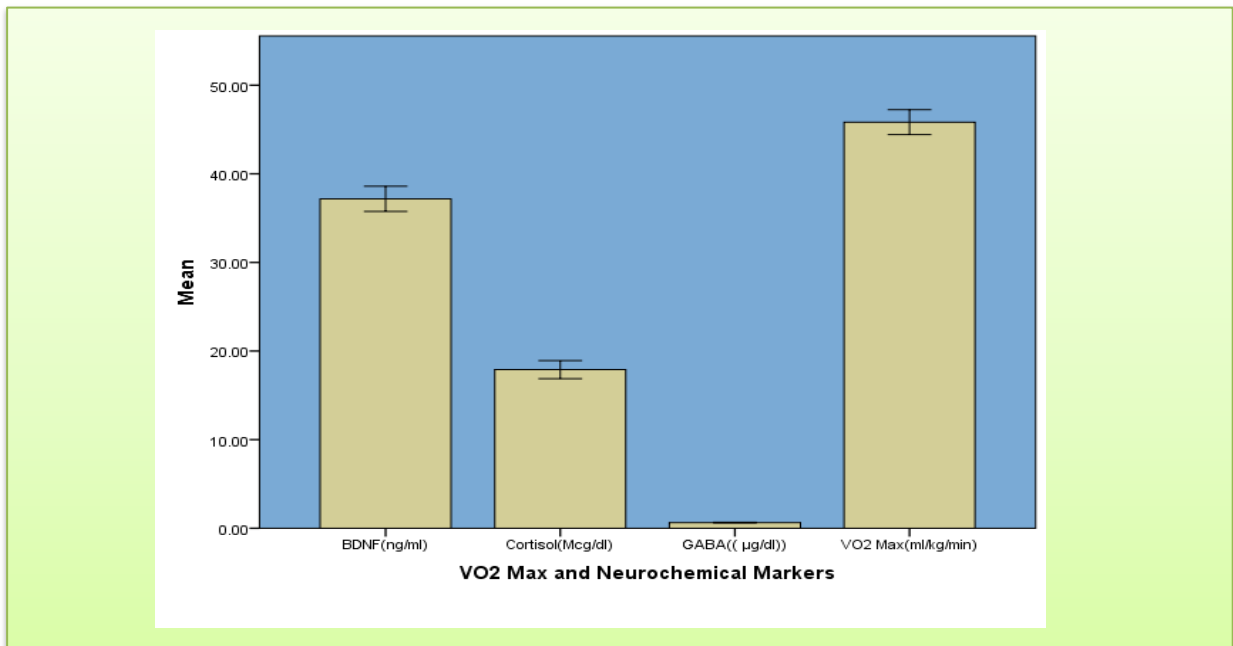


Figure 40: Graphical representation of the mean of VO₂ Max and Neurochemical Markers/Variables

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Aerobic Fitness Variables	Neurochemical Markers/Variables	N	df	(r) value	p value
VO ₂ Max (ml/kg/min)	GABA(µg/dl)	35	33	.393*	.020
	BDNF(ng/ml)	35	33	.241	.164
	Cortisol (Mcg/dl)	35	33	-.075	.667
Correlation is significant at the 0.05* and 0.01** level(2-tailed).					

Table 26: Bivariate correlation between Aerobic Fitness and Neurochemical Markers

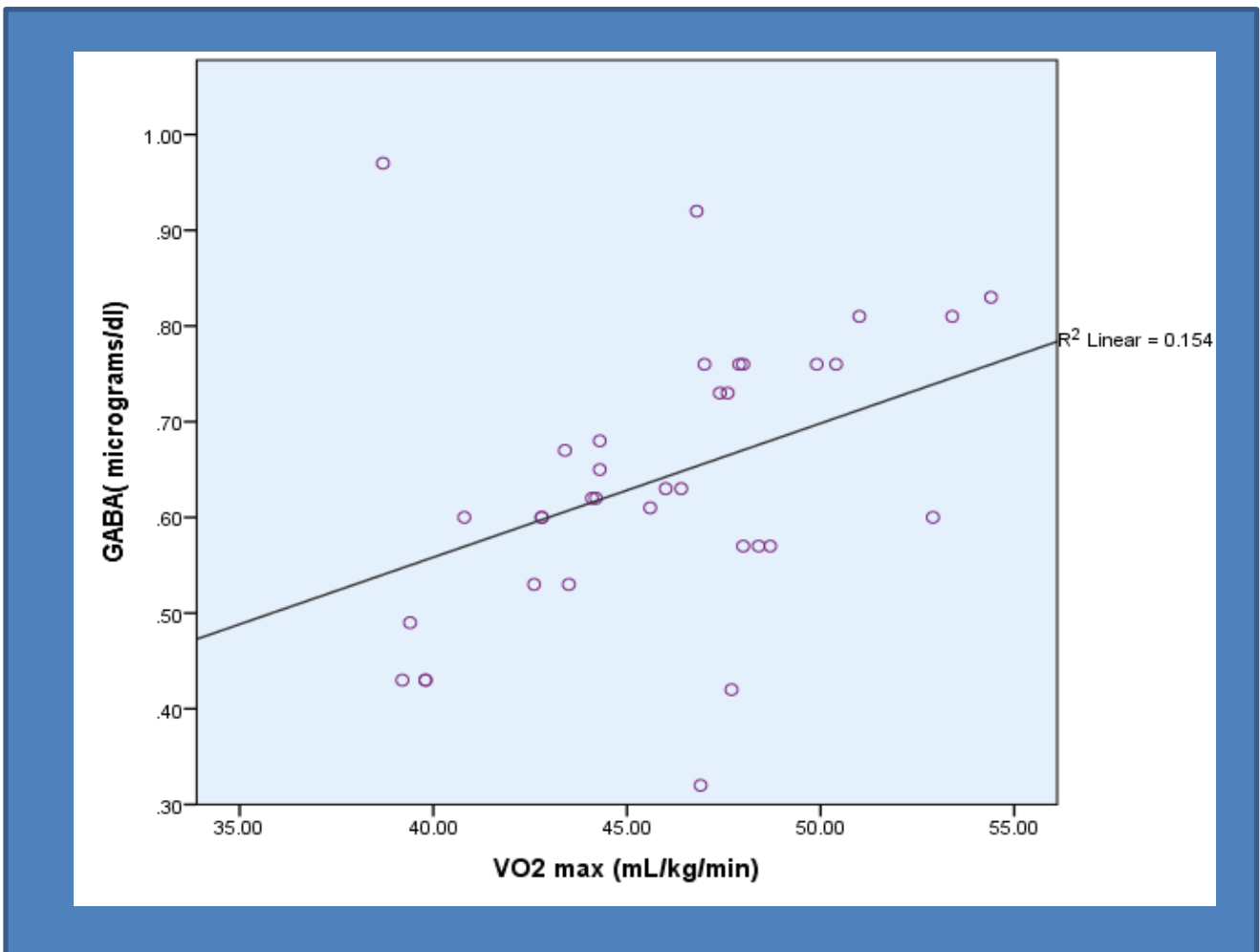


Figure 41: Scatter plot demonstrating the linear relationship ($r=.393^*$; $R^2 =0.154$) between VO₂ Max and GABA.

Results and Discussion

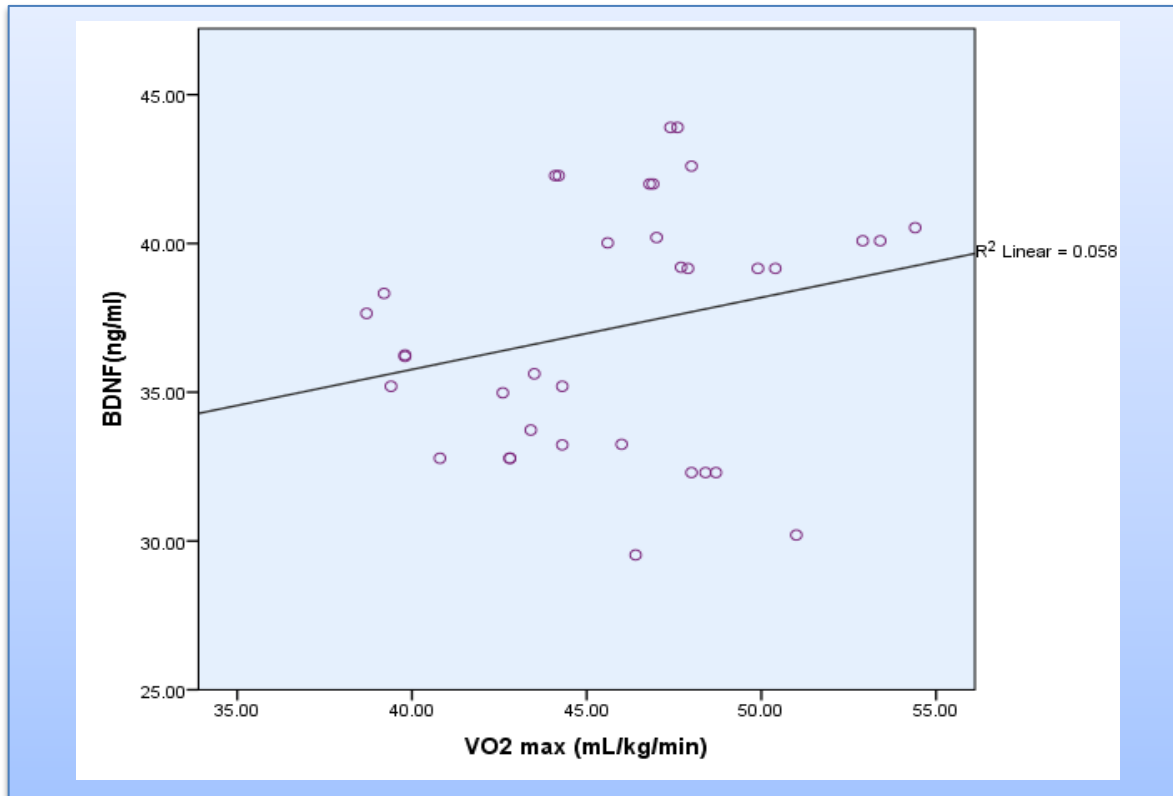


Figure 42: Scatter plot demonstrating the linear relationship ($r=.241$; $R^2 =0.058$) between VO₂ Max and BDNF.

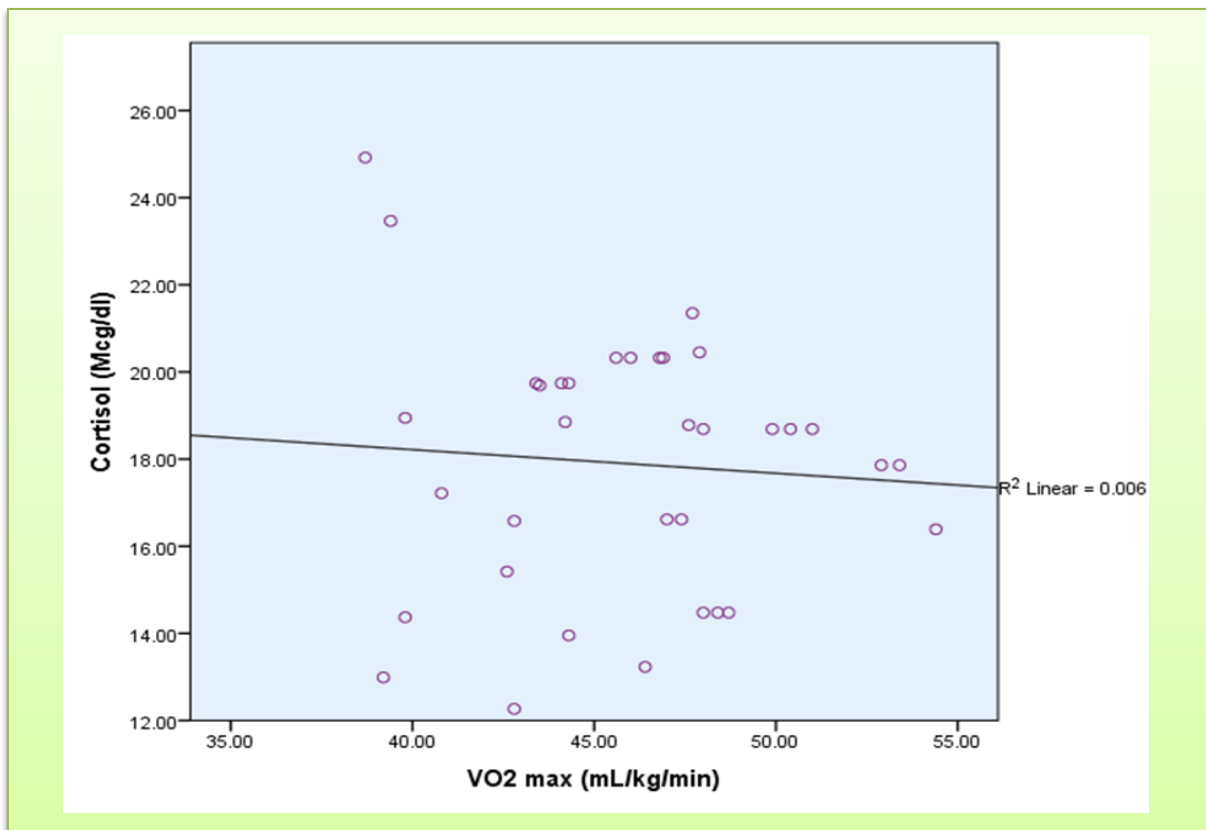
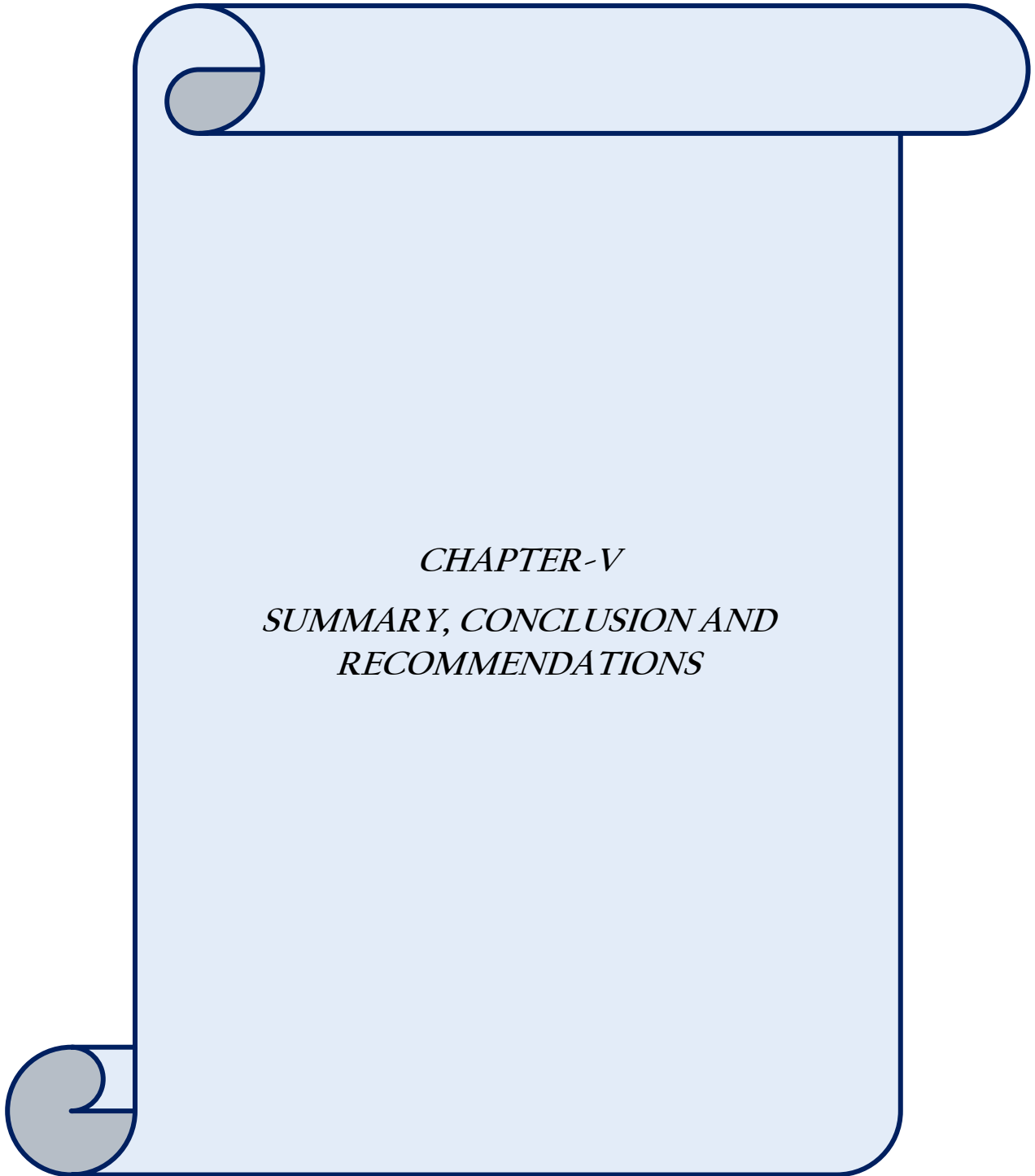


Figure 43: Scatter plot demonstrating the linear relationship ($r=-.075$; $R^2 =0.006$) between VO₂ Max and Cortisol.



5. Summary, Conclusion and Recommendations

This segment represents the concluding and crucial aspect of the thesis documentation. It encompasses a summary of the findings alongside a succinct overview of the complete study. The conclusion presents broad statements, in addition to brief suggestions stemming from the difficulties and limitations recognised throughout the research.

5.1 Summary

The main goal of this research was to explore potential links between cardiorespiratory fitness (VO₂Max), Pulmonary function, cardio autonomic (Heart Rate Variability), and selected neurochemical markers. Previous studies indicate that many have concentrated solely on the effects of exercise on cardiorespiratory fitness, lung function, cardio autonomic regulation (Heart Rate Variability), and neuroplasticity through neurochemical changes. By identifying particular gaps in existing literature across these areas, the researcher aimed to investigate the relationships across these domains simultaneously. Until now, no studies have directly investigated the relationship between cardiorespiratory fitness and individual elements from Pulmonary Function Tests, cardio autonomic and selected neurochemical markers in an integrated approach.

The method aligns with a cross-sectional study design where cardiorespiratory fitness serves as the independent variable, while the other dependent variables include indices from pulmonary function tests (PFT), cardiac autonomic indices (HRV), and neurochemical markers such as GABA, BDNF, and cortisol.

The current research was carried out in the Exercise and Sports Physiology Laboratory within the Department of Physical Education at Jadavpur University located in Jadavpur, Kolkata. A sample of 115 male participants was chosen using a convenient sampling technique, following a G*Power analysis to determine effect size. Normality tests were performed prior

Summary, Conclusion and Recommendations

to conducting parametric tests to assess the distribution of the data. In this study, the Pearson's correlation using a bivariate normal model was employed to explore the relationship between the chosen independent and dependent variables, with significance levels established at 0.05. The outcomes addressing the research question were effectively clarified through the quantified results obtained from the study. The research question was framed as: "What is the relationship between cardiorespiratory fitness (VO₂Max) and key physiological and neurochemical markers-including PFT indices, HRV indices, and circulating levels of GABA, BDNF and Cortisol in healthy young adults?" The study ultimately provided precise answers to this question based on its findings. Conclusion of the study reflected the comprehensive answer to the main research question framed in the introduction part.

The findings from the comparison between VO₂Max and the chosen PFT indices revealed a notable positive correlation with all selected indices, specifically FEV-1, FEV-3, and Vital Capacity. A high VO₂max alongside excellent performance in pulmonary function tests (like FEV₁, FEV-3, and VC) is a crucial sign of improved cardiorespiratory health, a lower risk of chronic illnesses, and increased lifespan.

The correlation analysis indicated that VO₂max had significant positive correlations with Mean RR, RMSSD, HF power, and HF nu, suggesting that increased cardiorespiratory fitness is linked to elevated parasympathetic activity and enhanced heart rate variability overall. Conversely, VO₂max exhibited significant negative correlations with LF power and LF nu, implying a diminished sympathetic influence in those with higher aerobic capacity. Mean HR displayed a negative but non-significant correlation with VO₂max, while SDNN and pNN50 demonstrated positive but also non-significant correlations. Collectively, these results imply that a higher VO₂max is primarily associated with improved vagal modulation and decreased

Summary, Conclusion and Recommendations

sympathetic dominance, indicating a more advantageous autonomic balance in individuals with better fitness levels.

The analysis of correlation between VO₂Max and the chosen neurochemical marker, GABA, revealed significant positive correlations, while BDNF exhibited a weak but positive association, and Cortisol displayed an insignificant yet negative correlation.

Considering the perspectives outlined above, the response to the research question can be understood as follows:

- The relationship between VO₂max and pulmonary function test (PFT) measures such as FEV-1, FEV-3, and vital capacity (VC) suggests that enhanced cardiorespiratory fitness is associated with improved lung function.
- A significant relationship was found between VO₂max and certain HRV indices (both time domain and frequency domain), indicating improved regulation of the autonomic nervous system.
- The relationship between VO₂max and specific neurochemical indicators was found to be robust, suggesting improved neurocognitive health via neurochemical regulation.

5.2 Conclusion:

The current research revealed a notable link between aerobic capacity (VO₂max) and various physiological and neurochemical factors. Results from pulmonary function tests (PFT) indicated a strong positive correlation with VO₂max, highlighting that improved respiratory efficiency is intimately connected to higher levels of aerobic fitness. Heart rate variability (HRV) metrics showed partial yet significant associations, implying that autonomic balance might play a role in aerobic performance, even though its impact seems to be more selective.

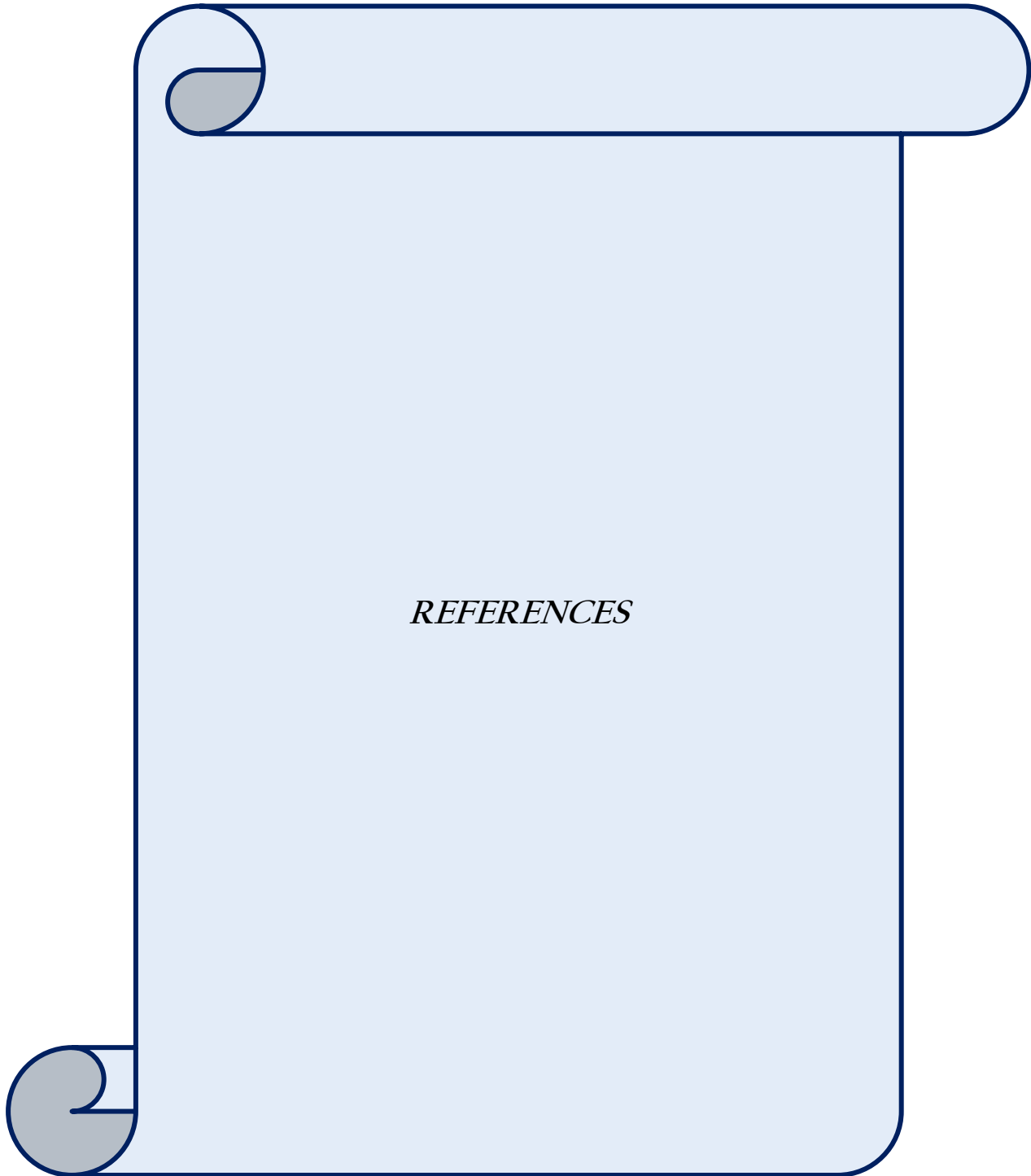
Summary, Conclusion and Recommendations

Within the neurochemical indicators, VO₂max showed a positive relationship with gamma-aminobutyric acid (GABA) and brain-derived neurotrophic factor (BDNF), while exhibiting a negative correlation with resting cortisol levels. These results imply that greater aerobic fitness is linked to improved inhibitory neurotransmission and neuroplastic capacity, as well as lower levels of basal stress hormones.

The findings collectively suggest that enhanced aerobic fitness (VO₂max) represents a comprehensive physiological condition characterized by effective lung function, balanced nervous system regulation, and positive neurochemical characteristics that promote resilience to stress and neural health. Future studies should investigate the causal relationships and training approaches that influence these systems to improve both physical health and neuropsychological well-being.

5.3 Recommendations:

- Upcoming research could be designed and conducted with a control group utilizing the current study's framework.
- A longitudinal study could be designed to gain a deeper insight into the underlying mechanisms that might contribute to the potential linear multiple relationships among the variables selected for this research. A study may be performed incorporating cognitive health variables with the existing study design.
- To reduce the risk of neurodegenerative diseases, it is recommended that everyone, irrespective of age or gender, should engage in regular physical activity.



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Annexure-I (Plagiarism Report)

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Jadavpur University
Kolkata-700 032

Annexure- II

(Institutional Ethical Approval and Trial Registration)

হাদবপুর বিশ্ববিদ্যালয়
কলকাতা-৭০০০৩২, ভারত



*JADAVPUR UNIVERSITY
KOLKATA-700 032, INDIA

Dr.Sridip Chatterjee
Dept. of Physical Education
Jadavpur University

RefNo: IEC/37/C/25

Date: 22.01.2025

Dear Sir/ Madam,

Institutional Ethics Committee (IEC) Approval

Title of the Study: "IMPACT OF CARDIORESPIRATORY FITNESS ON SELECTED
NEUROCHEMICAL AND CARDIO AUTONOMIC MARKERS"

The above application of Mr. Dilip Roy, Department of Physical Education, Jadavpur University has been considered on behalf of the Jadavpur University Institutional Ethics Committee in accordance with the procedures laid down by the University for ethical approval of all research involving human participants.

I am pleased to inform you that, on the basis of the information provided to the Jadavpur University Institutional Ethics Committee, the proposed research has been judged as per meeting appropriate ethical standards, and accordingly approval has been granted in the meeting dated 20.01.2025.

Should there be any subsequent changes to the project, which raise ethical issues not covered in the original application, P.I. should submit details to the Jadavpur University Institutional Ethics Committee for consideration.

Hope this will serve your purpose.

Thanking You,

Sankhayan Choudhury
(Prof. Sankhayan Choudhury)

CHAIRPERSON

Dr. Indrajit Banerjee
(Dr. Indrajit Banerjee)

CONVENER

Secretary Faculty Council of Arts
Jadavpur University
Kolkata-32

* Established on and from 24th December, 1955 vide Notification No.10986-Edn/II-42/55 dated 6th December, 1955 under Jadavpur University Act, 1955 (West Bengal Act XXIII of 1955) followed by Jadavpur University Act,1981 (West Bengal Act XXIV of 1981)

দুরভাষা: ২৪১৪-৬৬৬৬/৬১৪৪/৬৬৬৬/৬৪৪৪/৬৪৪৪
দুরবারী: (৯১)-০০০-২৪১৪-৬৪৪৪/২৪১০-৭১২১

Website: www.jaduniv.edu.in
E-mail: registrar@admin.jdyu.ac.in

Phone : 2414-6666/6194/6643/6495/6443
Fax : (91)-033-2414-6414/2413-7121

Clinical Trials Registry - India (ICMR-NIMS)

FULL DETAILS (Read-only) -> [Click Here to Create PDF for Current Dataset of Trial](#)

CTRI No	CTRI/2025/05/086537 [Registered on: 07/05/2025] Trial Registered Prospectively	
Acknowledgement Number	REF/2025/04/103228	
Last Modified On:	12/05/2025	
Post Graduate Thesis	No	
Type of Trial	Observational	
Type of Study Clarification(s) with Reply Modification(s)	Cross Sectional Study	
Study Design	Single Arm Study	
Public Title of Study Clarification(s) with Reply Modification(s)	Relationship among Cardiorespiratory Fitness, Selected Neurochemical and Cardio Autonomic Markers in Healthy Young Adults - A Cross Sectional Study	
Scientific Title of Study Clarification(s) with Reply Modification(s)	Impact of Cardiorespiratory Fitness On Selected Neurochemical and Cardio Autonomic Markers	
Trial Acronym	Nil	
Secondary IDs if Any	Secondary ID	Identifier
	NIL	NIL
Details of Principal Investigator or overall Trial Coordinator (multi-center study)	Name	Dilip Roy
	Designation	Ph.D Scholar
	Affiliation	Jadavpur University
	Address	Department of Physical Education, Jadavpur University, Kolkata Kolkata WEST BENGAL 700032 India
	Phone	9679157430
	Fax	
	Email	dilipr.pe.rs@jadavpuruniversity.in
Details Contact Person Scientific Query Clarification(s) with Reply Modification(s)	Name	Dr. Sridip Chatterjee
	Designation	Guide/Associate Professor
	Affiliation	Jadavpur University
	Address	Department of Physical Education, Jadavpur University, Kolkata Kolkata WEST BENGAL 700032 India
	Phone	9674764085
	Fax	
	Email	sridipchatterjee.ped@jadavpuruniversity.in

Annexure II

Details Contact Person Public Query	<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 30%;">Name</td> <td>Dilip Roy</td> </tr> <tr> <td>Designation</td> <td>Ph.D Scholar</td> </tr> <tr> <td>Affiliation</td> <td>Jadavpur University</td> </tr> <tr> <td>Address</td> <td>Department of Physical Education, Jadavpur University, Kolkata Kolkata WEST BENGAL 700032 India</td> </tr> <tr> <td>Phone</td> <td>9679157430</td> </tr> <tr> <td>Fax</td> <td></td> </tr> <tr> <td>Email</td> <td>dilipr.pe.rs@jadavpuruniversity.in</td> </tr> </table>	Name	Dilip Roy	Designation	Ph.D Scholar	Affiliation	Jadavpur University	Address	Department of Physical Education, Jadavpur University, Kolkata Kolkata WEST BENGAL 700032 India	Phone	9679157430	Fax		Email	dilipr.pe.rs@jadavpuruniversity.in										
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Email	dilipr.pe.rs@jadavpuruniversity.in																								
Source of Monetary or Material Support	Jadavpur University 188 Raja SC Mullick Road, Jadavpur 700032																								
Primary Sponsor	<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 30%;">Name</td> <td>Jadavpur University</td> </tr> <tr> <td>Address</td> <td>188, Raja Subodh Chandra Mallick Rd, Jadavpur, Kolkata, West Bengal 700032</td> </tr> <tr> <td>Type of Sponsor</td> <td>Other [Academic and Research State University]</td> </tr> </table>	Name	Jadavpur University	Address	188, Raja Subodh Chandra Mallick Rd, Jadavpur, Kolkata, West Bengal 700032	Type of Sponsor	Other [Academic and Research State University]																		
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Address	188, Raja Subodh Chandra Mallick Rd, Jadavpur, Kolkata, West Bengal 700032																								
Type of Sponsor	Other [Academic and Research State University]																								
Details of Secondary Sponsor	<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 50%;">Name</th> <th>Address</th> </tr> </thead> <tbody> <tr> <td>NIL</td> <td>NIL</td> </tr> </tbody> </table>	Name	Address	NIL	NIL																				
Name	Address																								
NIL	NIL																								
Countries of Recruitment	India																								
Sites of Study Clarification(s) with Reply	<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th colspan="2" style="text-align: right;">No of Sites = 1</th> </tr> <tr> <th style="width: 40%;">Name of Principal Investigator</th> <th>Name of Site</th> </tr> </thead> <tbody> <tr> <td>Dilip Roy</td> <td>Exercise and Sports Physiology Laboratory, Department of Physical Education, Jadavpur University</td> </tr> </tbody> </table>	No of Sites = 1		Name of Principal Investigator	Name of Site	Dilip Roy	Exercise and Sports Physiology Laboratory, Department of Physical Education, Jadavpur University																		
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Details of Ethics Committee Clarification(s) with Reply Modification(s)	<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th colspan="6" style="text-align: right;">No of Ethics Committees= 2</th> </tr> <tr> <th style="width: 15%;">Name of Ethics Committee</th> <th style="width: 15%;">Ethics Committee registered with DHR /CDSCO or not</th> <th style="width: 20%;">Ethics Committee Registration No.</th> <th style="width: 10%;">Approval Status</th> <th style="width: 10%;">Date of Approval</th> <th style="width: 10%;">Approval Document</th> </tr> </thead> <tbody> <tr> <td>Institutional Ethics Committee, Jadavpur University</td> <td>Yes</td> <td>1805/GO/Re/S/15/CPCSEA</td> <td>Approved</td> <td>22/01/2025</td> <td>Approval File</td> </tr> <tr> <td>NOC from Laboratory</td> <td>Yes</td> <td></td> <td>No Objection Certificate</td> <td>16/04/2025</td> <td>Approval File</td> </tr> </tbody> </table>	No of Ethics Committees= 2						Name of Ethics Committee	Ethics Committee registered with DHR /CDSCO or not	Ethics Committee Registration No.	Approval Status	Date of Approval	Approval Document	Institutional Ethics Committee, Jadavpur University	Yes	1805/GO/Re/S/15/CPCSEA	Approved	22/01/2025	Approval File	NOC from Laboratory	Yes		No Objection Certificate	16/04/2025	Approval File
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NOC from Laboratory	Yes		No Objection Certificate	16/04/2025	Approval File																				

Annexure II

Regulatory Clearance Status from DCGI	Status	Date	Aproval Document
	Not Applicable	No Date Specified	No File Uploaded
Health Condition / Problems Studied	Health Type	Condition	
	Healthy Human Volunteers	Physical Education Students within the age group of 20-30 years	
Intervention / Comparator Agent Clarification(s) with Reply Modification(s)	Type	Name	
	Intervention	Nil	
	Comparator Agent	Nil	
Inclusion Criteria	Age From	20.00 Year(s)	
	Age To	30.00 Year(s)	
	Gender	Male	
	Details	Only healthy males aged 20-30 years having at least 4 years training age.	
Exclusion Criteria	Details	Males under went any medical issues were excluded.	
Method of Generating Random Sequence	Not Applicable		
Method of Concealment	Not Applicable		
Blinding/Masking	Not Applicable		
Primary Outcome Clarification(s) with Reply Modification(s)	Outcome		
	<p>Researcher expects the following deliverables from the study:</p> <ol style="list-style-type: none"> 1. Identification of association of cardiorespiratory fitness with selected neurochemicals. 2. To realize the effect of cardiorespiratory fitness with selected cardio autonomic markers. 		
Secondary Outcome Clarification(s) with Reply Modification(s)	Outcome		
	On the basis of the scientific observation we may recommend chronic exercise training which may positively influence cardio autonomic markers & brain health		
Target Sample Size	<p>Total Sample Size="115" Sample Size from India="115" Final Enrollment numbers achieved (Total)= "Applicable only for Completed/Terminated trials" Final Enrollment numbers achieved (India)="Applicable only for Completed/Terminated trials"</p>		
Phase of Trial	N/A		
Date of First Enrollment (India) Clarification(s) with Reply	10/05/2025		
Date of Study Completion (India)	Applicable only for Completed/Terminated trials		
Date of First Enrollment (Global)	If country of recruitment is only India, global date would be not applicable.		
Date of Study Completion (Global)	Applicable only for Completed/Terminated trials		

Annexure-III

(Approved Letter for Laboratory Access)

যাদবপুর বিশ্ববিদ্যালয়
কলকাতা-৭০০০৩২, ভারত



*JADAVPUR UNIVERSITY
KOLKATA-700 032, INDIA

শারীর শিক্ষা বিভাগ, কলা অনুষদ / DEPARTMENT OF PHYSICAL EDUCATION, FACULTY OF ARTS

No Objection Certificate for Research Works

TO WHOM IT MAY CONCERN

Mr. Dilip Roy has been doing his Ph.D. in the Department of Physical Education, Jadavpur University as a regular research scholar(UGC-JRF). He has already been given with an Institutional Ethical Permission from Jadavpur University with Ref No: IEC/37/25 dated 22.01.2025 after reviewing his research proposal by the competent authority concerned.

In conformity with his research proposal he will be allowed to use the laboratory facilities (Exercise & Sports Physiology Laboratory, Department of Physical Education, JU) and henceforth the authority concerned has no objection for the research works entitled with "IMPACT OF CARDIORESPIRATORY FITNESS ON SELECTED NEUROCHEMICAL AND CARDIO AUTONOMIC MARKERS".

Place.....*Jadavpur University*
Date.....*16/4/25*.....

Sridip Chatterjee
16/4/25
Dr. SRIDIP CHATTERJEE
Head
Department of Physical Education
Jadavpur University
Kolkata-700 032

Signature and seal of the authority concerned
Exercise & Sports Physiology Laboratory
Department of Physical Education, JU

*Established on and from 24th December, 1955 vide Notification No.10986-Edn/1U-42/55 dated 6th December, 1955 under Jadavpur University Act, 1955 (West Bengal Act XXIII of 1955) followed by Jadavpur University Act,1981 (West Bengal Act XXIV of 1981)

দূরভাষা: ০৩০-২৪৫৭-২৪৮৬

Website : www.juphysicaleducation.org
E-mail : hod.ph.ed@jadavpuruniversity.in

Phone : 033-2457-2486

Annexure-IV

(Approval for Samples'/Participants' Recruitment)

যাদবপুর বিশ্ববিদ্যালয়
কলকাতা-৭০০০৩২, ভারত



*JADAVPUR UNIVERSITY
KOLKATA-700 032, INDIA

শারীর শিক্ষা বিভাগ, কলা অনুষদ / DEPARTMENT OF PHYSICAL EDUCATION, FACULTY OF ARTS

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In conformity with his research proposal, he will be allowed to have the male students of the Department of Physical Education, Jadavpur University, Kolkata-7000032, India, as samples for his study, and henceforth the authority concerned has no objection to the research work entitled "Impact of Cardiorespiratory Fitness on Selected Neurochemical and Cardioautonomic Markers"

Place..... JADAVPUR UNIVERSITY

Date...16/4/25.....

Head
Department of Physical Education,
Jadavpur University
Kolkata-700 032

Signature and Seal of the authority concerned/HOD

Department of Physical Education

Jadavpur University, Kol-700032

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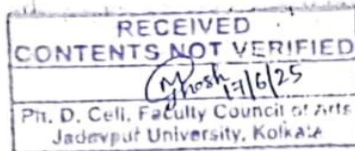
দুরভাস: ০৩৩-২৪৫৭-২৪৮৬

Website : www.juphysicaleducation.org
E-mail : hod.ph.ed@jadavpuruniversity.in

Phone : 033-2457-2486

Annexure-V

(Approval of correction of Ph. D Title)

MINUTES

Minutes of the meeting of the Research Advisory Committee(RAC) of the Department of Physical Education held on the 16th June'2025 at 12:30 PM in connection with the Pre-submission lecture of Mr. Dilip Roy, a regular Ph.D Scholar of the Department of Physical Education, under the Faculty council of Arts, Jadavpur University.

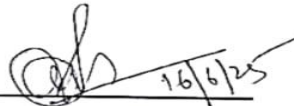
Members present:


1. Chairman: Dr. Sridip Chatterjee, Associate Professor & Head, Department of Physical Education, J.U
2. Member: Prof. A. K. Banerjee, Professor (Retd.), Department of Physical Education, University of Kalyani (External)
3. Member: Prof. Sudip Sundar Das, Professor, Department of Physical Education, J.U
4. Supervisor(Convener): Dr. Sridip Chatterjee, Associate Professor, Department of Physical Education, J.U.

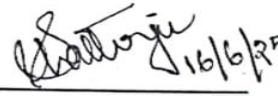
Sir,

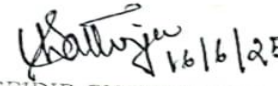
Mr. Dilip Roy presented his Pre-submission lecture in relation to his Ph.D. work and all members are satisfied & recommended that the thesis may be submitted for evaluation maintaining all the stipulated rules and regulations of the University. After modification the final title of the thesis is: "IMPACT OF CARDIORESPIRATORY FITNESS ON SELECTED PULMONARY CARDIOAUTONOMIC AND NEUROCHEMICAL MARKERS.

- a) Name of the scholar : Dilip Roy
 b) Name of the Supervisor : Dr. sridip Chatterjee
 c) Title of the research work : Impact of Cardiorespiratory fitness on Selected Pulmonary Cardioautonomic and Neurochemical Markers


 16/6/25
 Prof. Sudip Sundar Das
 Professor, Member


 Prof. A. K. Banerjee
 Professor (Retd.), Member 16/6/2025


 16/6/25
 Dr. Sridip Chatterjee
 Chairman & supervisor
 Head
 Department of Physical Education
 Jadavpur University
 Kolkata-700 032


 16/6/25
 (DR. SRIDIP CHATTERJEE)
 Associate Professor
 Department of Physical Education
 Jadavpur University
 Kolkata-700032

Annexure-VI

(Recommendation letter for Final Thesis Submission)

Received
in
grossly
17/6/25

PRE-SUBMISSION SEMINAR RECOMMENDATION OF
RESEARCH ADVISORY COMMITTEE
(2017 REGULATION)

IN VIEW OF THE FOLLOWING THE CANDIDATE IS A FIT AND PROPER PERSON TO SUBMIT THE THESIS FOR THE PH.D. DEGREE

1. WHETHER UNDERTAKEN COURSE WORK : WAIVED/QUALIFIED

2. PUBLICATION STATUS : COMPLIED

3. OPEN SEMINAR : Held on 16th June, 2025, 12.30 - 1.30 PM
Seminar Hall, Deptt. of Phys. Edu.

4. OPINION FOR SUBMISSION OF THE THESIS : YES/NO

(IF RECOMMENDED THE CANDIDATE MUST SUBMIT THESIS WITHIN 90 DAYS)

DATE: 16/6/25.....

SIGNATURE OF THE HEAD OF THE DEPARTMENT/ DIRECTOR OF THE SCHOOL & CHAIRMAN, PH.D. RESEARCH COMMITTEE WITH SEAL

DATE: 16/6/25.....

SIGNATURE OF THE CONVENOR PH.D. RESEARCH COMMITTEE (SECRETARY, FCA) WITH SEAL

SIGNATURE OF RAC MEMBERS:

1. A.K. Banerjee 16/6/2025

2. Chatterjee 16/6/25

3. 16.6.25
Head
Department of Physical Education
Jadavpur University
Kolkata-700 032

4. Chatterjee 16/6/25

(DR. SRIDIP CHATTERJEE)
Associate Professor
Department of Physical Education
Jadavpur University
Kolkata-700032

Annexure-VII

INFORMED CONSENT DOCUMENT (ICD)

Participant information sheet

INFORMATION FOR PARTICIPANTS OF THE STUDY

- 1. Title of the study: Impact of Cardiorespiratory Fitness on Selected Pulmonary Cardio autonomic and Neurochemical Markers**
- 2. Name of the research scholar: Dilip Roy**
- 3. Purpose of this project/study: To understand the habitual and long-term effects of exercise (VO₂ max) on the selected neurochemical and cardio autonomic markers.**
- 4. Procedure/methods of the study: Cross-Sectional Study**
- 5. Expected duration of the subject participation: 3 hours for four days/ participant**
- 6. The benefits to be expected from the research to the participant or to others and the post-trial responsibilities of the investigator: Aerobic fitness, Cardio Pulmonary health and serum level Neurochemical status and understanding of the correlational effects of exercise on them.**
- 7. Any risks expected from the study to the participant: No risks whatsoever**
- 8. Maintenance of confidentiality of records: Yes**
- 9. Compensation to the participants for foreseeable risks and unforeseeable risks related to research study leading to disability or death: No such risk**
- 10. Freedom to withdraw from the study at any time during the study period without the loss of benefits that the participant would otherwise be entitled: Yes**
- 11. Possible current and future uses of the biological material and of the data to be generated from the research and if the material is likely to be used for secondary purposes or would be shared with others, this should be mentioned: This data will be used purely for research and it will be used purely for doctoral research**
- 12. Address and mobile number of the research scholar, if any: Department of Physical Education, Jadavpur University, Kolkata -32**

Signature of Research Scholar with date

Signature of Participant with date

CONSENT FORM

Title of the Study:

Impact of Cardiorespiratory Fitness on Selected Pulmonary Cardio autonomic and Neurochemical Markers

Participant's name:

Address:

The details of the study have been provided to me in writing and explained to me in my own language. I confirm that I have understood the above study and had the opportunity to ask questions. I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without the medical care that will normally be provided by the hospital being affected. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s). I have been given an information sheet giving details of the study. I fully consent to participate in the above study. (I also consent / do not consent to use my stored biological samples for future scientific purposes: Yes/ No – if applicable)

Signature of the participant: _____ Date: _____

Signature of the witness: _____ Date: _____

Name and address of the witness:

Signature of the research scholar: _____ Date: _____

Annexure-VIII
(Seminar Presentation)

 **MANAV RACHNA**
विद्ययाचारिकशास्त्र

 **NAAC A++**
ACCREDITED

 युवा कार्यक्रम
एवं खेल मंत्रालय
MINISTRY OF
YOUTH AFFAIRS
AND SPORTS

 The Foundation
For Global
Community Health



 **ICSSPE**

3rd BRICSCESS Conference 2024
Faridabad NCR, INDIA
26th -29th February 2024

Oral Presentation Certificate

This is to certify that

Dilip Roy
has presented paper

entitled Impact of aerobic fitness on selected respiratory indices :
An Observational Pilot Study. in the

**“BRICS Conference on Exercise & Sports Science” organised at
Manav Rachna International Institute of Research & Studies.**


Prof. (Dr.) Sanjeev Gupta
Org. Secretary


Prof. (Dr.) J. Hans de Ridder
President


Prof. (Dr.) G. L. KHANNA
Chairperson

Powered by  **एनटीपीसी NTPC**

Industry partner 





ICPEES 2023
22nd - 24th March, 2023



Certificate of Appreciation

This is to certify that

Mr./Ms..... DILIP Roy Research Scholar / Student of
DEPARTMENT OF PHYSICAL EDUCATION , JADARPUR UNIVERSITY , KOLKATA

has contributed in the

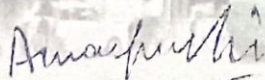
International Conference on Physical Education and Exercise Sciences


Organized by:

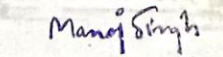
Department of Physical Education, Punjabi University, Patiala (Punjab) INDIA

as Presenter / Participant

Topic Entitled as "Applicability Of Heart Rate Variability As a Cardiac- Autonomic
Markers In Exercise and Sports Science."


Dr. Amarpreet Singh
Organizing Secretary


Dr. Nishan Singh Deol
Prof. & Head
Conference Director


Mr. Manoj Singh
Organizing Secretary

Annexure-IX

(Journal Publications)

Central European Journal of Sport Sciences and Medicine | Vol. 50, No. 2/2025: 41-51

ISSN (print): 2300-9705 | ISSN (online): 2353-2807 | DOI: 10.18276/cej.2025.2-04



EFFECT OF EXERCISE ON GABA: A SYSTEMATIC REVIEW OF THE LITERATURE

Dilip Roy^{A, B, D}

Department of Physical Education, Jadavpur University, Kolkata-700032, West Bengal, India ORCID:
0009-0004-0152-660X

Prosanta Paul^{B, D}

Department of Physical Education, Jadavpur University, Kolkata-700032, West Bengal, India ORCID:
0009-0006-4996-4371

Puneet Bhattacharya^{A, B}

Department of Physical Education, Jadavpur University, Kolkata-700032, West Bengal, India ORCID:
0000-0002-8811-818X

Sridip Chatterjee^{A, B}

Department of Physical Education, Jadavpur University, Kolkata-700032, West Bengal, India ORCID:
0000-0001-9292-5454 | e-mail:sridipchatterjee.ped@jadavpuruniversity.in

^AStudy Design; ^BData Collection; ^CStatistical Analysis; ^DManuscript Preparation; ^EFunds Collection

Abstract Physical exercise (PE) improves brain function by encouraging neuroplasticity via a number of different neurobiological processes. Gama-amino butyric acid (GABA) has potentiality to modify neuroplastic capacity of neurons through trophic action. L-glutamate of the brain naturally produces GABA and recent scientific analysis intensely focuses on its physiological influence on brain health. Investigation shows very less research between these two factors, and no comprehensive review study so far. The present study based on PRISMA-P 2015 guidelines accumulated latest information to better understand how physical exercise influences GABA levels in the brain. Using the PRISMA 2020 flow diagram, a rational approach was guaranteed during the screening process for existing literature that meets the criteria. These existing non-randomized controlled trials (Non-RCT) and randomized controlled trials (RCT) have shown that aerobic interventions boost GABA levels in the human brain that has a positive impact. This innate benefit may be considered as a form of medicinal and remedial treatment for depression, anxiety disorders, and in general cognitive health. These results, which are associated with increased GABA exposure and its mechanism, imply that exercise has the potential to be an intervention for enhancing psychological competence or cognitive health, executive function, and sport performance as well.

Key words: GABA, neurotransmitter, physical exercise, cognitive health and psychology

Introduction

Endogenous chemicals known as neurotransmitters are present in the central nervous system. These chemical messengers play a crucial role in the neural circuitry that controls muscle contraction during physical activity or exercise. Neurotransmitters can be categorized into three main types based on their functions: a) excitatory neurotransmitters, b) inhibitory neurotransmitters, and c) neuromodulators. Gamma-Amino Butyric Acid (GABA) is the primary inhibitory neurotransmitter, reducing neuronal excitability by regulating nerve transmissions. It is widely accepted that GABA is responsible for approximately 40% of the inhibitory neural control in the brain (Bowery & Smart, 2006). This trafficking is performed by activating ionotropic fast chloride receptors (GABA_A) or metabotropic receptors (GABA_B) in order to produce gentle and prolonged inhibitory signals (Pierrefiche et al., 1993) unlike the mechanism employed by the parasympathetic nervous system in the CNS.

The main emphasis of this article is on the impact of exercise on GABA. There is limited research available, but a small number of existing studies have identified a connection between these two factors. Intense physical exercise is linked to various unique alterations in brain state or function (Fu et al., 2014). There are several benefits that aerobic exercise has for brain skills (Klintsova et al., 2004; Swain et al., 2003; Xiong et al., 2009). It's also interesting to note that GABA is a well-known inhibitor of human vasopressin release (Chiodera et al., 1989). Intelligent and thoughtful researchers have been interested in this symbiosis between brain health and exercise in recent years. Because the nervous system is specifically designed for this kind of exercise, it may be possible to link the evolution of our brains to the increase in physical activity levels (Raichlen & Polk, 2013). There is mounting evidence that physical activity can positively impact brain function, particularly in the area of the central nervous system (Barha et al., 2016). Exercise itself has an endogenous influence on GABA which is found to increase its levels in central nervous system (CNS) and which as an autonomic consequence improves cognitive health. Studies on both human beings and animals indicate that GABA has the medicinal potential for lowering the impact of cognitive disorders as well as improving cognitive functioning and mood (Tinok et al., 2023). Imbalance of GABAergic neurotransmission may be a contributor not only in mood and anxiety disorders and even in epilepsy too (Perucca et al., 2023). Exercise's endogenous effects are currently being investigated as a necessary complementary treatment for improved health; beneficial physical, mental, and motor fitness for those desiring to perform better in their particular fields. Regular physical activity seems to improve cognitive behaviors that rely on underlying cortical neuroplastic mechanism (Cotman & Berchtold, 2002).

Aerobic exercise or activity has indeed been linked to improved neurocognitive function, as shown by Masley et al. (2009). As long as this neurocognitive performance aligns with executive functions, are crucial for enhanced athletic performance as well.

As natural as "mens sana in corpore sano," there is interactional relationship between physical fitness or health and cognitive health. This Latin proverb has come to mean, over time, that a sound body is the only thing necessary to create or maintain a sound mind. Actually, a number of observational studies have shown that individuals who are fit, exhibit better cognitive outcomes and less cognitive decline (Barnes et al., 2003; Heyn et al., 2004; Hillman et al., 2004; Larson et al., 2006; Lautenschlager & Almeida, 2006; Mummery et al., 2004; Roth et al., 2003; Singh- Manoux et al., 2005; Weuve, 2004).

The goal of this study is to explore the potential of exercise or physical activity as an intervention for better in cognitive health and prevailing GABA levels in human brain function. The literature on the GABA & exercise and sports & executive functions (EFs) is studied by the authors. Subsequently, the writers examine the research that

looks at how the intervention effects GABA levels and talks about how these changes could potentially lead to better performance in sports that require more concentration and focus. These findings collectively serve as the foundation for the final section, where the authors offer recommendations for further research in this field. -

Materials and Methods

Along with the updated (2020) elaboration, the Preferred Reporting Items for Systematic Reviews and Meta- Analysis Protocols (PRISMA-P) 2015 statement (Moher et al., 2015) was consulted and served as the framework for this review.

Operational Definition: The following definitions and the terms used in this review and have been followed throughout the paper.

Physical activity: Any type of skeletal muscle-driven physical activity that requires energy expenditure (Caspersen et al., 1985). It may consist of physical activity, interactive games, and sports initiatives.

Executive function (EFs): The terms “executive function” and “cognitive control” are also sometimes used interchangeably. The term pertains to an advanced level of cognitive functioning primarily regulated by the prefrontal cortex, specifically the frontal lobe. (Diamond, 2013).

Cognitive ability: Cognitive ability and intellectual functioning are related. It refers to the capacity of the human brain to process, store, and retrieve information as well as its capacity for memory, reasoning, and attention. (Shi & Qu, 2021).

Sports performance: Sports performance is a multifaceted term that combines biomechanical processes, psychological aspects, and the relevant skills. As a result of interactions between individual, environmental, and task characteristics, it is also prudent to say that sports performance is a composite trait. (Côté, et al., 2006).

Information Sources and Search Strategies: PubMed, Google Scholar, Science Direct, and the Web of Science were the electronic databases that were utilized for the literature search. The researchers themselves carried out the literature search. Search terms were used in combination like “Physical activity” OR “Exercise” OR “Yoga” OR “Sports” OR “Games” OR “Sports science” AND “GABA”.

Eligibility Criteria: Each study was subjected to the subsequent inclusion criteria: Only published in English, exclusively experimental studies, up to date publications (published by September, 2024), and study designs that evaluated the benefits of exercise, physical activity, or yoga-based interventions are the requirements for this category of articles. Physical exercise includes acute aerobic exercise i.e. a single bout of moderate intensity aerobic exercise performed on a cycle ergo meter for 30 minutes at a workload equivalent to 60% of maximal cardio respiratory fitness, graded exercise on a bicycle ergo meter to reach a target heart rate(HR) of $\geq 80\%$ of predicted maximum HR (220-age), high-intensity-interval training(HIIT), 12 week intervention based on either 60 minutes walking or yogic activities and session of a 60 minute yoga postures(anasanas).

Data Extraction: Examining the article titles, the researchers independently screened the articles. Together with the second, third and fourth reviewers (PP, PB and SC), the first reviewer (DR) examined the abstracts in addition to the titles to assess an article’s applicability to the subject. Following the researchers’ completion of the information extraction process, the qualitative data was verified for accuracy once more. The ensuing data was extracted: The information provided includes (i) the publication year and the nation of origin; (ii) methodological details, such as the study design, experimental context, sample characteristics, study duration, physical activity type, outcome measures, and instruments; and (iii) important revelations about the impact and efficacy of exercise

on the GABAergic pathway. Cross-referencing the bibliographies of the chosen articles allowed for the final identification of pertinent studies.

Results

Study Selection: By searching the databases, 37 articles in all were found. The remaining papers' titles and abstracts were checked for potential inclusion criteria after duplicates were eliminated. Just six studies fulfilled the inclusion criteria and were included in this review after a careful evaluation of the full-text publications which is reflected in 'Figure 1'.

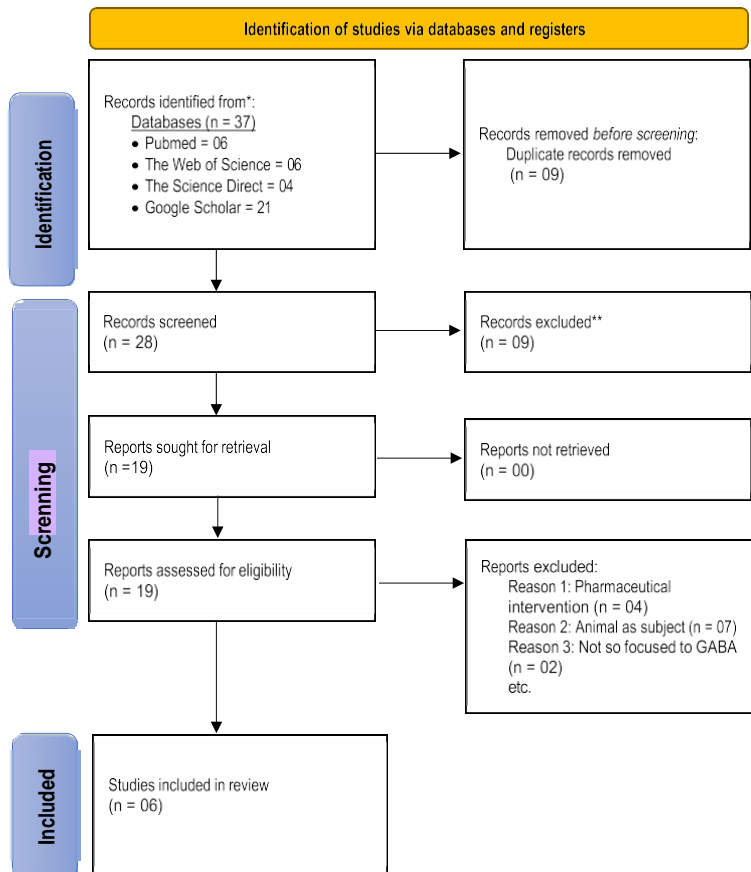


Figure 1. PRISMA 2020 flow diagram for new systematic reviews which included searches of databases only

Study Characteristics: The featured studies' attributes were highlighted in 'Table1'. Two articles are RCTs out of the six. The topic of one of them whether GABA levels, mood swings, and anxiety are unique to yoga or connected to physical activity was covered. In this study, participants aged 18 to 45 were recruited and the research was conducted in clinical settings within the United States of America (Streeter et al., 2010). The other one is based on the participants having Major Depressive Disorder compared to healthy control participants to evaluate the

Vagal-Gamma-Aminobutyric Acid theory (Streeter et al., 2018). In addition to the RCTs included in this analysis, three other studies examined the effects of yogasana or exercise on GABA levels. (Coxon et al., 2017; Maddock et al., 2016; Mooney et al., 2016). While the remaining one found only the prescribed yoga poses increased brain GABA levels by 27 %. (Streeter et al., 2007).

Measurement Protocol: The GABA levels were measured with a variety of instruments while Magnetic resonance spectroscopic imaging (MRSI) scans were utilized in the majority of RCTs and non-RCTs of this study to measure GABA levels (Streeter et al., 2010; Streeter et al., 2007).

Discussion

Recent research suggests brain health may be connected to maintain a steady balance between excitatory and inhibitory process. Cortical excitability must be carefully regulated between excitatory and inhibitory activity to ensure optimal brain function. This complex balance is modulated by inhibitory and excitatory neurotransmitters, especially GABA for inhibition and glutamate (Glx) for stimulation. Existing research literature indicates that physical activity can influence GABA levels. It may even help maintain or increase GABA concentrations in the brain (Novak et al., 2024).

Humans fall into one of those living species that produce GABA. It is synthesized from glutamate via the glutamic acid decarboxylase (GAD) enzyme requires PLP (the active form of vitamin B-6), as a cofactor. GAD enzymes have two forms: GAD 65 and GAD 67 controlled by GAD 1 and GAD 2 respectively. GAD genes perform a critical role in the brain releasing the inhibitory neurotransmitter GABA. GAD 65 and GAD 67 are found in axon terminals and cell bodies accordingly. Due to the presence of PLP acts as an allosteric cofactor for GAD enzymes and inorganic phosphate, phosphocreatine, pH levels, magnesium, adenosine triphosphate(ATP), GAD 65 function at a restricted fraction of its maximum catalytic ability. GAD expression is controlled at both the transcriptional and post-translational levels, and it is essential for maintaining the glutamate-GABA balance. GABA transaminase (GABA-T) found in glial cells removes released GABA from synapses and transforms it into glutamate, which contributes to the glutamine pool. Glutamine is transported from glial cells to the presynaptic terminal and transformed into glutamate. Subsequently glutamate is converted back into GABA by glutamic acid decarboxylase (Braga et al., 2024).

With regard to the effects of physical activities, such as yoga or exercise, on the level of GABA in the brains of apparently healthy individuals, the current study aimed to thoroughly evaluate all published RCTs and Non-RCTs that were included for this study.

In the brain, it serves as the principal inhibitory neurotransmitter and plays a significant role in the spinal cord as well. The research was also intended to present a summary of the available qualitative data on cause -and- effect linkages. In the end, the final analysis comprised only six studies. According to research, physical activity significantly improves the human brain's GABA level. Higher brain GABA concentrations as a result of this effect are correlated with better cognitive performance, which may have a positive impact on sports performance as a result of improved EFs. With regard to EFs neurotransmission that involves GABA, plays a role in working memory, attention control and inhibitory regulation. Changes in GABA levels have been associated with decision making skills, impulsiveness and difficulties with attention, particularly in those diagnosed with ADHD (Sideraki & Drigas, 2024).

Even though the results were based on a limited number of included studies, the current literature review generally affirms the benefits of physical activity. Anxiety and mood disorders are associated with decreased

GABAergic activity. Exercise and yoga are good for one's anxiety and mood. The researchers noted that elevated thalamic GABA levels are linked to improved mood and less anxiety (Mooney et al., 2016). It is widely accepted that physical activity has a positive impact on cognitive development. It complies with a study found that aerobic exercisers compared to control showed an overall rather than specific improvement in cognition (Jonasson et al., 2017). School going students in a review study reported improved cognitive function as a result of physical activity. Cognitive assessments took into account a variety of cognitive outcomes, such as executive functioning, working memory, and attention (Zeng et al., 2017). It is interesting to note that while some studies have reported that exercise and sport can improve EFs, many others have suggested that EFs is a prerequisite for peak athletic performance (Ball, 2022; Paul et al., 2024). A number of researchers have examined the correlation between EFs and performance in order to comprehend the significance of EFs for sports performance, especially in soccer and found a positive relationship between them (Huijgen et al., 2015; Verburgh et al., 2014; Vestberg et al., 2017). Young athletes with greater technical and tactical skill have shown improved inhibitory control (Verburgh et al., 2014; Huijgen et al., 2013). A crucial component of tactical performance, which is linked to the actions taken by both individual players and the team, is the players' capacity to choose and produce efficient responses to changing, unpredictable game conditions. (Mesquita, 1998).

It explicitly raises the possibility that increased cognitive flexibility may also be essential for improved sports achievement. Remarkably, Improved EFs, increased cognitive flexibility, and a higher level of GABA in the central nervous system may all co-exist with physical activity and exercise. Thus, GABA may prove to be a crucial neuronal marker in the future for identifying athletes who perform better in competition.

This is the rationale behind the priority of this literature review. There haven't been any reviews like this in this particular area yet. The effects of exercise and yoga poses on the GABA level in the brain have been the subjects of a few experimental studies. There was just two RCTs on the relationship between GABA levels in the human brain and physical activity in this current review.

The question is whether physical activity has a clear link with higher GABA levels in the brain and better cognitive function. The research has unequivocally demonstrated how physical or yogic exercise increases GABA levels. Increased GABA level is necessary for the control of emotions. Reduced symptoms of anxiety and depression and increased parasympathetic activity demonstrated by elevated heart rate variability (HRV) have been found to be linked to yoga based intervention (Streeter et al., 2010; Streeter et al., 2018). But the research using Long-Term Integrated Amrita Meditation (LT-IAM) and Short-Term Integrated Amrita Meditation (ST-IAM) as interventions showed dissimilar results. LT-IAM practitioners demonstrated greater GABA plasma level than the LT-Control group while ST-IAM practice significantly reduced anxiety and depression levels without affecting GABA plasma levels (Lozano Montes et al., 2021). It might be the subject of upcoming studies. However, four Non-RCTs were included in this study. Three of the four studies unequivocally show that the brain's GABA level has increased. (Coxon et al., 2017; Maddock et al., 2016; Streeter et al., 2007). Even so, distinct brain regions have shown elevated GABA concentrations. Whereas the other study did not identify any specific brain region and the remaining study did not attempt to measure GABA levels, two studies found cortical GABA concentration. The M1 GABAergic mechanism was shown here to be somewhat down regulated (Mooney et al., 2016). According to this study, it is not possible to identify which specific physical activity is in charge of a given region-based GABA concentration in the brain or to identify which kind of physical intervention is most appropriate for the higher level of GABA concentration. The researchers examined the literature associated to the different aerobic exercise or yoga intervention and GABA

as there is limited number of research works done on this topic. Although the present literature review provides an extensive and up-to-date analysis of the impact of physical exercise on the GABA level in the human brain, it is important to acknowledge certain limitations when interpreting the results. Initially, although there may be more unpublished and non-English research on the subject, the current review only included full-text publications written in English. Furthermore, given the paucity of empirical research, it is necessary to exercise caution when drawing conclusions about the beneficial effects of physical activity on the GABA level of the human brain. More research is therefore required.

Conclusions

This article reviews the results of various types of studies that, taken together, point to the possibility that physical activity interventions, which raise GABA levels in the human brain, may be useful in treating anxiety disorders, depression, and general cognitive decline. Exercise boosts neurogenesis and synaptogenesis while preventing neurodegeneration and the onset of depression (Pahlavani, 2024). These improved cognitive state usually denotes several mental capacities, including language, learning, reasoning, focus, attention and visuospatial functioning (Fisher et al., 2019). Exercise is an effective intervention for depression, both as a stand-alone treatment and as a supplement to improve emotional well-being, according to both RCT and non-RCT researches. Provided that there is sufficient proof to support the idea that engaging in regular aerobic exercise can improve a variety of EFs, even in healthy populations (Guiney & Machado, 2012). In conclusion, current review study suggests that exercise can be used either independently or in conjunction with other therapies, to improve cognitive function, EFs and sports performance simultaneously improving GABAergic mechanism and GABA concentration too.

Recommendations

An inquiry into how exercise affects GABA levels in the brain may support that there is a hypothetical triangle relationship among executive function, sports performance, and cognitive health.

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Table 1. Characteristics of the included studies.

Reference	Sample (Population)	Study design	Intervention	Study location	Context/Comparison with	Main results (Outcomes)
Mooney et al. (2016)	10 healthy young adults(3 females, mean age 23± 2 years, range 18-33 years)	Non-Randomized Controlled Trial	Single bout of moderate intensity aerobic exercise.	The University of Auckland	Ten healthy participants went through three experimental sessions.1 st session is for VO ² peak test. For the 2 nd and 3 rd session identical group is either for experimental intervention or control intervention.	A single spell of aerobic exercise with moderate intensity modifies primary motor cortex(M1) inhibition.Intracortical inhibition throughGABA _B path way may be down regulated followed by acute aerobic exercise.
Streeter et al. (2010)	The Yoga subjects (n=19) and the walking group (n=15).	Randomized Controlled Trial	Yoga intervention and walking intervention.	At Boston University School of Medicine General Clinical Research Unit.	Subjects were randomized to yoga or a metabolically matched walking intervention for 60 minutes 3 times a week for 12 weeks.	The study justified that increased thalamic GABA levels result in improved mood and decreased anxiety. The group assigned for yoga found positive correlations between changes in mood scales and changes in GABA levels.
Streeter et al. (2007)	Eight Yoga practitioners and Eleven comparison subjects.	Parallel-groups design.	A 60 minute yoga session and a 60 minute reading session.	At medical school-affiliated centers-Boston University School of Medicine, McLeanHospital, HarvardMedical School, Boston University School of Public Health and Boston V.A. Healthcare System.	Yoga group completed a 60 minute yoga session while the comparison group went through a 60 minute reading session.	The Yoga practitioner group underwent with 27% increase in GABA levels after the yoga session (0.20 mmol/kg) but the comparison subject group met no changes after the reading session (-0.001 mmol/kg) (t=-2.99,df=7.87,p=0.018).
Maddock et al. (2016)	Thirty –eight (22 females and 16 males) healthy, normal weight volunteers	Non-Randomized	Graded exercise on a bicycle ergometer with prescheduled duration and intensity.	University of California Davis Medical Center Sacramento,California 58179	MRS acquisition has been done with three different 'study' followed by the control 'study'.	Exercise induced with increased cortical GABA level. Exercise for an experimental group is here found to be a factor responsible for unlike brain state and a note worthy alterations in brain metabolism compared to sedentary group.
Coxon et al. (2017)	n=10 Right handed individual, eight male and two female.	Non-Randomized	Twenty minutes' HIIT exercise.	Monash University,Clayton;VIC, Australia	Magnetic Resonance Spectroscopy before and after twenty minutes of HIIT exercise.	The most of the participants experienced increased GABA concentration in sensory motor cortex.
Streeter et al. (2018)	Subjects with Major Depressive Disorder (MDD) and healthy control participants(HC) n=15+17	Randomized Controlled Trial	A 12-week yoga intervention	The Boston University Medical Centre	MEGAPRESS at 4 Tesla	Evidence of increased brain GABA linked to particular yoga poses and breathing techniques showed that participants with MDD were on par with those without depression.

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Team Sports and Executive Functions: A Comparative Observational Pilot Study

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PURPOSE: This study aimed to compare the executive functional ability among participants regularly practicing and participating in four different sports, including Cricket, Volleyball, Kho-Kho, and Kabaddi, and the active control group.

METHODS: This pilot study included 125 university youths aged 19-25 years. Twenty-five participants were selected for each of the four different sports disciplines, including Cricket, Volleyball, Kho-Kho, and Kabaddi, to meet the purpose of the study. Twenty-five active, healthy male participants served as the control group. Moreover, participants in the control group did not regularly engage in organized sports; however, they were all recreationally active and healthy. The Executive Functions (EFs) of all sampled participants were assessed using the Tower of London (TOL) and Stroop Color and Word Test (SCWT). Mean, standard deviation, one-way analysis of variance (ANOVA), and Tukey's honest significant difference (HSD) post-hoc tests were used for data analysis and interpretation.

RESULTS: One-way ANOVA demonstrated significant differences among groups in both tests; thus, the post-hoc Tukey's HSD test was conducted, which gave pairwise comparisons between and within groups. Pairwise comparison of the TOL test indicated significantly higher EFs in Kabaddi players than those in the Volleyball ($p < .01$), Kho-kho ($p < .05$), and the control ($p < .001$) groups; however, there was no significant difference between the Kabaddi and Cricket groups. The Cricket group demonstrated higher EFs than the control group ($p < .05$). The pairwise comparison results of the SCWT test indicated significantly higher EFs in Volleyball ($p < .001$) and Kho-kho ($p < .05$) players than those in the control group.

CONCLUSION: This study demonstrates that people involved in regular physical and team sports activities have higher EFs than non-trainer active control individuals.

Key words: Prefrontal cortex, Cognitive flexibility, Neurocognition, Executive function, Physical activity

INTRODUCTION

Executive functions (EFs) are commonly described as a set of high order cognitive processes controlled by the frontal and sub cortical areas, especially the prefrontal cortex of the brain. EFs develop and mature across the lifespan, slowly from childhood being less specialized, through adolescence with synaptic pruning processes up to early adulthood, characterized by complete maturation [1,2]. EFs comprise of basic cognitive processes such as inhibition [inhibitory control, including self-control (behavioral inhibition) and interference control (selective attention and cognitive inhibition)], working memory (WM), and cognitive flexibility which enhance some areas of the psychological domain such as reasoning, problem solving, planning, attention etc. [3-5]. The concept of executive programming and its links to the pre frontal lobe began appearing in

the mid-19th century [6], while the term was first used by Karl Pribram in 1973 [7]. These mental processes control the human goal directed behavior through three main dimensions which are working memory, inhibition and cognitive flexibility. In 1994 Kramer et al., did a breakthrough research on the inhibition behaviors and planning, task coordination, initiation and processing of semantic information. The relation between physical activity and cognition has been equated through several documented literatures, while the specific descriptors used to describe the subcomponents of executive function have been modified slightly in the physical activity literature and typically described as planning, scheduling, inhibition, and working memory [8]. There are multiple evidences that indicate a positive impact of physical activity and sports on EFs. Johannes W. de Greeff et al. [9], found positive effects for both acute physical activities as well as for longitudinal physical activity programs on ex-

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ecutive functions. Valentin Benzing et al. [10], reported that regular practice of physical activity acts as a therapy to increase the EFs even in neurodivergent children. Few other evidences claimed that continuous involvement in physical activity and sports helps in activation of the prefrontal cortex, cerebellum, and basal ganglia, which directly impact executive functioning through their complex motor tasks [11-13]. Several researchers have proposed that, different types of sports may influence EFs in terms of movement, motivation, and emotional enhancement, social interaction and cooperation [14-16]. Team sports may also be a resulting factor for better EFs [17]. Every team sport is played based on open skills in the form of a group, and they are otherwise termed as such.

In this present study authors included four team sports in which two (Kho-Kho & Kabaddi) are popular indigenous games (Indian) and other two (Cricket & Volleyball) are ball games which are popular across the globe. Based on the different distinctive patterns, movements and skills these four team sports players may need different level of EFs ability.

No study is performed regarding indigenous games (Indian) and cricket on EFs while very few studies were done on volleyball so far that is why the researchers have attempted so in the current study.

The purpose of the present observational study was to compare the executive functional ability among participants regularly practicing and participating in four different types of team games-Cricket, Volleyball, Kho-Kho, Kabaddi and the active control group.

METHODS

1. Participants

The researchers recruited a total of 125 subjects for this study. 25 subjects from each discipline i.e., Cricket (n=25), Kho-Kho (n=25), Volleyball (n=25), and Kabaddi (n=25) along with the group of subjects who were recreationally active and healthy were considered under the active control group (n=25). For the recruitment of the university level players, researchers and the university sports board jointly organized an orientation program and explained about the study, only willing players were considered and included in this study.

However, to form active control group the researchers distributed handouts to the different departmental students of the parent institute, Jadavpur University. Those who are willing to participate and fulfill the criteria of this study are asked to join in the experiment. All the willing subjects are asked to fill the individual consent form. Finally, five distinctive groups were formed through purposive sampling to meet the

purpose of experiment.

2. Location of the study

The study was conducted at the Exercise and Sports Physiology laboratory, Department of Physical Education, Jadavpur University.

3. Inclusion and exclusion criteria

Players who have university sports achievements in their respective fields and at least three year's regular active involvement in inter university level sports competition were considered as subjects in this pilot study. The age sex matched subjects aged between 19-25 years assigned for the control group who did not participate in any organized sport activities in regular basis, were all recreationally active and healthy individuals. All the subjects of this study were stayed in the hostel and also regular students of the university thus they followed a similar lifestyle in terms of biological clock and diet pattern.

4. Administration of test

For measuring executive ability, the researcher collected data by using Tower of London (TOL) test and Stroop Color and Word Test (SCWT) from verified online sources. The Tower of London test is usually used in applied clinical neuropsychology for the assessment of EFs [25].

The TOL test comprises of three wooden pegs of different lengths mounted on a strip of wood and three colored balls (red, green, blue) that are manipulated on the pegs to reproduce a pre-defined picture end state. However, there are some rules based on mental skills which need to be followed to complete the task, first of all subject can move only one ball at a time, secondly they cannot place the balls anywhere else other than the three pegs, thirdly subjects can only place three balls on the left peg, two on the middle peg, and one ball on the right peg to finally make the pre-defined pattern in a possible number of moves and time period. Number of moves of each level will be displayed in the upper right corner of the screen [18,19] (Fig. 1). In case of any error from the participants' end, the

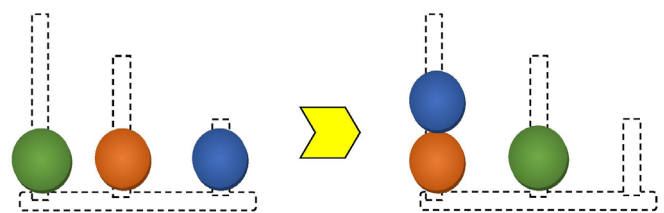


Fig. 1. Tower of London test.

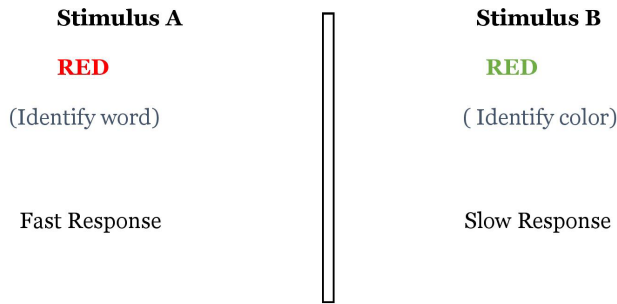


Fig. 2. Stroop Color and Word Test.

‘reset button’ helps to return to the starting position. After completion of all the levels, the final score displayed on the screen which will be considered as the final score of the participant. This test is widely used for measuring planning and problem solving ability of an individual.

SCWT is a neuropsychological test broadly used for both experimental and clinical purposes. Both represent the “jumble condition” in which participants are required to perform in response to congruent and incongruent stimuli. In congruent condition participants are asked to identify the word instead of colors. For example, the word ‘Red’ written in red color ink so in this condition participants are required to identify the word only. Conversely in incongruent condition participants are asked to identify the colors instead of words. For example, the word “Green” is printed in red ink. Thus, in this condition, participants are required to identify the name of the color ink instead of reading the word [20] (Fig. 2). Twenty levels are there and the complexity of the levels increases gradually. The SCWT is widely used to measure the Stroop effect [21], ability to inhibit cognitive interference; previous study also reported its application to measure other cognitive functions such as attention, processing speed, cognitive flexibility [22] and working memory [23]. In this present study the researcher collected data by using online verified tool. After collecting the numerical data researcher analyzed the data through descriptive and inferential statistics. Fig. 3, provides the detailed Trial Profile with the enumeration of the primary outcomes.

5. Statistical analysis

Tukey Honestly Significant Difference (HSD) [24] test was used to check the numerical normality and it was found that the data was normally distributed. Mean and Standard deviation were performed as descriptive statistics and One-way Analysis of Co-Variance (ANOVA) was computed as inferential statistics to compare cognitive outcomes of players involved in Cricket, Kho-Kho, Volleyball, Kabaddi games and the

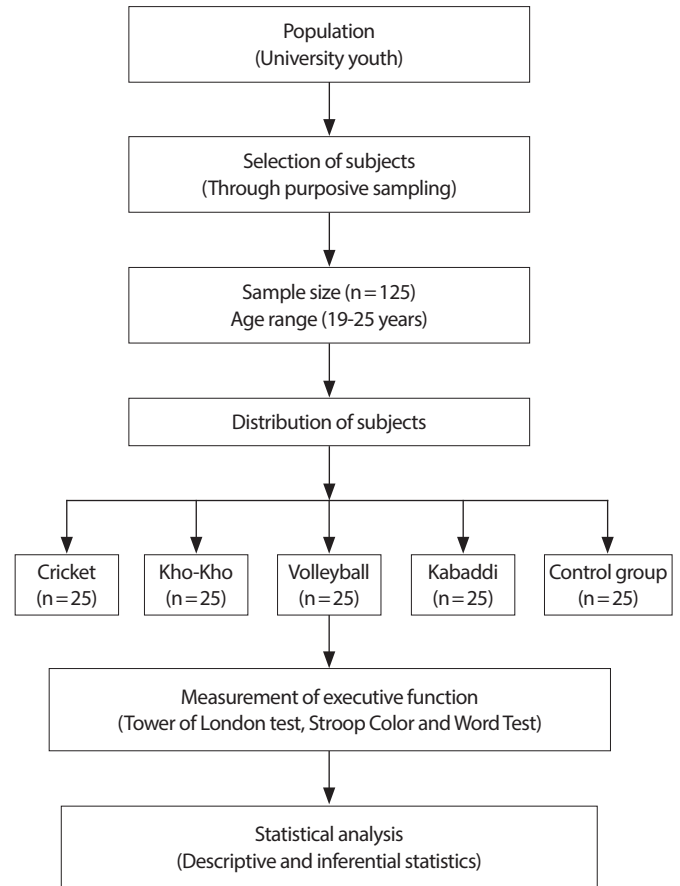


Fig. 3. Schematic diagram of Trial Profile.

active control group. In this present study independent variables were four different discipline of sports with age matched control group and the dependent variable were the obtained scores of EFs task measured through TOL and SCWT. The level of significance was set at $p \leq .05$.

RESULTS

Descriptive statistics and inferential statistics were performed based on the obtained data acquired through TOL test and SCWT of all Cricket, Volleyball, Kho-Kho, and Kabaddi and age-sex matched active control group which is shown in Table 1. Significant differences among groups were found in both tests through the One-way ANOVA thus *Post Hoc* Tukey HSD test was conducted which gave pair wise comparisons between and within groups detail as shown in Table 2. Pair wise comparison result of TOL test using Tukey HSD *Post Hoc* Test clearly indicates significantly higher EFs in Kabaddi players in comparison to Volleyball ($p < .01$), Kho-Kho players ($p < .05$) and the control group ($p < .001$) while there was no significant difference between Kabaddi and Cricket group. Cricket

Table 1. Descriptive and Inferential statistics of different group based on EFs test

	Tower of London test					Stroop Color and Word test					
	N	Mean	SD			Mean	SD				
Cricket	25	32.4	2.87			91.8	3.78				
Volleyball	25	30.6	3.25			93.8	2.18				
Kho-Kho	25	31.2	3.67			92.6	3.57				
Kabaddi	25	34	2.66			91.2	5.45				
Control	25	28.92	4.05			88.8	5.82				
Total	125	31.42	3.70			91.64	4.61				
Sources	Sum of squares	df	Mean square	F-Ratio	p-value	Sources	Sum of squares	df	Mean square	F-ratio	p-value
Between groups	364.68	4	91.17			Between groups	346.8	4	86.7		
Within groups	1,339.84	120	11.16	8.16	<.00001	Within groups	2,292	120	19.1	4.53	<.001
Total	1,704.52	124				Total	2,638.8	124			

Table 2. Pairwise comparison (*Post Hoc* Tukey HSD) between and within groups based on TOL and SCWT

Pairwise comparison of TOL			Mean difference	Q ₀₅ =3.9169 Q ₀₁ =4.7085	p Value	Pairwise comparison of SCWT			HSD ₀₅ =2.6176 HSD ₀₁ =3.1466	Q ₀₅ =3.9169 Q ₀₁ =4.7085	p Value
Group	N	Mean SD				Group	N	Mean ± SD			
Cricket	25	32.4±2.87	1.80	2.69	.32	Cricket	25	91.8±3.78	2.00	2.29	.488
Volleyball	25	30.6±3.25				Volleyball	25	93.8±2.17			
Cricket	25	32.4±2.87	1.20	1.80	.710	Cricket	25	91.8±3.78	0.80	0.92	.966
Kho-Kho	25	31.2±3.67				Kho-Kho	25	92.6±3.57			
Cricket	25	32.4±2.87	1.60	2.39	.44	Cricket	25	91.8±3.78	0.60	0.69	.988
Kabaddi	25	34±2.66				Kabaddi	25	91.2±5.45			
Cricket	25	32.4±2.87	3.48	5.21*	.003	Cricket	25	91.8±3.78	3.00	3.43	.11
Control	25	28.92±4.05				Control	25	88.8±5.82			
Volleyball	25	30.6±3.25	0.60	0.90	.969	Volleyball	25	93.8±2.17	1.20	1.37	.86
Kho-Kho	25	31.2±3.67				Kho-Kho	25	92.6±3.57			
Volleyball	25	30.6±3.25	3.40	5.09*	.004	Volleyball	25	93.8±2.17	2.60	2.97	.22
Kabaddi	25	34±2.66				Kabaddi	25	91.2±5.45			
Volleyball	25	30.6±3.25	1.68	2.51	.391	Volleyball	25	93.8±2.17	5.00	5.72*	.000
Control	25	28.92±4.05				Control	25	88.8±5.82			
Kho-Kho	25	31.2±3.67	2.80	4.19*	.02	Kho-Kho	25	92.6±3.57	1.40	1.60	.78
Kabaddi	25	34±2.66				Kabaddi	25	91.2±5.45			
Kho-Kho	25	31.2±3.67	2.28	3.41	.119	Kho-Kho	25	92.6±3.57	3.80	4.35*	.021
Control	25	28.92±4.05				Control	25	88.8±5.82			
Kabaddi	25	34±2.66	5.08	7.60*	.000	Kabaddi	25	91.2±5.45	2.40	2.75	.301
Control	25	28.92±4.05				Control	25	88.8±5.82			

Here the value of 'Q' indicates the significant result.

group demonstrated higher EFs in comparison to the control group ($p < .05$). On the other hand, pair wise comparison results of SCWT test using Tukey HSD *Post Hoc* Test clearly indicates significantly higher EFs in Volleyball ($p < .001$) and Kho-Kho ($p < .05$) players in comparison to the control group.

DISCUSSION

The present study aimed to compare the executive functional ability

among participants involved in Cricket, Volleyball, Kho-Kho, Kabaddi and the active controls. This study may be first time attempt where indigenous games (Kho-Kho & Kabaddi) and Cricket have been considered to be an intervention as a comparative model on university level players.

Existing research literature has exhibited participation in team sports, might show stronger associations with EFs than other types of sports and physical activity that require less cognitive engagement [25]. Studies with physical activity intervention have previously demonstrated that in case of

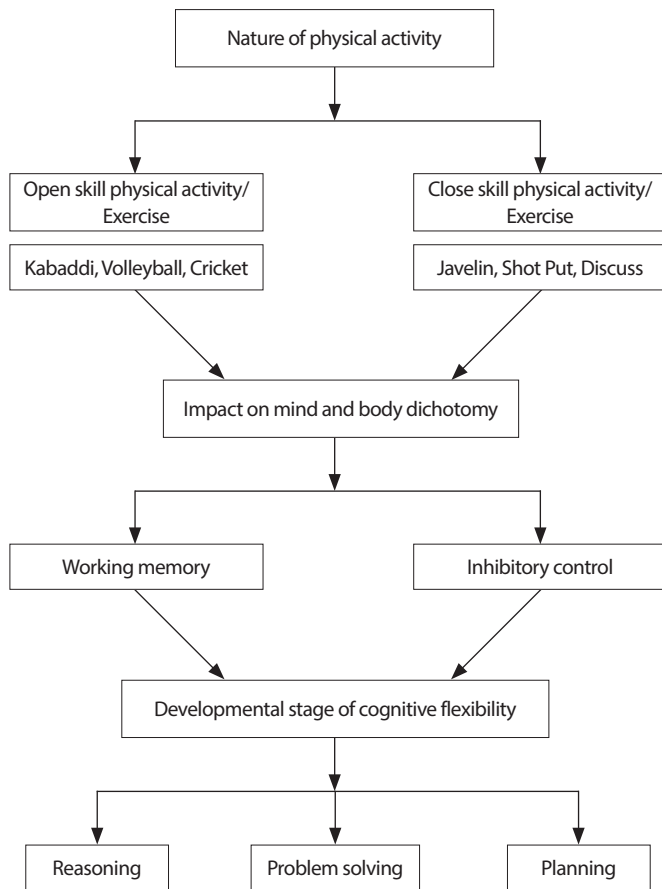


Fig. 4. The mechanism of EFs through physical activity and sports.

healthy children, adult, older population and even in ADHD children, regular practice of physical activity or involvement in sports has definitive positive effect on EFs. Few researchers have mentioned that development of EFs through sports activity rely on the movement involved in the activity [26,27]. Based on environmental impact on motor skills, motor skills can be classified as open or closed skills [28]. Team sports i.e., Football, Volleyball, Cricket, Kabaddi require to perform open skills which include complex cognitive process like attention, active decision making, perception, planning, strategy development, ongoing adaptability [28-30]. On the other hand, athletic events i.e., javelin throw, discus throw, shotput etc. closed skills which require lesser cognitive involvement, minimum variation of movements and are performed in a predictable environment [28,29]. People involved in open skills need to accommodate themselves in a continually changeable atmosphere and they are typically hypothesized with better EFs rather than those who involved in closed skills [29,31,32]. The mechanism of EFs through physical activity and sports has been shown in Fig. 4.

Soccer is a team sport as well as a ball game. It typically needs to be

performed with open skill implementation. Previous research work on EFs on soccer player highlighted increased EFs [33]. It may relate with the other open skill team sports as well. Research work of EFs on elite volleyball players represented minimal degree of cognitive flexibility for highly specialized athletes and a maximum level for spiker outside hitters [24].

In this study, a significant relationship was observed between team sports practitioners and EFs. The sum up, based on the result in this study through TOL and SCWT measurement clearly indicates that, people involved in sports and physical activity have higher EFs than the active control group. The limitations being if the measurement of sedentary individuals could have given a more clear understanding about the importance of physical activity or sports activity and EFs. The sociodemographic status of the participants was not considered in this study. The present study was conducted on 125 subjects, a larger sample size with more sports disciplines may be measured in the future, to give a more specified result.

CONCLUSION

The findings of the present study highlight the development of EFs through physical activities and team sports. Positive and significant relationships have been drawn within the limitations of this study; between team sports activities and EFs. This study demonstrate that people involve in Kabaddi game have comparatively higher level of EFs than other three team sports (Kho-Kho, Cricket, Volleyball). Simultaneously the study indicated athletes of every included team sports have comparatively greater EFs than the control group. In short it is clearly signified that people involved in team sports activities have higher inhibitory control, self-control and cognitive flexibility compared to the non-trainer controls.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

Conceptualization: S Chatterjee; Writing Original draft: P Paul; Review and Editing: P Bhattacharya, D Roy.

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Impact of exercise on brain neurochemicals: a comprehensive review

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Abstract

Background Physical activity influences neuro-cognition through organic and peptide molecules of the brain. The organic molecules constitute neurotransmitters and neuromodulators while the peptide molecules include neurotrophic factors. Regular exercise, when repeated overtime, may cause the baseline neurochemical level to rise or fall and help in improvement of neuro-cognition. Several outstanding reviews have summarized these findings; however, the neurobiological basis of these results has received less attention.

Aim To explore the emergence and effects of physical exercise on three signaling pathways i.e., the neurotransmitters, neurotrophins and neuromodulators.

Methods To fulfill the purpose of the study, several robust literatures were reviewed based on the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA). Studies that directly matched and fulfilled the primary objective were screened, appraised and presented in a systematic and comprehensive manner.

Results Chronic exercise and long-term training showed exponential rise in all the three types of neurochemicals. While aerobic and graded exercise depicted linear rise in neurotransmitters and strength, training showed no significant changes in neurotrophins.

Conclusions The comprehension of exercise and its positive effect on neurochemicals in the improvement of neuro-cognition, neurogenesis and brain functions have been pooled in this study. Single bouts of exercise have been given equal pertinence as chronic exercise in development of a complete psychophysiological well-being. This review magnifies that aerobic exercise of moderate intensity when performed in a regular and precise way improves all three classes of neurochemicals and modulates mental health and wellness.

Keywords Physical exercise · Neuro-cognition · Neurotransmitters · Neurotrophins · Neuromodulators

Introduction

Constantly growing evidence confirms that physical activity or exercise is the most effective way to bring about a healthy body and mind. It is a well-documented fact that the synergetic role of exercise and a proper diet help maintain a body free from metabolic and non-communicable diseases.

However, comprehensive exercise to enhance brain health is now an ongoing research area since a few years [1]. Pioneer studies of the past have elaborated on the expression of neurochemicals in the improvement of brain function and cognition in animals with regular movement, similar benefits of exercise and its effect on neurochemicals in the human body are being demonstrated since few years now [2]. Physical exercise is associated with the synthesis and release of several brain chemicals which help enhance various brain functions [3].

This comprehensive study provides a review of the human intervention literature and examines the influence of physical activity, exercise and fitness training on cognition, mental well-being, brain structure, and brain function through the release of (1) Neurotransmitters, (2) Neurotrophins and (3) Neuromodulators. There are several neurochemicals released in the brain as a result of physiological changes in response

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to exercise [4]. The proper communication between the neuromuscular junctions, synapses and production of lactate during exercise acts as underlying precursors which enhance neurochemical release [5].

This comprehensive review highlights the influence of exercise on monoamine metabolic systems, catecholamines [6] and the improvement in neurogenesis, vasculogenesis and synaptogenesis through exercise-induced neurotrophin release [7]. Metabolic and anti-oxidative reserves are positively improved with release of exercise-induced neurochemicals and neuromodulators [8]. Thereby this review in a nutshell elaborates the effects of physical exercise on the synthesis and release of various neurobiological chemical secretions of the brain in the human population (Figs. 1 and 2).

Existing body of knowledge and provocation of thought

The present available literature on acute and chronic exercise and its relation to feedback, regulatory, modulatory, cellular and physiological mechanisms of the brain, are quite scattered and expressed in various pockets but never comprehensively compiled in a collective manner. There are elaborate studies or original articles on each of these neurochemicals, implicating their individual relationship with physical exercise. Moreover, explicit scrutiny of accessible literature showed that a mechanistic model on the effects of physical exercise focusing on the major classes of neurochemicals could be initiated. Thus, the thought to conduct a

comprehensive review to understand the effects of physical exercise on three major neurochemical groups arose.

Purpose of this review

The ultimate purpose is to summarize the effects of different types, intensities and duration of exercise on brain neurochemicals through the following three perspectives:

1. To understand the exercise mediated effects on brain functions through neurotransmitter release.
2. To recognize the neurotrophic effects of physical exercise and their role in neurogenesis.
3. To realize the effects of physical exercise on neuromodulators and their role on brain health.

Methods and acquisition of evidence

Methodical analysis of reviewed literature, suggests robust effects of physical activity on cognition and well-being. This review systematically draws out various studies on the effects of physical activity and neurochemicals based on the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines [9]. The extracted studies were checked for eligibility and tabulated using the Population, Interventions, Control, Outcomes and Study Design (PICOS) guideline [10, 11]. A total of 58 studies were obtained which were tabled under three sub headings fulfilling the objective of the study.

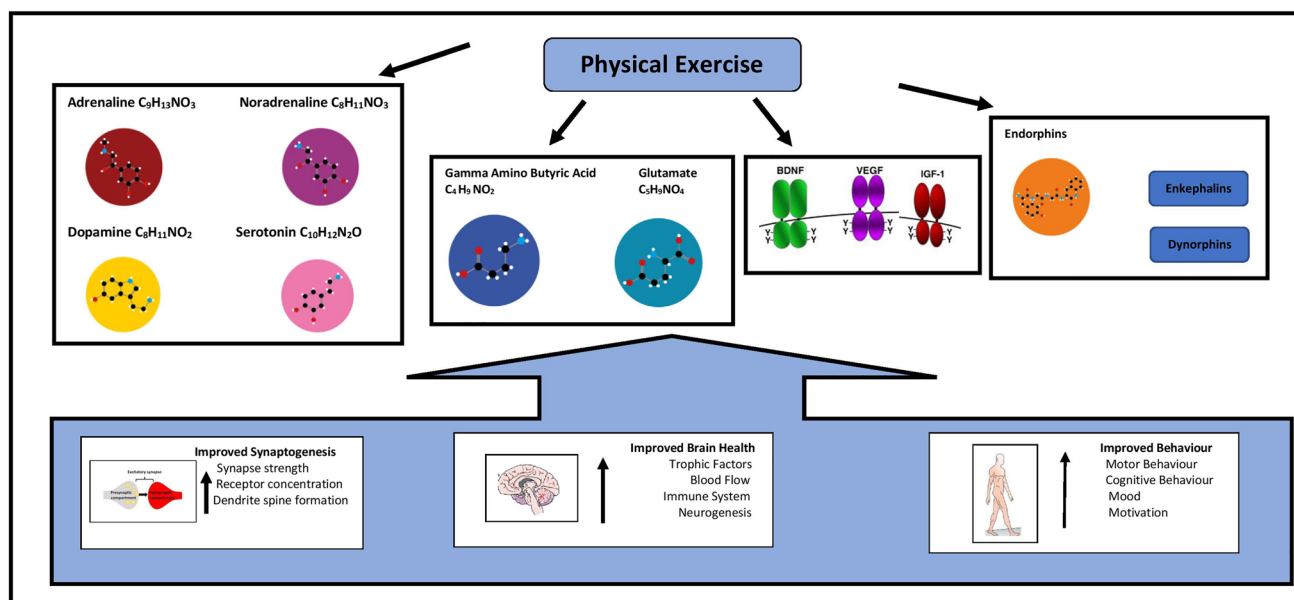
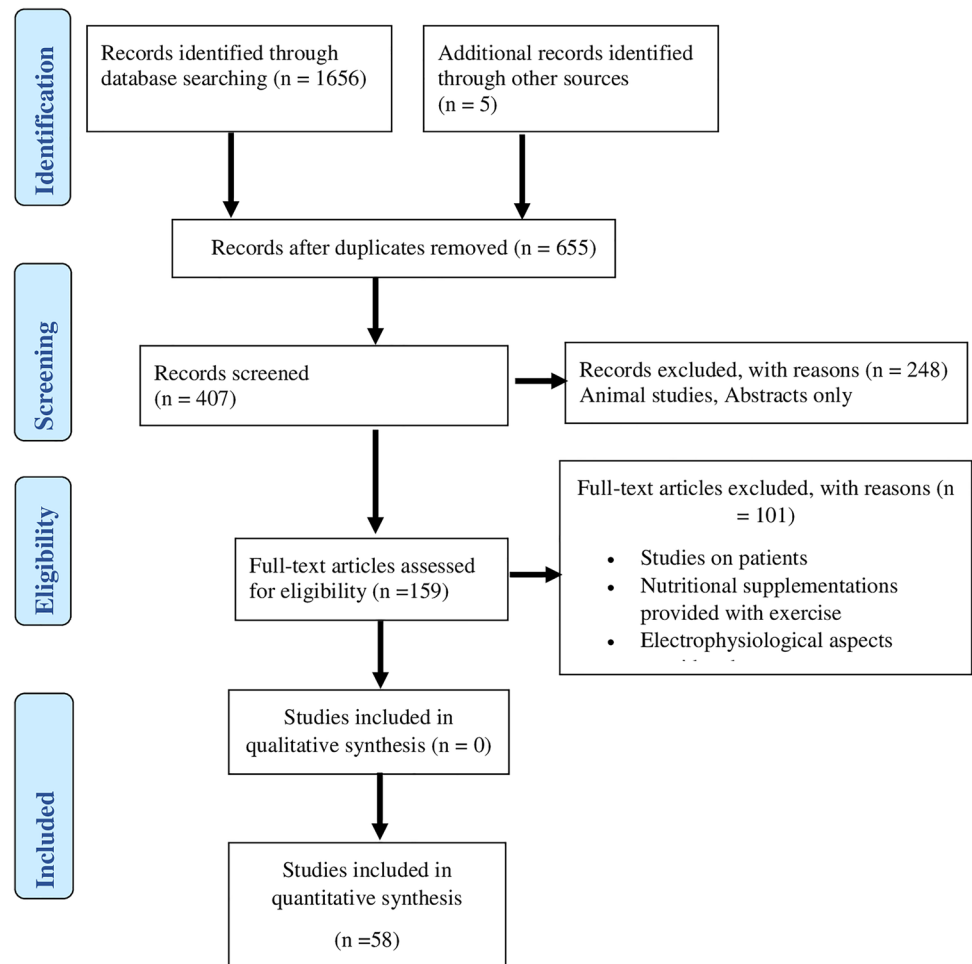


Fig. 1 Interplay between neurochemicals and physical exercise with its effects

Fig. 2 PRISMA flow diagram



Inclusion and exclusion criteria

Studies that met the eligibility criteria based on Population, Interventions, Control, Outcomes and Study Design (PICOS) were incorporated in this review study [10, 11]. Research studies conducted on healthy population; (P) with physical exercise as the intervention either immediate or long term of different intensities; (I) incorporated on active individuals and control groups of different ages and gender; (C) that evaluated the levels of neurotransmitters, neurotrophins and neuromodulators (O) were selected. Randomized control trials or non-randomized control trials were the selected designs (S). Articles published only in English language and on human subjects were included while animal studies were not considered. Only full test papers were included so that the mechanisms could be clearly studied. Articles with studies on brain injured or diseased patients were not included.

Literature search and data extraction

During the review designing stage, all the probable search terminology and keyword combinations were tested. The methodological plan of the present study was to search and analyze previous studies that investigated the effects of physical exercise on various neurochemicals of the human brain. The bibliographic searches were conducted by two researchers (P.B and D.R), in the following databases: PubMed, PubMed central, Web of Science, Scopus, Sport Discus and Cochrane Central Register for Controlled Trials until September 2022. The keywords used to find the various articles included: “physical exercise”, “physical activity”, “graded exercise”, “exercise”, “training”, “fitness”, “cognitive functions”, “cognition”, “neurochemicals”, “brain chemicals” and also the names of all the chemicals individually. The two researchers (P.B and D.R) thoroughly read the titles and abstracts to decide

on selecting the studies after which a complete scanning of the selected papers was conducted, blindly. The data extraction was conducted keeping the purpose of the review in mind and all the differences in opinion were resolved by a third researcher (S.C). Reference lists of the articles selected were also checked for eligibility.

Mechanism and observations

The underlying physiological mechanistic benefits of regular exercise, training or physical activity on the three sets of neurochemicals have been elaborated below. A total of 58 studies were selected based on the eligibility criteria and presented in three tables. Table 1 constitutes studies on the impact of physical exercise on neurotransmitter release, Table 2 pooled exercise effects on neurotrophins, while Table 3 explored exercise effects on neuromodulators.

Neurotransmitters and their mechanism during exercise

Body's chemical messengers which help develop a better communication of the brain with the rest of the body are called the neurotransmitters. These help in enhancing the muscle–neuronal pathways through the synapses [12], in the development of motor acquisition, muscle memory and neuro-protection for healthy aging [13]. It has been reported that enriched environments like physical exercise, stress free surrounding, etc. help the neuromuscular junctions to function more efficiently [14].

The release of neurotransmitters during exercise is based on the structural role of communicators and some precursor substances like lactate. Lactate is an organic molecule which is mainly produced when the body breaks down carbohydrates in the tissues to produce energy. Studies on various animals and humans have shed light on this important metabolite that is released from muscle cells during and following intense physical exercise [15]. Lactate is able to cross the blood–brain barrier, made by astrocytes of the brain, and can be used as an alternate energy source to glucose. It has been implicated in memory processes, and neuronal plasticity [16, 17]. In the brain, lactate serves as a precursor to glutamate, which is the main excitatory neurotransmitter [18].

Exercise-oriented fatigue, also causes changes in the central nervous system, which arise from the proximal regions, and moves to the neuromuscular junctions [19]. The monoamines serotonin (5-Hydroxytryptamine; 5-HT), dopamine (DA), and noradrenaline (NA) play a key role in signal transduction between neurons during such changes [20]. Let's take a deeper look at these neurotransmitters.

Glutamate and gamma amino butyric acid (GABA)

Inhibitory GABA and excitatory glutamate work together to control many processes, including the brain's overall level of excitation. Glutamate and GABA do not cross the blood–brain barrier and must therefore be synthesized within the central nervous system [21].

From various observations on brain carbohydrate metabolism, electrophysiology, and cortical excitation–inhibition balance, it can be seen that physical activity leads to an expansion of the tissue pool of glutamate and GABA, causing increased neuronal activation when compared to the sedentary state individuals [22]. This may also take place by up-regulation of genes which control glutamatergic system and synaptic plasticity [1]. It has also been reported in recent studies, that the astrocytes and glial cell functions are potentiated with regular exercise; this morphological change may also be a contributor in increasing neurotransmitter pooling to enhance hippocampal plasticity and growth [23]. However, most of the studies are on animal models and scarcely on human populations.

Catecholamines

Catecholamines contain a nucleus and a catechol group also called the benzene group with two hydroxyl assemblies, an ethylamine side chain and a single amine group. These catecholamines are synthesized at the nerve terminals and the cell bodies of the neurons. Tyrosine hydroxylase (TH, tyrosine-3-monoxygenase) catalyzes the conversion of its substrates tyrosine and molecular oxygen to 3, 4-dehydroxy-1-phenylalanine (L-DOPA). It is the most important enzyme in catecholamine synthesis, being the initial and rate-limiting step in the synthesis of Dopamine, Nor-epinephrine, and Epinephrine. The catecholamine exists in low (micro-molar) concentrations in the brain in regard to neurotransmitters, such as Glutamate and GABA. However, catecholamines have considerable importance in the regulation of multiple aspects of the central nervous function and are vital therapeutic targets. The mechanism of synthesis of monoamine catecholamines is known to be modulated by exercise both peripherally and centrally. In the brain, these neurotransmitters when released innervate the noradrenergic and dopaminergic pathways, which in turn innervate the hippocampus, amygdala, dorsolateral prefrontal cortex and the basal ganglia. These are all found mainly in the substantia nigra and ventral tegmental regions of the brain involving cognition and memory functions [24].

Dopaminergic cells are found in two nuclei of the mid brain–substantia nigra and the ventral tegmental nucleus. The neurons of these cells project in three pathways the nigrostriatal pathway, the meso-cortical pathway and

Table 1 Pooled Evidence of Effects of Exercise on Neurotransmitters

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
1. Hartley et al. [33]	Subjects: seven male age: 20–24 years Mean age: 21 years Mean height: 176cms Mean weight: 70.1kgs	Pretest posttest design	After the pre-training tests were completed, the subjects participated in a 7-week training program consisting of 3-h sessions of distance running, basketball, and volleyball on three mornings per week. Heart rates which were spot checked during the sessions end	Rest vs mild vs moderate vs heavy exercise	Norepinephrine levels did not change from resting values ($2.0 \pm t$ 0.38 (mean and SE) pg/l during mild work, but the concentrations increased slightly at moderate loads (2.5 zt 0.2 l) and still further with heavy exercise (4.0 zt 1.11) Cortisol and epinephrine became elevated above resting values only during the heavy work	After physical training, lower plasma norepinephrine responses to moderate and heavy work and higher insulin levels at all loads were observed. Many of the changes which result from physical conditioning may be mediated through the endocrine system Plasma hormones;
2. Winder et al. [34]	Subjects: Six healthy male subjects Age: 30 ± 1 years	Longitudinal study	Intervention: seven-week endurance training on bicycle ergometer six five-minute bouts of pedaling workloads that elicited the VO2Max by end of each bout Each work load separated by two mins of rest. On alternate days running at a pace, they could maintain for 40 min (5–8 kms)	Pre-training vs post-training	Plasma NE reduces from pre-training levels $2.95 \pm 0.32 - 1.60 \pm 0.09$ ng/ml Plasma E reduces from pre-training levels $0.53 \pm 0.13 - 0.14 \pm 0.03$ ng/ml	Study demonstrates that the plasma catecholamine response to exercise is less after training The major adaptation occurred within three weeks after the start of training

Table 1 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
3. Winder et al. [35]	Subjects: healthy male $n=6$ Age: 30 ± 1 years Weight: 81 ± 5 kgs	Pre-test post-test design	Intervention: 9 weeks Endurance training Alternate on bicycle ergometer and running Six five min bouts of pedaling workloads that initiated Maximal O ₂ consumption at the end of each bout separated by 2 min rest Alternate days subject ran at a pace 3–5 miles for 40 min. Daily workloads kept constant for four weeks, after which the capacity was increased to levels that elicited VO ₂ Max Exercise test: At 3-week interval during the training, participants performed an exercise test to a 90-min bicycle ergometer at 58% of initial VO ₂ Max, as well as at the beginning of the training program to fix the VO ₂ Max levels for the subjects	Sub-maximal exercise vs maximal training	Pre-training plasma Epi increased from resting values of 0.08 ± 2 ng/ml to 0.64 ± 0.04 at the end of the 90-min exercise bout. Plasma nor-epinephrine e increased from 0.26 ± 0.05 ng/ml to 1.81 ± 0.40 during this long-term bout of exercise The catecholamine response was much lower after training	Training induced reduction in catecholamines levels. Maximal adaptation and reduction within 3 weeks of training

Table 1 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
4. Lehmann et al. [36]	Subjects: Twelve healthy male Non-trained subjects <i>n</i> = 6 Age: 27 ± 2 years Marathon runners <i>n</i> = 6 Age: 32 ± 5 years	Pretest posttest study	Interventions: Graded treadmill exercise with initial running velocity <i>v</i> = 8 km.h/l (5% slope) To individual exhaustion by 2 km.h/l steps after a 3-min running period with a break of 30 secs	Non-trained vs Marathon trained	Endurance trained subjects show lower plasma noradrenaline levels during exercise and a higher adrenergic receptor density than in non-endurance trained subjects (<i>P</i> < 0.01) No significant differences in plasma catecholamines occurred between the groups before and during moderate exercise, and at exhaustion	Correlations between the exercise-induced catecholamine responses the VO2Max uptake
5. Fleg et al. [37]	Subjects: 24 Male only Age: 22–77 years Group I: 22–37 years Group II: 44–55 years Group III: above 65 years Weight: (kgs) 92.7 – 0.25 (age) <i>R</i> = 0.42 <i>P</i> = 0.05		Intervention: Motor-driven treadmill at constant speed of 3.5mph (except for three subjects aged 72,72,74) their modified speed was 3 mph and 2.5 mph respectively Modified Balke Protocol – treadmill inclined by 3% every 2 min starting from the level until the subject was exhausted	Rest vs. Maximum exercise in the three age groups	Although HR increases linearly with progressive exercise loads, both E and NE increase exponentially Both plasma E and NE overshoot post-exercise	Concluded that exercise mediated increase in plasma catecholamine concentrations appears to be exaggerated in the older subjects during maximal and sub-maximal exercise even after normalization for relative effort
6. Brooks et al. [38]	Subjects: 10 Males: 10 Age: 32.3 ± 10.6 years Weight: 71.3 ± 6.9kgs	RCT	30 s sprint on a non-motorized treadmill	Pre- vs Post-exercise	7 fold increase in AD from 0.2 + 0.2 to 1.4 + 0.6 n mol.l ⁻¹ Six fold increase in NA from 2.2 + 0.6 to 13.4 + 6.4 nmol.l ⁻¹ β-endorphin given in Table 3	Anaerobic metabolism, duration of exercise and sympathetic tone play an important role in this increase in AD and NA
7. Schwarz et al. [39]	Subjects: 10 Males: 10 Age: 25.7 ± 2.9 years Weight: 69.8 + 5.6	RCT	Cycle ergometer first step 50 W increasing by 50 W every 3 min until volitional exhaustion Intensity of exercise at 63% VO2 max Duration: 89 ± 15 min		The catecholamines A and NA increased linearly during exercise	Intense endurance training increases β-endorphin and has a positive effect only when duration of exercise is beyond one hour

Table 1 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
8. Rogers et al. [40]	Subjects: Nineteen males 10 well-trained males 9 minimally trained males Minimally trained subjects: Age: 28 ± 5 years Weight 76 ± 1 kgs Training: $6,212$ kJ/week Well-trained subjects: Age: 33 ± 7 years, weight: 73 ± 1 kg Training: $27,796$ kJ/week		Treadmill and Bicycle ergometer were kept as options for training. Treadmill exercise started at 3.75 mph and 2.5% elevation for a 4-minute warm-up period, followed by increase in elevation or speed was increased every minute until volitional fatigue Cycle ergometer exercise started at 50 W (306 kmp/min) for four minutes These exercise testing sessions were conducted twice once in winter and once in spring	Minimally trained vs well-trained subjects	Free NE excreted in urine: Minimal trained: Rest: 0.44 ± 0.03 4 min exercise; 0.73 ± 0.07 Max exercise: 4.14 ± 0.38 (ng/ml) Well trained: Rest: 0.56 ± 0.05 4 min exercise: $0.90-0.11$ Max exercise: 5.86 ± 0.72 (ng/ml) Free E excreted in urine: Minimal trained: Rest: 0.05 ± 0.01 4 min exercise; 0.10 ± 0.02 Max exercise: 0.63 ± 0.14 (ng/ml) Well trained: Rest: 0.09 ± 0.02 4 min exercise: 0.17 ± 0.05 Max exercise: 1.03 ± 0.23 (ng/ml)	During exercise training, pre-junctional receptors could develop increased sensitivity to catecholamines to achieve catecholamine excretion similar to pre-training levels

Table 1 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
9. Kohrt et al. [41]	Subjects: 106 older adults 24 younger adults Age: Older group 64 ± 1 yr Younger group: 24 ± 1 yr		Intervention: After 12 h fasting at 7am all subjects were kept at 30 min supine lying, followed by 10 min standing Treadmill for 15 min with 75–80% VO2max intensity based on the Maximal Exercise test all the subjects underwent to maintain the age-based VO2max range for the subjects	Resting vs Sub-maximal exercise in older vs younger group	Basal NE and E levels no significant difference between older and younger adults NE response to standing was exaggerated in older adults: (696 t 39 vs. 512 t 61 pg/ml; $p < 0.05$), whereas NE and E responses to exercise requiring -78% of VO ₂ max were attenuated in older adults: (NE: 1,444 t 74 vs. 1,983 t 222 pg/ml; E: 109 t 10 vs. 228 t 29 pg/ml; both $P < 0.01$) Increments in NE and E during exercise were more closely associated with age (NE: $r = -0.38$; E: $r = -0.46$; both $P < 0.05$) and VO ₂ max (NE: $r = 0.43$; E: $r = 0.52$; both $P < 0.05$) than with adiposity (NE: $r = -0.29$; E: $r = -0.25$; both $p < 0.05$)	The results show that (1) compared to young, older people have a blunted catecholamine response to exercise at a given relative intensity, and (2) exercise training results in a marked reduction in metabolic and hemodynamic stress during exercise at a given absolute intensity in older people
10. Greiwe et al. [42]	Subjects: 9 Males: 3 Females: 6 Age: 28 ± 8 years	Pre-test post-test study	Intervention: 10-week training and fifteen-minute treadmill exercise bouts performed at 60, 65, 70, 75, 80 and 85% of VO ₂ Max before and after training	Trained vs Untrained states of the same subjects	Plasma NA concentrations increased significantly with increase in exercise intensity (60–85%) of VO ₂ Max Plasma A response Plasma Epi response to exercise too showed an increase with increase in exercise intensity. However, the increase was not significant	NE release from sympathetic nerve endings is not parallel to the release of Epi from the adrenals with increase in intensity of exercise NE response is mediated by large muscle group activity and higher work rate after exercise

Table 1 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
11. Strobel et al. [43]	<p>Subjects: Seventeen male healthy adults with 4-7years. of training</p> <p>Anaerobically trained subjects:(ANTA)</p> <p>$n = \text{nine}$</p> <p>Age: 23.1 ± 2 years</p> <p>Height: 185 ± 6 cms</p> <p>Weight: 73.7 ± 6.1 kgs</p> <p>Aerobically trained subjects: (ATA)</p> <p>$n = \text{eight}$</p> <p>Age: 23.8 ± 2.7 years</p> <p>Height: 181 ± 7 cms</p> <p>Weight: 70.0 ± 4.8 kgs</p>	Pre-test post-test study	<p>Interventions: Three treadmill exercise tests and one SX test, exercise started at running speed of 8 km.h-1 for 3 min and increased to 2 km; h-1 every 3 min until exhaustion</p> <p>Second exercise test at 8% inclination at three submaximal workloads of 5 min duration (45%, 60% and 75%) of aerobic threshold</p> <p>SX test at 8% inclination at running velocities corresponding to 116% VO2Max (ATA) and 140% VO2Max for (ANTA)</p> <p>Tests was preceded by a 30-min warm-up</p>	Aerobically trained vs Anaerobically trained	<p>Results showed that plasma NE increased 80-fold in ANTA and 70-fold in ATA 1 min after SX test in comparison to pre-start values and two hours later returned to prestart values. The increase in plasma NE 1 min after SX was about 29% higher in ANTA than in ATA ($P < 0.034$)</p> <p>Plasma EPI increased 40-fold in the ATA and 50-fold in the ANTA plasma 1 min after exercise compared to pre-start values, after 2 h of recovery the plasma EPI returned to normal values. The increase in plasma EPI between the groups after exercise was significantly higher in ANTA than in ATA ($P < 0.009$)</p>	Results conclude that increments in Plasma NE and EPI with SX is significantly higher than ANTA and ATA which was related to maximal accumulated oxygen deficit and blood lactate concentration

Table 1 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
12. Jacob et al. [44]	Subjects: Nineteen female adults Untrained Group (UT) <i>n</i> = 6 Endurance Trained group (ET) <i>n</i> = 7 Sprint Trained Group (ST) <i>n</i> = 6	Pre-test post-test study	Intervention: 2 days Day 1: 5 min warm-up, continuous progressive treadmill protocol for VO2Max determination, after warm-up speed increased by 2 km.h ⁻¹ every 2 min until the subjects were exhausted On D2, two days after D1 but no more than a week later, velocity test was performed 6 s against load supramaximal bouts on bicycle ergometer increased by 1 kg until inability to pursue further, with 5 min passive recovery between groups followed by Wingate test the same day after a 30 min recovery	Untrained vs Endurance trained vs Sprint trained	Maximal plasma adrenaline (Amax) and noradrenaline concentrations determined just after the Wingate test were greater by 5–eightfold and 7–10 respectively than the resting values and also significantly greater than warm-up in the three groups, however the Amax, NAmax and the ratio between the two was not significantly different between the three groups	The researcher concludes the comparison with male studies the female results no difference on the catecholamines dependent on the training status or intensity Thus, training has no effect on catecholamine responses to supramaximal exercises and thus sex differences in response to training do occur

Table 1 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
13. Jacob et al. [45]	Subjects: Nineteen male Middle distance runners' subjects: six Long distance runners' subjects: six Untrained subjects: Seven	Pre-test post-test study	MDR training program consisted of aerobic and anaerobic training sessions. MDRs trained for maximal speed running (anaerobic training: once a week), prolonged sprint (anaerobic training; twice a week) and undertook aerobic training three times a week to increase their maximal oxygen consumption (V_{O2max}). In contrast, LDRs undertook only aerobic training sessions three times a week to increase their V_{O2max} and maximal aerobic capacity	Long distance runners vs middle distance runners vs untrained subjects	Concerning the plasma catecholamine concentrations in response to exercise, MDR and LDR Amax values [3.73 (1.53) nmol l ⁻¹ , 3.47 (0.74) nmol l ⁻¹ , respectively, for MDR and LDR] were significantly greater than those of UT [1.48 (0.32) nmol l ⁻¹] who also exhibited the lowest NAmax values [11.09 (6.58) nmol l ⁻¹] compared to MDR and LDR [20.43 (3.51) nmol l ⁻¹ ; 15.85 (4.88) nmol l ⁻¹ , respectively, for MDR and LDR]	These results suggest that long-term endurance training can enhance plasma catecholamine concentrations in response to supramaximal exercise. However, as there were no significant differences between MDR and LDR Amax and NAmax values, the effect of the intensity of training remains to be clarified

Table 1 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
14. Botcazou [46]	Subjects: Twelve adolescent girls Training group: TG <i>n</i> = 6 Control group: CG <i>n</i> = 6	Longitudinal study	Interventions: 6 sprint test Day 1: Cycle ergometer on which sprint trails of 6 s against loads increased by 1 kg after each trail until the subjects were exhausted 5 min resting periods was allotted between successive trails Day 2: After a stipulated break-fast warm-up for 15 min at 50% of VO2Max, after 3 min of recovery the 6 s sprint test was performed, the cycling was done at the same load as on Day1, the velocity and power was recorded TG group performed in sprinting training program for 6 months at 3 days/week while CG group performed their normal daily work the 6 s sprint test was performed before training (P1) after training (P2) and after detraining 5 months later (P3)	P1 vs P2 vs P3	TG Group warm-up induced a significant increase of A concentrations only P2 (<i>P</i> < 0.05) Plasma A concentrations obtained after 6 s-sprint test (AEX) were significantly higher from resting concentrations only in P2. Moreover, they were higher than in P1 and P3 There were no differences throughout the 30 min of recovery for all periods. No differences were found in A response for the control group (CG) in P1 and P2 Plasma A concentrations obtained after the 6 s-sprint test was significantly higher in TG than in CG after P2 Plasma noradrenaline concentrations NA concentrations increased significantly in TG and CG after the warm-up and after the 6 s-sprint test in all periods. There were no significant differences between TG and CG concerning NA concentrations measured at rest, after the 6 s-sprint test (NAEX) and during the recovery	This result show that sprint training has no effect on sympathetic nervous activity in adolescent girls The increase of plasma A concentrations observed in our trained adolescents in response to physical exercise is in accordance with transversal studies conducting in adult men, plasma NA concentration were not

Table 1 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
15. Winter et al. [47]	Subjects:30 Males: 30 3 groups of 10 subjects each Age: 22.2±1.7 years	Randomized Cross Over Design	Intervention 1- Control group 15 min sedentary Intervention 2- Exercise Group: Moderate exercise group 40 min of low impact running (aerobic condition) Intervention 3—Exercise Group: Intense exercise two sprints of three mins each separated by 2 min until exhaustion(anaerobic condition)	Relaxed group vs Moderate exercise group Intense exercise group	Plasma-Dopamine: Significant linear increase in levels across three-time samples for all three conditions Linear Trend NA: Significant interaction between condition and time sample. Post Hoc Analysis showed intense condition gave significantly steeper levels of NA after exercise in comparison to the other two conditions Quadratic Trend A: ANOVA yielded significant interaction between time sample and condition Post Hoc test shows higher changes for the intense group as compared to the relaxed group Quadratic trend	Vocabulary learning was faster by 20% after intense physical exercise, strongest increases in catecholamines epinephrine and dopamine along with BDNF

Table 1 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
16. Maddoek [22]	Subjects: 38 Females: 22 Males: 16	RCT	Intervention 1 for GABA: Graded exercise—bicycle ergometer 50–100 W and increased by 25–40 W every 2–4 min for 18 min followed by 1 min cool down Intervention 2: For Glutamate Graded exercise for 20 min on cycle ergometer first to reach the target heart rate and then at constant load Intervention 3: For Control Group Same as intervention 2 but the subjects will just sit on the cycle and not pedal	Exercise Group vs Control Group	Reliable changes after exercise Glutamate: Increased Glutamate content in visual and anterior cingulate cortices GABA: Increased GABA in the visual cortex Downward drift in Glutamate in the control group	Distinct positive changes in brain metabolism following exercise

Table 1 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
17. Wochynski et al. [48]	<p>Subjects: Fifty – five cadets Age: 20 years Group A SAGI trained (Special Aviation Gymnastic Instrument Training) $n = 41$ Height: 176.64 ± 5.78 cms Weight: 71.03 ± 6.94 Group B Control Group $n = 14$ Height: 173.62 ± 5.12 cms Weight: 67.59 ± 6.36</p>	Pretest posttest design	<p>Intervention: Group A: Consecutive exercises: Looping: 2 series of spins on blocked looping, with 10 spins forward then backward Interval between series lasted 20 s Gyroscope: 2 series of the dynamic turns, each lasting 60 s. for 3 min Interval between series lasted 20 s Aero wheel: 2 series of turns. Each series consisted of 3 turns sideways to the right and then left. Each series was repeated 4 times of 3 turns alternating direction for 3 min All exercises on each instrument were repeated thrice Group B: Exercises that improved general fitness with motor ability, light aerobics, gymnastics, outdoor runs, body functional abilities, higher load, goal techniques, repetitions and interval techniques Thirds training session was common for both the groups including marching, drills and other military activities</p>	Exercise group vs Control group	Statistically significant increase in catecholamines levels was seen after training in all three sessions In comparison to the before training baseline	The exercises produce statistically significant increase in plasma AT adrenaline, noradrenaline, and dopamine in all 3 training sessions, depending on their intensity. The significant difference between group A and group B in both BT and AT values in training session III indicates that catecholamines are good markers for the assessment of the exercise adaptation level. The SAGI training scheme improves the general physical fitness of the examined cadets in comparison with the control group

Table 2 Pooled Evidence of Effects of Exercise on Neurotrophins

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
Brain-derived neurotrophic factor (BDNF)						
1. Ferris et al. [64]	Subjects: Fifteen Male: Eleven Female: Four Age: 25.4 ± 1.0 years Height: 174.7 ± 1.9 cms Weight: 71.0 ± 3.1 kgs	Randomized Control Study	Intervention: Round 1: Graded exercise test stationary bicycle (GXT) Round 2 and 2: 30 min endurance rides at fixed intensity levels Vth – 20 And Vth + 10	Rest vs Graded exercise test vs Endurance test	BDNF values increase from baseline after Vth + 10 endurance significantly increased by 13%, while after Vth -20 endurance, no significant rise was seen post exercise	BDNF levels significantly increased with graded exercise in healthy populations both male and female to improve neurological health
2. Winter et al. [47]	Subjects:30 Males: 30 3 groups of 10 subjects each Age: 22.2 ± 1.7 years	Randomized Cross Over Design	Intervention 1- Control group 15 min sedentary Intervention 2- Exercise group: Moderate exercise group 40 min of low impact running (aerobic condition) Intervention 3—Exercise Group: Intense exercise two sprints of three mins each separated by 2 min until exhaustion (anaerobic condition)	Relaxed group vs Moderate exercise group vs Intense exercise group	Results showed peripheral serum BDNF levels at baseline, immediately after exercise and after vocabulary, the values differed for the three conditions (F (2,52) D5.88, $p = 0.006$; intense > moderate: $t(26) = -3.33, p = .003$) ANOVA showed a quadratic trend $F(1,26) = 4.38, p = 0.05$ Post hoc tests revealed significantly stronger changes across times samples for the intense as compared to the relaxed condition	Vocabulary learning was faster by 20% after intense physical exercise, there was a sustained serum BDNF level during learning which predicted immediate learning success after an intense exercise

Table 2 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
3. Schiffer [65]	<p>Subjects: Twenty-seven healthy sports student's male</p> <p>Age: 22.2 ± 1.8 years,</p> <p>Height: 183.1 ± 5.9 cm</p> <p>Weight: 77.8 ± 8 kg</p> <p>Assigned to three groups:</p> <p>Sh: Strength Group</p> <p>Em: Endurance Group</p> <p>C: Control group</p>	Pre-Test – Post-Test Study	<p>Intervention:</p> <p>Sh Group: Complete body strength training anterior thigh leg extension machine was used, chest press, leg press, lateral raise, lateral pulley seated row, hyperextension, with strength training loads 3 sets at 70–80% of IRM</p> <p>Em Group: With 8–10 repetitions per session with crunches and lower back extension until exhaustion</p> <p>Em Group: Ran 45 min with a heart rate of 80% of HR at the aerobic-anaerobic threshold</p>	Endurance group vs Strength Group vs Control	<p>There was no influence proven by time [$F(2,24) = 0.940$, $p = 0.342$, $f = 0.356$].</p> <p>group [$F(2,24) = 0.250$, $p = 0.781$, $f = 0.25$] and interaction of time x group [$F(2,24) = 0.157$, $p = 0.855$, $f = 0.293$] seen on BDNF</p>	This study concludes that 12 weeks of intensive strength training is insufficient to induce adaptations in basal BDNF plasma concentrations

Table 2 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
4. Seifert et al. [66]	Subjects: Twelve healthy adults Exercise group: 7 healthy males Age: 29 ± 6 years Control group: 5 healthy males Age: 31 ± 7 years	Randomized controlled trial	Intervention: Three months seven days a week Graded exercise on cycle ergometer was used to assess VO2Max Exercise group performed cycle ergometer cycling first five mins at light intensity then increasing workload to 70% VO2Max, maintained for 15 min Recovery for 30 min in which incremental cycling was performed. For 4 min at 60%, 70%, 80%, 90% and 100% of VO2Max and each 4 min bout was separated by 6 min of recovery, this was performed for 3 months Control subjects continued sedentary lifestyle with a diet aiming to maintain energy balance	Plasma BDNF	BDNF ng/ml in the exercise group show At rest: 2.5 + 2.4 At exercise: 4.4 + 2.4 Three-month follow-up at rest: 5.5 + 2.3* After exercise: 5.9 + 3.9 BDNF ng/ml in Control group At rest: 1.2 ± 0.5 After exercise: 1.3 ± 0.32	Three months of endurance training increased the release of BDNF from the human brain at rest and although acute exercise per se did not influence the release of BDNF, the arterial BDNF level was elevated during exercise compared with rest, which proves BDNF as a potential to improve brain health

Table 2 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
5. Goekint et al. [67]	Subjects: Thirty-two age sex matched and total muscle strength matched individuals Experimental group $n = 16$ Control group $n = 15$	Non-RCT study	Intervention: Three days a week for ten weeks. Total muscle strength (IRM) was first calculated for six different exercises. Determination of IRM in the first session was reassessed at 6th, 12th, 20th and 30th session. Subjects maintained current activity level with no other aerobic exercise or any other training, while control group was advised no physical activity but their daily routine for this ten weeks	Experimental group vs control group	The serum BDNF levels before and after intervention showed no significant changes over time ($p = 0.12$) No difference between the experimental and control group ($p = 0.37$). When looking at the changes (deltas) in BDNF level, too no difference was found. ($p = 0.55$)	One training session of strength training alone did not significantly change peripheral BDNF levels thus researcher furthers the benefits of combined effect of physical exercise as a whole in cognitive development
6. Erickson et al. [68]	Subjects: One hundred and twenty Aerobic Exercise group: $n = 60$ Age: 67.6 ± 5.81 years Stretching Control group: $n = 60$ Age: 65.5 ± 5.44 years	Randomized controlled trial	Intervention: Aerobic group: walking, 50–60% of HRR (1–7 weeks), 60–75% of HRR (remainder of the program), 40 min Control group: stretching and toning exercise Frequency: three times per week Duration: 12 months	Exercise group vs Control group	BDNF increased in the Control group from Baseline-21.32 (9.32)—to after intervention 23.77 (8.04) Exercise Group from Baseline 23.41 (9.67)—to after intervention 24.04 (10.83)	BDNF increased and memory improved in both groups. Increased hippocampal volume was associated with greater levels of BDNF

Table 2 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
7. Griffin et al. [69]	<p>Subjects: 47 healthy male students</p> <p>Age: 22 ± 2 years</p> <p>Height: 180 ± 7 cm</p> <p>Weight: 82 ± 11 kg</p>	Controlled trial	<p>Intervention: All performed cognitive tasks and Stroop test</p> <p>EX-group: Graded exercise</p> <p>During the first testing session, all participants performed a set of cognitive tasks, including the face–name matching task and the Stroop task. Following this, the EX-group completed a graded exercise test, which served as the acute exercise bout, while CON participants had a 30 min rest</p> <p>Two chronic exercise protocols for subgroups of the EX-group: C-EX3 and C-EX5 3-week training</p> <p>Two aerobic protocols for subgroups A-EX3 and A-EX5 5-week training</p> <p>The CON group remained sedentary both during the testing sessions and during the 3-week or 5-week interval between sessions</p> <p>Duration: 3 weeks or 5 weeks</p>	<p>Exercise group (EX) vs Control group (CON)</p>	<p>Post hoc analysis showed a significant increase in serum BDNF concentration immediately post-GXT (60 min: $1294.0 \pm 820.5 \text{ pg}\cdot\text{ml}^{-1}$), relative to baseline (0 min: $974.7 \pm 741.6 \text{ pg}\cdot\text{ml}^{-1}$, $p=0.05$)</p> <p>3 weeks of aerobic training had a significant effect on the serum BDNF response to acute exercise (Fig. 6a). There was a significant effect of time ($p=0.0075$, $F(3,33)=4.725$;</p> <p>5 weeks of aerobic training also has a significant effect on the serum BDNF response to acute exercise (Fig. 6b). There was a significant effect of time ($p=0.0001$, $F(3,42)=8.973$)</p>	<p>Graded exercise – acute aerobic exercise selectively improves hippocampal-dependent learning with increased BDNF levels. Exercise induced cognitive functions are associated with BDNF linked mechanism</p>

Table 2 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
8. Ruscheweyh et al. [70]	Nordic walking group: 20 older adults Age: 60.1 ± 6.2 years Gymnastics group: 21 older adults Age: 62.5 ± 6.4 years Control group: 21 older adults Age: 58.1 ± 6.7 years	Longitudinal interventional study	Intervention: Nordic walking: 50–60% of maximal exertion, 50 min Gymnastics: 30–40% of maximal exertion, 50 min Frequency: five times per week Duration: 6 months	Serum BDNF, MRI, and cognitive function	There was a trend for increase in BDNF with increasing physical activity over 6 months. Cognitive function improved in intervention groups	High physical activity was positively associated with gray matter volume increases mainly in the pre-frontal cortex and the cingulate gyrus
9. Heyman et al. [71]	Subjects: Eleven male cyclists Age: 23.3 ± 5.1 years Mean height: 183cms Mean weight: 77kgs	Pre- and Post-test design	Intervention: Bicycle ergometer exercise for 60 min at 55% Wmax pedaling followed by intense endurance performance test at 75% Wmax 77% intensities	Moderate vs intense exercise	Exercise had pronounced effects which showed rise in BDNF levels increase during exercise and reduced to basal levels after 15 min of recovery. BDNF levels rise with intense exercise of acute intensity. (ANOVA time effect, $P < 0.01$)	Peripheral BDNF increase is exercise-induced and promotes the antidepressant effects of exercise
10. Cha et al. [72]	Subjects: Eighteen healthy male Age: 19 ± 1 years Height: 173.22 ± 7.65 cms Weight: 78.25 ± 14.25 kgs	Pretest posttest design	Intervention: Maximal graded exercise treadmill test following American College of Sports Medicine guidelines for measuring V02Max were followed	Rest vs maximal exercise	Positive correlations between V02Max and immediately after exercise – IAE serum BDNF ($r = 0.753, p < 0.0001$), IAE plasma BDNF ($r = 0.667, p = 0.003$) and IAE platelet BDNF ($r = 0.649, p = 0.004$) Significantly positive correlation between treadmill running time and changes in serum and plasma BDNF ($r = 0.669, p = 0.002; r = 0.642, p = 0.004$, respectively) from rest to immediately after exercise was also seen	The concentrations of serum, plasma and platelet BDNF are all increased by treadmill VO_2 max performance in healthy college men, thus influence of one bout exercise on BDNF levels (platelet, serum and plasma) with correlation to cardiorespiratory fitness levels

Table 2 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
11. Schmolesky et al. [73]	Subjects: 45 Age: 18–25 years Gender: Male Quota Sampling	Study design: RCT	Intervention: four different aerobic exercise intensity (80%–60%) conditions on cycle ergometers (Vigorous, Moderate, Sedentary control) Duration 20–40 min, referred as Vig20, Vig40, Mod20, Mod40, Con 20 and Con40 Control group remained seated during the exercise period	Control group vs Exercise Group	32% increase in sBDNF levels relative to baseline. Concentrations of sBDNF were 45% higher in the four exercise conditions Vig20 = 26.38 ± 34.89%, Vig40 = 28.48 ± 19.11%, Mod20 = 41.23 ± 59.65%, Mod40 = 30.16 ± 72.11% and decreased consistently among the controls (Con20 = -14.48 ± 16.50, Con40 = -10.51 ± 26.78)	Sedentary controls the serum BDNF reduced by 13% and the long duration group gave a 10% rise in BDNF levels. Physical exercise caused an average ~ 32% increase in sBDNF levels. Vig conditions that experienced a significant increase in sBDNF levels, followed by Mod and control conditions
12. Tsai et al. [74]	Subjects: 60 males Lower fit Exercise group n = 20 Age: 23.10 ± 2.20 years Higher fit Exercise Group n = 20 Age: 22.20 ± 2.17 Non-exercise group N = 20 Age: 22.20 ± 1.70	Pre-post-test design	Intervention: VO2Max test to divide them into three groups, followed by 30 min acute aerobic exercise on a motor driven treadmill	High exercise group vs low exercise group vs nonintervention group	Post-exercise BDNF levels were significantly higher than the pre-exercise levels in both the Exercise intervention groups But there was no significant correlation among the BDNF levels and behavioral ERP performance before and after acute exercise in any of the three groups	Exercise BDNF is an important molecular mediator for neural efficiency in the human brain functioning and its improvement with aerobic exercise cannot be neglected
13. Leckie et al. [75]	Subjects: 90 (Two groups) Group 1: walking exercise group n = 47 Age: 67.23 ± 5.39 years Group 2: Stretching control group n = 45 Age: 66.38 years ± 5.83	Intervention 1 year	Exercise group: Walking 10 min with increased walking duration weekly by 5 min until 40 min durations achieved at Week 7, and then continued till the end at 40 min Control Group: Four muscle toning exercises	Age vs BD	Control group: Toning and stretching group the population shows a decrease in BDNF levels for the oldest individuals Positive linear rise in the moderate intensity walking group was seen in relation to age	Cognitive outcomes in elderly population are influenced by exercise interventions depend on the intensity and type of exercise

Table 2 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
14. Saucedo Marquez et al. [76]	For Experiment 1 Subjects: 8 active men Age: 28 ± 5 years For Experiment 2: Subjects: 21 men Age: 21 ± 4 years	Cross over randomized design	Participants performed a continuous exercise (CON) protocol at 70% of maximal work rate and a high-intensity interval-training (HIT) protocol at 90% of maximal work rate for periods of 1 min alternating with 1 min of rest (both protocols lasted 20 min)	Rest vs Continuous exercise vs HIIT exercise	Both exercise protocols significantly increase BDNF levels compared with a rest condition (CON $P=0.04$; HIT $P<0.001$), with HIT reaching higher BDNF levels than CON ($P=0.035$) (experiment 2)	These results suggest that shorter bouts of high-intensity exercise are slightly more effective than continuous high-intensity exercise for elevating serum BDNF
15. Hotting et al. [77]	Subjects: Eighty-one healthy adults Males = 41 Females = 40 Age: 22 years (18–29 years) SD: 2.36 Mean BMI: 21.7 kg/m^2 SD: 1.85	Pretest posttest group	Intervention: Learning: 20 Polish/German words auditory stimuli Exercise: High-intensity exercise: ~80% HRmax Low-intensity exercise: <57% HRmax Relaxing group Watching a silent movie Learning: Vocabulary test 1 Vocabulary test 2	Low-intensity exercise group vs high-intensity exercise group vs relaxing group	Serum BDNF only increased after exercising in the high-intensity exercise group. Time \times Group $F(4, 148) = 17.99, p < 0.001, \eta^2 = 0.327$ The analysis per time point showed that groups did not differ with respect to BDNF at $t0$ and at $t1$ (all $F < 0.50$, all $p > 0.60$) but that there was a significant effect of Group after exercising at $t2, (2, 74) = 8.68, p < 0.001$	Present study concluded that high-intensity exercise increased the release of BDNF and cortisol in humans
16. De la Rosa et al. [78]	Subjects: Eighty-six healthy mean Age: 17–68 years Four groups Young Sedentary group (YSG) $n=21$ Age: 17–25 years Young Trained Group (YTG) Age: 18–25 years $N=16$ Middle-Aged Sedentary Group (MSG) Age: 47–67 years $N=25$ Middle-Aged Training Group (MTG) $N=25$	Randomized Control Study	YTG: Seven years of exercise experience in tennis, taekwondo, running and football MTG: amateur rugby players. 35 + 15 years of practice MSG: Involved in not more than 150 min of light exercise weekly	YSG vs YTG vs MSG vs MTG	Effects of exercise training ($F(1,80) = 50.11; p < 0.0001$), age ($F(1,80) = 289.6; p < 0.0001$) and the interaction between these factors ($F(1,80) = 11.94; p = 0.0009$) Also effect of exercise on BDNF levels was higher in the YTG than the MTG groups Post Hoc Analysis showed increase in BDNF levels with age and a decrease with physical exercise was more intense in the young group	BDNF improves memory with regular exercise and mitigates age-related brain losses with modulation of stress, these act as preventative strategies against brain aging

Table 2 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
17. Kujach et al. [79]	Subjects: Thirty-Six Young adults Males N=36 SIE (Sprint Intensity Exercise) Group n=20 Age: 21.0±0.9 years Control Group (CTR) n=16 Age: 21.7±1.3 years	One-way repeated study design	Interventions: SIE protocol constituted 5 min warm-up exercise and six sets of 30 s of all out cycling exercise followed by 4.5 min of rest on a cycle ergometer	Exercise group vs Control group	The acute SIE exercise significantly alters serum BDNF concentration immediately post exercise, ($p < 0.01$) while one hour post exercise, the BDNF concentration decreases and was not significantly different from baseline	SIE may have beneficial result on cognitive functions and correlate to the blood L.A levels increase after an acute bout of exercise which has several neuroprotective effects
18. Arazi et al. [80]	Subjects: Thirty older men assigned into three groups Strength Group: n = 10 Age: 60.8 ± 1.8years Height = 177.8 ± 8.9 cm Weight = 90.6 ± 16 kg Endurance Group: n = 10 Age: 60.7 ± 1.7 y, Height: 181 ± 5.4 cm, Weight: 85.9 ± 13.4Kg Control Group: n=10 Age: 60.9 ± 0.9 y Height: 179.6 ± 8.2 cm Weight: 87.7 ± 9.7 kg,	Controlled randomized design	Intervention: 45 min includes: 10 min of standard warm-up, 30 min of main exercise and 5 min of cool down Strength exercises: two circuits resistance exercise with repetitions of 65–70% one rep max Endurance exercises: Running with 65–70% of maximal heart rate	Rest vs strength training vs endurance training	The endurance and strength groups demonstrated small to moderate significant increases ($p = 0.003$, $F = 15.642$) in the BDNF levels from pre-to post-exercise (endurance, $ES = 0.15$ (–0.7, 1.02 CI, small), 17.7%, $p = 0.002$; strength, $ES = 0.42$ (–0.48, 1.29 CI, moderate), 15.5%, $p = 0.003$). A	Findings of the study revealed that acute strength and endurance induced changes in BDNF in older adults but there was no statistically significant changes between the treatment groups in the variables at post-exercise
19. Kang et al. [81]	Subjects: Twenty Females Age: 68–80 years Aquatic exercise group n = 10 Control group n = 10	Pre-test – Post-test Study	Intervention: Duration: 16 weeks Three times a week 60 min exercise intensity increased 1–4 weeks 40–50% of heart rate reserve (HRR) Next 5–8 weeks 50–60% HRR 9–12 weeks 60–65% HRR 13–16 weeks 65–70% HRR	Aquatic exercise group vs Control group	The BDNF levels increased significantly over time in the exercise group ($p < 0.05$) The intergroup comparison showed a significant difference in the change ($p < 0.05$) and a significant group x time interaction was also found ($p < 0.05$)	Aquatic exercise in the early stages of aging in women can increase the BDNF expression and increase cognitive function

IGF—1

Table 2 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
20. Poehlman [82]	Subjects: Eighteen Males: Ten Age: 66.3 ± 2.1 years Females: Eight Age: 65.9 ± 1.9 years	Repeated measure design	Interventions: Cycling exercise three times a week for eight weeks Week 1: net expenditure of 150 kcal per session at 60% of VO2Max By week 8: exercise intensity increased to 75% of their VO2Max with energy expenditure of 300 kcal per exercise	Male vs Female and Rest vs Exercise	Interventions: IGF-1 increased by 14% in the total group from 76 ± 4.8 to 86 ± 5.6 ng/ml, where $p = 0.05$ By gender there was an increase in males by 19% pre- to post-exercise 78 ± 7.0 to 93.2 ± 7.8 ng/ml Where $p < 0.01$, In women a non-significant increase was seen from 73 ± 7 to 79 ± 8 ng/ml where $p = 0.01$	Results show a sexual dimorphism in response to IGF-1, men showed a significant increase while in older women the rise was blunted, the researcher suggest that the change may be mediated by GH and IGFBP-3
21. Cappon J et al. [83]	Study 1: Subjects: Ten Males: Nine Females: One Age: 22-35 years 29 ± 4 years Study 2: Subjects: Nine Males: Seven Females: Two Age: 23-32 years 28 ± 3 years	Pretest posttest study	Intervention: Four exercise protocol separated by five days Session 1: Progressive cycle ergometer Session 2, 3 & 4: Ten mins of constant power-high-intensity exercise performed 45 min after one of the three liquid meals Session 2: A progressive cycle ergometer test was conducted to measure VO2max, three weeks after which on the exercise day they were made to do three exercise bouts with one-hour gaps between each of 10 mind power cycle ergometer		Results for Session 1: Mean IGF-1 levels went 14% above pre-exercise, after a ten min exercise protocol and remained elevated above pre-exercise levels up to 20 min into recovery Results for session 2: IGF-1 was sampled every four hours no significant change was observed in 24 h	Researcher proposed two mechanisms of increased IGF-1 levels with physical fitness: c. An exercise GH-IGF-1 interaction d. GH-independent direct effect of exercise on IGF-1 levels

Table 2 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
22. Schwarz et al. [58]	Subjects: Ten adult healthy male Age: 27.5 ± 1.7years	Pre–post-test study	Intervention: Three sessions at least one week apart one session consisted 10 min constant cycle ergometer exercise, one at high intensity and one at low intensity. In control group rest in comfort was given During the control session, the subject performed no exercise but rested comfortably	Exercise vs control	During resting control session IGF-1 levels dropped mean fall was 6.8 + 2.4% 10 min low-intensity exercise mean IGF-1 levels increased by 7.7 + 2.7% they fell back 10 min after exercise High Intensity exercise mean IGF-1 levels increased by 13.3 + 3.2% (<i>P</i> < 0.002) There was no significant difference between the IGF-1 levels among high- and low-intensity protocols	This study suggests that IGF-1 secretions are not related to GH, as GH increased significantly to high-intensity exercise but IGF-1 increased to both low and high-intensity exercise Plus, circulating IGF-1 and IGF-II reached their peak rise much before GH, accompanying exercise is, in fact, not related to GH
23. Elias et al. [84]	Subjects: Seven Male Age: 37 ± 3 years Body Mass: 78.2 ± 3.6kgs Height: 171.1 ± 3.2cms	Pre–post-test study	Intervention: Subjects exercised to exhaustion on a treadmill using the Bruce multistage protocol (Bruce 1971) with a 3-min pre-exercise baseline (standing) stage followed by 3 min of warm-up at 1.7 mph 5% grade	Rest vs Exercise	IGF-1 levels rose with exercise (P<0.01) reached peaked values 15-30 min after exercise, after which they slowly fell below baseline 60 min post exercise and then slowly rose to baseline again. There was a prompt correlation between Plasma IGF-I and Leptin before after and up to 180 min post exercise. concentrations rose promptly (P,01) with exercise reaching (<i>r</i> =0.741, <i>P</i> <.0001)	Acute exercise leads to decline in gonadotrophin decline with decline in plasma leptin may be due to rise in IGF-1 levels

Table 2 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
24. Chadan et al. [85]	Subjects: Seven healthy volunteers Female: Seven Age: 62–69 years Age: 65 ± 1 years Height: 164 ± 1.2 cms Weight: 73 ± 3kgs	Repeated measure design	Interventions: Walking in a flat oval track, with specified intensity once a week for four weeks All tests were of repeated measures design. Four sessions: A. low-intensity short duration, (LS heart rate = 100 bpm for 25 min) B. low intensity, long duration (LL, heart rate = 100 bpm for 50 min) Moderate intensity, short duration (MS, heart rate = 120 bpm for 25 min) D. moderate intensity, long duration (ML, heart rate = 120 bpm for 50 min) All activity was performed in groups with heart rates being continuously monitored. Each subject completed the four different activity bouts	LI SD vs LI LD vs MI SD vs MI LD	Physical activity had no effect on IGF-1 levels in elderly women and was independent of GH rise	Researcher concludes that physical exercise may modulate bioavailability of IGF-1 by altering the IGF1Rs in elderly population thereby contributing to increase in muscle mass as observed in physically active older adults

Table 2 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
25. Bermon et al. [86]	Subjects: Thirty-two older adults Males: Sixteen Females: Sixteen Age: 67 ± 80 years Strength training = 8 Sedentary Control: N = 8	Pretest post design	Intervention: Strength training program: Leg press, knee extension, chest press for eight repetitions, three times a week for seven days a week. Trained subjects started at 80% of 1-RM) With Fifteen minute warm-up (cycling and calisthenics) and 10 min cool down (stretching)	Training group vs Sedentary group	Exercise Group showed total IGF-1 increase immediately and 6 h (+ 7.5%, $P < 0.01$) after the standardized strength test Free IGF-1 also increased immediately (+ 93.8%, $P < 0.001$) and 6 h (+ 31.3%, $P < 0.001$) after the test No significant shifts were seen in the sedentary population	Acute bout of strength exercise increases total and free concentration of IGF-1 in elderly subjects
26. Borst et al. [87]	Subjects: Thirty-one healthy sedentary men and women Age: 25–50 years Three Groups Group I: Single-set resistance training $n = 11$ (I-SET) Group II: Multiple set resistance training $n = 11$ (III-SET) Group III: Non-exercising Control Group $N = 09$	Pretest posttest design	Intervention: Resistance training protocol Three days a week for 25 weeks Each session 20-90 min with 5 min warm-up, stretching and 5 min cool down I-SET performed one circuit of torso flexion, leg extension, chest press, biceps curl, triceps extension II-Set training performed three repetitions of the same exercises Training load was set at 60–70% of 1-RM, after the subjects were able to perform 10-12repetitions of each exercise the load was increased by 1.8–2.7 kg for the next session A rest of 2 min was given between sets	Sedentary group vs I-SET training group vs III-SET training group	Results show significant increase in IGF-1 after 13 weeks of resistance training I-SET showed 20.5% increase with no further increase during the second half, while in III-SET there was an 18.5% increase during the first half with no increase in the second half of the study	The study makes an inference that the increase in strength corresponds with the increase in IGF-1 in the total span of the study, thus could be that IGF-1 is partially responsible for the improvement in strength

Table 2 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
27. Chichharo [88]	Subjects: Seventeen professional cyclists of International Cycling Union, Mean Age: 27 ± 1 years Weight: 66.9 ± 2.5 kgs Height: 179.6 ± 1.8 cms	Repeated measure design	Interventions: 3518kms in 21 stages over a period of three weeks with one day rest	Before and after prolonged endurance competition	The mean values of IGF-1 at the start of competition t_0 were significantly lower than at t_1 and t_3 Values increased by 68.4% at t_1 and 77.5% at t_3 above starting levels. ($p > 0.05$)	There is an increased demand of IGF-1 in the tissues during this type of endurance exercise, but further investigation needed
28. Nindl [89]	Subjects: Ten healthy adults Males $n = 10$ Age: 21 ± 0.6 years Weight: 78.6 ± 6.4 kgs Subjects: Ten young, healthy, fit men (age: 21.0 ± 2.1 yr, height: 177.1 ± 6.7 cm, weight: 78.6 ± 6.4 kg)	Pretest posttest design	Interventions: Acute, heavy-resistance exercise protocol included squats, leg bench press, lateral pull downs, the relative loads for each exercise alternated between 1 and 5 RM loads calculated at 70% and 85% of exercise at IRM. With a 90 s rest period in between each exercise	Control group vs Exercise group	The results were measured thirteen hours of overnight sleep after the exercise protocol performed at 15:00 to 17:00 h. No exercise effects were found in free or total IGF-1 measures. However, there were changes in other IFG proteins and receptors	Results suggest that impact of resistance exercise on circulating IGF-1 depends on the complete IGF system and causes alterations in the system that can be detected through systemic circulation
29. Schiffer [65]	Subjects: Twenty-seven healthy sports students Age: 22.2 ± 1.8 years, Height: 183.1 ± 5.9 cm Weight: 77.8 ± 8 kg	Pre-Test – Post-Test Study	Intervention: Strength Ability: Knee extensor Isometric and dynamic muscle force on leg extension machine At 120 degree and 90 degree Endurance tests on a treadmill (Woodway, Weil am Rhein, Germany) started at a running speed of 7 km/h, increasing with every stage by 1.5 km/h till exhaustion	Endurance group vs Strength Group vs Control	Basal plasma concentrations of IGF-1 decreased significantly after the intervention in all groups (Sh: from 243.1 ± 52.4 to 222 ± 57.4 ng ml^{-1} ; Em: from 246 ± 24.2 to 232.1 ± 36.6 ng $\cdot ml^{-1}$; C: from 225.1 ± 47.5 to 211.9 ± 56.6 ng ml^{-1}). ANOVA showed no interactions for time and group for IGF-1 [$F(2,24) = 0.212$, $p = 0.810$, $f = 0.333$]	The basal IGF-1 adaptations depend on exercise modes, also functional adaptations after strength and moderate endurance training do not induce specific alterations for basal plasma concentrations of IGF-1

Table 2 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
30. Goekint et al. [67]	Subjects: Thirty-two age sex matched and total muscle strength matched individuals Experimental group $n = 16$ Control group $n = 15$	Non-RCT study	Intervention: Three days a week for ten weeks. Total muscle strength (IRM) was first calculated for six different exercises. Determination of IRM in the first session was reassessed at 6th, 12th, 20th and 30th session. Subjects maintained current activity level with no other aerobic exercise or any other training, while control group was advised no physical activity but their daily routine for this ten-week training	Experimental group vs control group	The 10-week training period did not have significant effect on IGF-1 concentration ($28.4 + 21.2$ ng/ml). Acute strength training session did not exceptionally influence the concentration in the experimental group ($284.3 + 13.5$ ng/ml) in comparison to the control group ($281.2 + 12.2$ ng/ml)	Only a strength training session did not significantly change peripheral IGF-1 levels thus researcher further the benefits of combined effect of physical exercise as a whole in cognitive enhancement
31. Jeon et al. [90]	Subject: Twenty junior high school students Exercise group $n = 10$ Age: 15 years Height: 161.2 ± 2.5 cms Weight: 56.3 ± 6.8 kgs Control group $n = 10$ Age: 15 years Height: 162.6 ± 3.4 cms Weight: 55.7 ± 7.7 kgs	Pretest posttest study	Intervention: Exercise group performed supervised aerobic exercise three days a week for eight weeks Control group continued their normal sedentary activities Maximal oxygen uptake (VO2max) of all the exercise group participants was measured to prescribe aerobic exercise intensity for the purpose of the intervention	Exercise group vs Control group	Results: In the exercise group IGF-1 significantly increased from ($p < 0.05$), from 420.0 ± 172.3 ng/ml to 432.3 ± 165.2 ng/ml	The results of this study suggest that chronic aerobic exercise has a positive effect, enhancing resting IGF-1 expression in adolescents whose brains are still developing

Table 2 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
32. Kraemer [91]	Subjects: Seven Healthy men Age: 23.1 ± 2.4 years Height: 170.1 ± 4.0 cms Body Mass 74.4 ± 10.3 kgs	Pretest Posttest study	Intervention: Experimental heavy-resistance exercise protocol consisted of three sets of eight different resistance exercise with 1 min rest between each set performed at 10RM	Randomized Control Trial	The total serum IGF-1 showed no significant differences between control and recovery day values at any particular point of time No significant change was seen between pre- and post-exercise concentrations of IGF-1 within or between trials. Non-exercise control day and experimental trail day also showed no significant differences in serum IGF-1 levels $388+83$ nmol/l and $386+93$ nmol/l respectively	In this study serum GH increased dramatically but serum IGF-1 levels did not change over 24 h after exercise which indicate that IGF-1 concentrations may be independent of GH stimulations after exercise
33. Kujach et al. [79]	Subjects: Thirty-Six Young adults Males $N=36$ SIE (Sprint Intensity Exercise) Group $n=20$ Age: 21.0 ± 0.9 years Control Group wevs(CTR) $n=16$ Age: 21.7 ± 1.3 years	One-way repeated study design	Interventions: SIE protocol consisted 5 min warm-up exercise and six sets of 30 s of all out cycling exercise followed by 4.5 min of rest on a cycle ergometer	Exercise group vs Control group	The acute SIE exercise significantly alters serum IGF-1 concentration immediately post exercise ($p < 0.01$) while one hour post exercise, the IGF-1 concentration decreased and was not significantly different from baseline	SIE may have beneficial result on cognitive functions and correlated to the blood LA levels increase after an acute bout of exercise
34. Kang et al. [81]	Subjects: Twenty Females Age: 68–80 years Aquatic exercise group $n=10$ Control group $n=10$	Pre-test – Post-test Study	Intervention: Duration: 16 weeks Three times a week 60 min exercise intensity increased 1–4 weeks 40–50% of heart rate reserve (HRR) Next 5–8 weeks 50–60% HRR 9–12 weeks 60–65% HRR 13–16 weeks 65–70% HRR	Aquatic exercise group vs Control group	Aquatic exercise group showed significant increase in IGF-1 over time ($p < 0.01$) The inter-group comparison showed a significant difference in the change ($p < 0.05$), and a significant effect of the group X time interaction was found ($p < 0.05$)	Regular aquatic exercise in elderly population of women during early stages of aging can increase the IGF-1 levels and help maintain cognitive functions

VEGF

Table 2 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
35. Kraus et al.2003 [61]	Subjects: Sixteen males Male Sedentary (SE) <i>n</i> = 8 Age: 22.1 ± 1years Height: 178.5 ± 2.3cms Weight: 84.6 ± 11.9kgs Exercise trained male (ET) <i>n</i> = 8 Age: 30 ± 3years Height: 175.1 ± 4.1kgs Height: 174.9 ± 5.4cms	Pretest posttest design	Interventions: Five days after determination of VO2Max, with a 5 min warm-up at 75 W for SE and 150 W for ET, after which the work load was increased by 25 W every minute until fatigue sets in. Five days later, all subjects performed one-hour cycle ergometer at 50% maximum power output	SE vs ET	Results showed increase in VEGF in ET at 0 and 2 h post exercise Rest: 32.2 ± 6.5 ng/ml 0 h: 45.3 ± 7.6 2 h: 45.2 ± 10.0 4 h: 36.1 ± 7.6 There was no increase in VEGF in SE at any point of time Rest: 41.3 ± 6.4 ng/ml 0 h: 44.7 ± 7.3 2 h: 48.8 ± 8.1 4 h: 48.0 ± 11.3	In peak post exercise, it was seen that VEGF was increased in both the SE and the ET groups Thus, suggesting that circulating VEGF is elevated in response to traditional systemic exercise in both groups, although there is considerable variation
36. Gustaffson et al. [92]	Subjects: Eight healthy males Age: 24 (22–26) years Height: 182 (176–186) cm Weight: 79 (67–90) kg	Pretest posttest design	Interventions: One-legged knee extension exercise over seven 45-min training sessions). Four of the subjects trained their right leg and four trained their left leg. Subjects kicked at a rate of 60 rpm with average workload 60–70% of performance capacity After 24 h from the 7th training, an exercise session with identical workloads as in the 1st training session to evaluate physiological response	Rest vs exercise	The basal VEGF mRNA and protein expression increased two fold over the training period (<i>P</i> < 0.05)	Before training, VEGF mRNA expression was predominantly located in cells between the skeletal muscle fibers After training increases in mRNA levels were noted in cells between skeletal muscle fibers but also within the fibers

Table 2 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
37. Kang et al. [81]	Subjects: Twenty Females Age: 68–80 years Aquatic exercise group $n = 10$ Control group $n = 10$	Pre-test – Post-test Study	Intervention: Duration: 16 weeks Three times a week 60 min exercise intensity increased 1–4 weeks 40–50% of heart rate reserve (HRR) Next 5–8 weeks 50–60% HRR 9–12 weeks 60–65% HRR 13–16 weeks 65–70% HRR	Aquatic exercise group vs Control group	The results for intra-group and inter-group analyses of changes and interactions for VEGF are shown in Table 5. No significant differences were found in VEGF over time in either group and there was no group \times time interaction. 189.9 ± 29.50 198.1 ± 20.26	The blood VEGF levels in the present study did change significantly and could have been affected by the exercise period, content, intensity, or gymnastic changes
38. Kujach et al. [79]	Subjects: Thirty-Six Young adults Males $N = 36$ SIE (Sprint Intensity Exercise) Group $n = 20$ Age: 21.0 ± 0.9 years Control Group (CTR) $n = 16$ Age: 21.7 ± 1.3 years	One-way repeated study design	Interventions: SIE protocol constituted 5 min warm-up exercise and six sets of 30 s of all out cycling exercise followed by 4.5 min of rest on a cycle ergometer	Exercise group vs Control group	Meanwhile, the peripheral levels of BDNF, IGF-1, and VEGF were significantly increased after an acute bout of SIE compared to those in CTR. In response to acute SIE, blood LA levels significantly Increased and correlated with increased levels of BDNF, IGF-1, and VEGF	In the present study, acute SIE led to an improvement in prefrontal-dependent cognitive performance. Also, SIE resulted in significant elevations of serum BDNF, IGF-1, and VEGF levels and these changes are accompanied by an increased peripheral LA concentration. These findings suggest that acute bouts of SIE are beneficial to improve cognitive performance 20 min following exercise in young adults

Table 3 Pooled Evidence of Effects of Exercise on Neuromodulators

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
Endocannabinoid system						
1. Carr et al. [101]	Subjects: Seven women volunteers between 18 and 30 years	Pretest posttest design	Intervention: two months Before which some exercise tests were conducted Training protocol consisted conditioning exercises, bicycle ergometer one hour a day for six weeks at 85% of maximal HR. The exercise was increased on plateau from 20, 30, 40 and 45 mins respectively during ensuing three weeks	Control vs exercise 1 vs exercise 2 vs exercise 3	Results show acute rise in beta endorphins and beta enkephalin highly significant ($p < 0.01$)	Results show rise in plasma beta endorphins and beta enkephalins, and training augments this effect
2. Howlett et al. [102]	Subjects: Eighteen normal young women Age: 20–23 years	Pretest posttest study	Intervention: eight weeks training running for five weeks with steady increase from four miles (6–4 kms) a day initially to 10 miles (16 kms) a day during second four weeks. With three hours a day in moderately strenuous activities such as cycling or tennis Testing exercise on a treadmill was performed during the afternoon in the early follicular phase at the beginning of T1, middle T2 and end T3 of the training program. Each testing set was for one hour with three successive 20 min runs at 80% of VO2Max aerobic capacity	Intensity of training T1 vs T2 vs T3	The first treadmill run before training all subjects showed a definite rise in plasma endorphin, above basal values from 40 to 1706 ng/l The tendency was the ones with higher basal immunoreactivity during exercise, in the later run tests the rise and fall was varied and significantly different from control group for each test at 1% level	Results conclude that release of large amounts of both β -endorphin and enkephalin before the training and virtual abolition of release physiological stimulus to exercise. They could also contribute to menstrual disturbances in women during exercise but it requires further research

Table 3 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
3. Farrell et al. [103]	Subjects: $n = 14$ males Trained subjects: 15 years of training experience $n = 7$ Untrained subjects: No such training experience $n = 7$	Observational study	Interventions: Submaximal testing for VO2Max Subjects ran continuously for 7 min at 60% VO2Max 3 min at 100% VO2Max 2 min at 110% VO2Max	T vs UT	Results showed resting levels were similar in both groups, and remained statistically unchanged for T and UT, during 60% VO2Max, and significant increase was visible at 100% VO2Max, at 110% VO2Max the T group showed, 10.8 ± 2.0 fmol ml ⁻¹ in comparison to 6.6 ± 1.0 fmol ml ⁻¹ Even at 5 min post exercise, β -EP is significantly above resting values and higher for T group ($P < 0.05$)	Results conclude plasma response of β -Ep to supramaximal exercise in trained subjects exceeds that found in untrained subjects. This response can be dependent on other catecholamine Responses in exercise state, need further investigation
4. Rahkila et al. [104]	Subjects: Ten experienced male endurance athletes Age: 23–26 years Weight: 60–84 kg Height: 174–192 cm Training: 60–170 km/week during the study	Repeated measure design	Interventions: VO2Max was determined on a motor driven treadmill, The velocities of the treadmill were determined which would require 50%, 60%, 70%, 80%, 90% and 100% of the individual VO2Max 10 min warm-up at 50% VO2Max preceded by 100% test, where 10 min running exercises were performed at random order with an interval of 2–5 days	50% vs 60% vs 70% vs 80% vs 90% intensity of exercises	Treadmill running for 10 min at 92% and 98% of VO2Max increases plasma concentration of β -e and β -LPH which was significant, this increase showed nonlinear relationship with intensity but more associated with Lactic acid levels	Increase in β -e and β -LPH were accompanied with blood lactate levels and thus intensive running with an anaerobic response does cause an increase in the beta endorphins in endurance athletes and aerobic exercise did not elicit a significant response

Table 3 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
5. Goldfarb et al. [105]	<p>Subjects: Twelve College men Untrained athletes: <i>n</i> = 6 Age: 25 ± 4 years Weight: 77.3 ± 4.4 kgs Height: 186 ± 3.1 cms Trained Athletes: <i>n</i> = 6 Age: 28 ± 2.2 years Weight: 75.3 ± 1.4kgs Height: 184 ± 4.3cms</p>	<p>Pretest posttest study</p>	<p>Intervention: Determination of VO2Max at 50 rpm, after which within two weeks three submaximal tests were conducted, 5-6 min of warm-up with resistance to ergometer either 60, 70 to 80% of VO2Max based on the VO2Max data, resistance-adjusted cycling and 30 min exercise with 20 min of recovery time were fixed</p>	<p>Trained vs Untrained</p>	<p>There were no significant changes in B-EP at 60% VO2max. Cycling at 70% VO2max increased B-EP at 30 min in the trained group to 10.48 ± 1.77 pmol.l and the untrained group to 11.65 ± 1.19 pmol.l This represents an approx. 2 1/twofold increase in B-EP concentration. Cycling at 80% VO2max increased B-EP at 30 min to 18.08 ± 3.21 and 20.65 pmol .l the trained and untrained group respectively. Exercising at 80% VO2max increased B-EP approximately 4 1/twofold by 30 min</p>	<p>The study concludes that exercise at 60% VO2max does not increase B-EP concentrations, and B = EP concentrations are independent of lactate secretions, as the increase in B-EP at 70% and 80% VO2Max were similar to untrained subjects but lactate concentrations varied greatly and are not strongly correlated. These data also indicate that exercise intensity influences the extent of B-EP concentration but that training status does not alter this relationship</p>
6. Pierce et al. [106]	<p>Subjects: eight female ballistic dance specialized aerobic athletes Age: 29.7 ± 4.0 years Weight: 51.8 ± 3.0kgs Height: 165.1 ± 4.11 cms Performing min of three aerobic session per week</p>	<p>Pretest posttest design</p>	<p>Intervention: 45 min high-intensity aerobic routine led by an expert</p>	<p>Rest vs aerobic exercise</p>	<p>Result of paired <i>t</i>-test showed β-IER (Mean ± SD) was significantly increased following aerobics bout 12.0 + 1.3 pg β-EP/ml-1 over the pre-exercise levels at rest 8.6 + 1.4, (<i>p</i> < 0.05) Exercise dependence scores ranged between 2.0 and 6.0 out of a possible maximum score of 14. Thus, exercise dependence scores were not correlated to the β-IER scores</p>	<p>Results conclude that intensive aerobic exercise leads to increased β-IER levels which on the other hand are independent of a tendency toward exercise dependence</p>

Table 3 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
7. Kraemer et al. [107]	Subjects: Eight Healthy adult males $n = 8$ Age: 24.7 ± 1.6 years Height: 178.4 ± 2.9 cms Weight: 82.1 ± 4.4 kgs	Pretest posttest design	Intervention: Heavy resistance exercise with identical ordered six exercises 5 vs 10 RM with rest period 1 min vs 3 min an total work calculated in joules Two series with eight exercise at S5/3 and H10/5	Series 1 vs Series 2	The results showed β -EP significant rise in levels for H 10/1 protocol when the RM shifted from 5 to 10 and rest from 1 to 3 min	The results concluded that patterns of response of plasma β -EP and other stress hormone were similar during other heavy-resistance exercise still here specific indication to the duration of rest and intensity of load has been clearly obtained which may act as key stimulus to increase levels of beta endorphins
8. Heitcamp et al. [108]	A group of 16 healthy male runners volunteered to take part in the test	Pretest posttest design	Intervention: Treadmill protocol; Initial treadmill speed was at 6 km.h-1 was increased 2 km. = .h-1 every three mins with a constant gradient at 5%, after signal exhaustion subjects were encouraged to continue and complete the current 30 s measurement Marathon run protocol has a forest course gravel path 6 km length which has to be covered seven times, with total change in elevation 490	Test 1 vs Test 2	Results The β -endorphin for the treadmill test concentration 3 min after exercise was 4.6 times ($P < 0.001$) higher than at rest and even 30 ($P < 0.001$) and 60 min ($P < 0.05$) after exercise it remained higher In the marathon protocol 1 h after running β -endorphin concentrations increased significantly ($P < 0.05$) and continued to increase after 2 h ($P < 0.01$). The steepest increase was measured within the final hour of running ($P < 0.001$), increasing above baseline to 6.9folds	Conclusion form the results shows that β -endorphin concentrations increase with intensity and duration of exercise Secondly, the elimination of both hormones after exercise was slower after the marathon than after the incremental test. Thirdly, the increase in ACTH and β -endorphin concentration during the marathon was not linear but exponential

Table 3 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
9. Sparling et al. [109]	<p>Subjects: Twenty-four active males Age: 23.77 ± 9.4 years Height: 183.77 ± 6.2 cms Weight: 74.577.9 kg Three test conditions: n = 8 Cycling n = 8 Running n = 8 sedentary n = 8</p>	Pre- and post-test design	<p>Interventions: Exercise began with 5 min warm-up, followed by either cycle ergometer or Treadmill slows to increased intensity which elicits a heart rate of 70–80% of maximum heart rate. (140–160 bpm) Once the steady intensity was achieved, they continued for 45 min The control group was in same conditions kept in sitting condition for 50 min</p>	Three exercise groups: Running vs Cycling vs sedentary	<p>Post Hoc Analysis resulted to show a significant elevation in the levels of plasma anandamide in runners ($p < 0.01$) and cyclists ($p < 0.05$), but not sedentary Controls: Plasma 2-Ag showed similar results</p>	The rise in the systemic anandamide occurs parallel to the rise in central endocannabinoid system. This highlights the psychological role of exercise and new neuro-humoral mechanism
10. Heyman et al. [71]	<p>Subjects: Eleven male cyclists Age: 23.3 ± 5.1 years Mean height: 183 cms Mean weight: 77 kgs</p>	Pre- and Post-test design	<p>Intervention: Bicycle ergometer exercise for 60 min at 55% Wmax pedaling followed by intense endurance performance test at 75% Wmax 77% intensities</p>	Moderate vs intense exercise	<p>Plasma levels of endocannabinoids concentrations increased significantly during exercise and also recovery ($p < 0.01$) for the three compounds AEA, OEA and PEA Increase in AEA per unit time was under the 15 min recovery (0.035–0.04 pmol/ml/min) compared to the moderate exercise phase (0.006–0.006 pmol/mL/min) ($p < 0.05$)</p>	Evidence highlights exercise as a physical stressor that increases peripheral AEA levels and this is mediated may be by BDNF signaling which in turn influences neuro-plastic and antidepressant effects of exercise

Table 3 (continued)

Study reference	Population	Study design	Intervention	Comparators	Outcomes	Conclusion
11. Raichelen et al. [110]	Subjects: Ten regular treadmill runners (6 male, 4 female) Body mass: 67.35 kg Age: 31 + 12.9years	Pre- and post-test design	Interventions: Exercise protocol with four different intensities for 30 min The lowest corresponds to a walking speed with age-adjusted maximum HR (heart rate) Age-adjusted maximum heart rate (AAMHR) lowest corresponded to a moderate walking speed intensity I-HR < 50% AAMHR II-HR ~ 70% AAMHR includes slow jog intensity III-HR ~ 80% AAMHR: medium-intensity run IV-HR ~ 90% AAMHR: high-intensity run	I-HR vs II-HR vs III-HR vs IV-HR	Results showed that II-HR and II-HR led to a significant increase in AEA levels post exercise, major significant change was seen only in exercise intensities between 70 and 85% of AAMHR	Exercise induced changes in the Endocannabinoid system benefit psychological state, pain, management and cognitive health

mesolimbic pathway, all involved in exercise-induced neurocognition [25].

Serotonin (5-hydroxytryptamine; 5-HT), a neurotransmitter produced from the amino acid tryptophan (TRP), which travels through the blood–brain barrier by a specific carrier and is hydroxylated by the action of tryptophan hydroxylase. This hydroxylation is the rate-limiting step in the biosynthesis of 5-HT [26]. Thus, tryptophan is the precursor to serotonin, and it needs to cross the blood–brain barrier. Here, aerobic exercise performance reduces the levels of competitive amino acid and increases the chances of tryptophan to cross over and in turn increase the serotonin levels in the brain [27].

Epinephrine is an alpha- and beta-adrenergic agonist, belonging to the catecholamine family. It is a naturally occurring sympathomimetic amine, which stimulates vascular alpha-adrenergic receptors, causes vasoconstriction, thereby increasing vascular resistance and blood pressure. Norepinephrine plays a role as a vasoconstrictor agent, an alpha-adrenergic agonist, a sympathomimetic agent which directly stimulates adrenergic receptors [28]. Both these amines have reported 1.5 to 20 times increase in their basal concentrations reliant on the exercise characteristics like its intensity, duration and type [29].

Peripherally, acetylcholine is released from the neuromuscular junctions as well as from preganglionic fibers of the autonomic nervous system; it causes muscle contraction during physical movement [30]. When exercise is initiated, the brain acetylcholine levels increase, primarily in the hippocampus and cortex. This increase in acetylcholine causes the generation of hippocampal theta, which helps to augment synaptic plasticity and memory production [31, 32].

The studies on release of neurotransmitters are tabulated in Table 1.

Neurotrophins and their mechanism during exercise

Neurotrophins belong to the protein family, a class of growth factors capable of inducing the survival [49] development, and function [50] of neurons. Neurotrophins are peptide molecules that enhance neurogenesis, improve brain function, neuro-cognition, etc. Regular exercise when repeated over time may cause the baseline neurochemical level, to rise or fall and induce the survival, development and functioning of neuron cells [51]. Neurotrophins, regulate the development, maintenance and functions of the mammalian nervous system through activation of two different classes of receptors — the tyrosine kinases and tumor necrosis factor (TNF) receptor family, a super family of cytokine receptors [52].

Recent studies show that the regulation of the Brain-Derived Neurotrophic Factor (BDNF) protein, is controlled by the expression of the BDNF gene in the neurons, and the level of gene expression is controlled by a sequence of

neurotransmitter interactions [53]. Likewise, peripheral factors, including blood level of circulating hormones like estrogen, corticosteroids and insulin-like growth factor 1 (IGF-1) also influence BDNF and its function in the brain [54]. The neurotransmitter systems of acetylcholine, Gamma Amino Butyric Acid GABA, serotonin, and noradrenaline all act as mediators in regulation of BDNF in the hippocampus. There is immense research on exercise-induced BDNF and skeletal muscle as a secretory organ where BDNF is helping in development of muscle memory and neuro-sprouting to build cognitive reserves [55].

Insulin-like growth factor 1 (IGF-1), synonymously called Somatomedin C, is a neuropeptide hormone similar in molecular structure to insulin, which plays an important role in childhood growth, and shows anabolic developments in adults. It is produced primarily in the liver. IGF-1 regulates a variety of processes both peripherally and centrally including muscle hypertrophy, neurogenesis, neuronal survival, differentiation and enhancement of other neurotrophins including BDNF, etc. [56, 57] Peripheral levels of IGF-1 increase with exercise and build up cognition, memory and exercise-induced neurogenesis. This increase also enhances the BDNF secretions [56, 58].

Vascular Endothelial Growth Factor (VEGF), formerly known as the vascular permeability factor [59], is a signal protein formed from cells that stimulate the development of blood vessels. It is a sub-family of the platelet-derived growth factor family of cystine-knot growth factors, which play a pertinent role in vasculogenesis and angiogenesis [60]. It is a well-researched fact that endurance exercise training increases the muscle capillary supply. However, the muscle capillary supply and exercise-induced angiogenesis are regulated by VEGF [61]. Enriched environments like physical exercise for prolonged periods result in increased VEGF, which is also an important ‘somatic regulator’ of adult neurogenesis [62, 63].

The studies on release of neurotrophins are tabulated in Table 2.

Neuromodulators and their mechanism during exercise

Neuromodulators are neurochemicals that act in synergy with the neurotransmitters to enhance the excitatory or inhibitory responses, they include the endogenous opioid peptides, namely β -endorphins, enkephalins, dynorphins and endocannabinoids. Acute exercise causes significant increases in peripheral levels of endogenous opioids; this effect is intensity-dependent, corresponds to acute exercise-induced changes in hypothalamic–pituitary–adrenal (HPA) axis hormones, and in mood upliftment [58]. Cannabinoids appear to modify motor behavior by altering the communication between other transmitter systems present in the

basal ganglia. They appear to increase gamma amino butyric acid (GABA) transmission and inhibit glutamate transmission along with the reuptake of dopamine [93]. Thus, it can be predicted that low-level skills such as running, which are controlled to a higher degree by the basal ganglia than high-level skills, such as basketball, football or tennis may more readily activate the endocannabinoid system. Although further research is required in these areas. There are evidences of the synergic effects that endocannabinoids have with dopamine, cannabinoids increase the firing rates of dopaminergic neurons in the ventral tegmentum, substantia nigra, and the medial forebrain bundle. Further, withdrawal from cannabinoids, on the other hand, results in a decline in dopaminergic activity in the medial forebrain bundle [94–96]. This evidence suggests that the activation of endogenous cannabinoids through exercise could account for exercise addiction. Although, these possibilities deserve further scientific inquiry. The endocannabinoid system has reported to show adaptive responses to exercise in the form of vasodilation that could help increase blood flow during exercise. This is seen in the case of anandamide, which acts as a vasodilator and produces hypotension [97, 98]. On the other hand, exogenous cannabinoids have been seen to act as bronchodilators which could facilitate breathing during exercise [99, 100].

The studies on release of neuromodulators are tabulated in Table 3.

Discussion on the findings

A comprehensive analysis has been provided in this review study on the major avenues of the effects of physical exercise on brain neurochemicals. There have been various studies on neurochemicals and exercise with reference to animal brain models. The spectrum of neuro-protection through exercise therapy is also seen [111, 112]. However, this review attempts to concise neurochemicals in respect to physical exercise, keeping the neurophysiological mechanism under highlight.

Findings and discussion on exercise and neurotransmitters

A total of 17 studies on neurotransmitters and exercise have been summarized in Table 1, the collective evidence recorded neurotransmitter and catecholamines studies since 1972 till 2017. The trend of research in exercise-induced neurotransmitter research has shifted from a general response to physical-graded exercise variations and lately to more specific domains like effects on hypoxia, obesity, diabetes or cardiovascular dysfunction mainly to highlight the therapeutic side of exercise. However, these specific

variations have not been tabulated here as the present study includes effects only on healthy population. A total of 423 subjects constituted the total population under study, 364 males and 59 females. Studies that focused on older adult population included 114 males, while adolescent age group included 12 females. The results over the years have been conflicting; longitudinal studies showed noradrenaline is mediated by large muscle group activity and higher work rate exercise [42]. Overall catecholamine adaption occurs within three weeks after the start of training, while the response to exercise reduces there on [34, 35, 54]. Thus, catecholamines are good markers to indicate exercise adaptation level [48]. Studies with well-trained subjects and more intense exercise showed a greater effect on catecholamine response. Thus, the difference between non-trained and trained could be compared better. These studies showed lower catecholamine increase in well-trained subjects than the untrained or control groups. This could be due to higher adrenergic receptor density [36]; or due to increased pre-junctional receptors which lead to excretion of catecholamines, pulling the levels down to the same as pre-training levels [40]. Few studies also expressed the precursor release of blood lactate and accumulated oxygen deficit as a possible correlation leading to catecholamine increase [43]. Older adults and female population have been scarcely researched on. Of what is available in the as-researched evidential outcome, shows a blunted catecholamine response in both sections of the population [41, 44, 46]. Further research to unravel the exact causes of such responses is an area to work on.

Distinct positive changes in brain metabolism following graded exercise, aerobic exercise, and anaerobic exercise showed a linear trend of rise for plasma dopamine, and a quadratic trend for GABA and glutamate. Evidence of improvement in vocabulary learning was visible which lays the need to study these neurotransmitters from the aspect of neurogenesis and memory enhancers apart from their therapeutic mediations [22, 27].

Brain and muscle crosstalk with respect to neurotransmitters concluded in this review work that, exercise-induced catecholamine release brings in positive changes in brain metabolism following graded exercise, aerobic exercise, and anaerobic exercise [34, 36, 38]. Exercise-persuaded improvements in various neurochemical secretions had a positive impact on body adaptations, learning and cognitive fitness along with morphological changes and improvements in synaptic plasticity.

Findings and discussion on exercise and neurotrophins

A total of 38 studies have been pooled together in Table 2, which synthesize the benefits of exercise-induced brain-derived neurotrophic factor (BDNF), insulin-like growth

factor 1 (IGF-1) and vascular endothelial growth factor (VEGF) on brain health. A total of 1541 subjects underwent different exercise patterns from 2006 to 2022. Brain and muscle crosstalk with respect to neurotrophins, has been a novel area of research. Therefore, the studies are more in number and quite recent. Overall, 1229 male underwent these studies, of which 878 were young and middle-aged adults, while 507 were older adults. Research on female subjects was much lesser, 314 subjects constituted the research findings.

The results denoted that BDNF significantly increased with intense graded exercise of short duration which is anaerobic in nature, while significant changes were also seen with endurance training of aerobic nature and short-term duration [64, 66, 69, 71, 72]. However, 10-week and 12-week strength training showed statistically insignificant rise in BDNF [65, 67]. Long-term aerobic exercise like 6-month Nordic walking and 12-month aerobics reported to cause rise in BDNF through structural changes observed in the hippocampal regions and increase in gray matter volume in the cingulate and prefrontal cortex. Both these studies were performed on the elderly and implicated neuroprotective benefits of exercise on such vulnerable population [70–75]. On the other hand, a study on young adults reported an increase in BDNF levels through an intervention of acute high-intensity exercise. This study also showed improvement in vocabulary test scores which were taken simultaneously showing advances in memory, neuro-cognition and overall brain health [77]. Findings and evidence depict BDNF to elevate in circulation with all types of exercise. However, the most significant statistical rise was seen in practitioners with seven years and beyond of training experience [78], and insignificant changes were seen with strength training exercise [65, 67].

Compiled research studies on IGF-1 summarize two mechanisms of action: significant rise in exercise-induced IGF-1 secretions, one independent of GH release [42, 83, 91] and the other dependent on GH secretions [82, 83]. Few studies stated that the exercise-induced changes were interdependent on the entire IGF- system which led to the increase in overall bioavailability of IGF-1 [85, 88]. One finding that unraveled clearly was that chronic aerobic exercise and sprint intensity exercise led to the improvements in IGF-1 levels [42, 82, 90], while specific strength training exercises did not [67, 89, 91]. Though, it was also reported that strength training with chronic aerobic segments of warming up, cycling, and cool down, which can better be called as combined training showed superior levels of IGF-1 production [86, 87]. Research evidence on female subjects was scant and showed blunted results in comparison to the male population. Long-duration aquatic aerobic exercise shows significant rise in IGF-1 levels, on the other hand, four weeks walking with different aerobic exercise for long and

short duration caused rise in GH, but no significant improvement in IGF-1 took place [81, 85].

The next neurotrophic factor VEGF reported exercise-induced structural and functional changes, and the most minute finding in a particular study depicting its role in angiogenesis by [92] shows after variations in leg–knee extension exercises, and VEGF levels rise. Another very recent study depicts VEGF to increase with regular physical exercise not only in and around the muscle fibers but also in between the muscle fibers which improves muscles regenerative capacity [113]. These studies evidently show the induction of central and peripheral growth factors with regular exercise and physical activity to ensure successful brain functions.

As expressed earlier from the mechanistic point of view, it was evidently seen in several reported studies that exercise improved neurotrophic release and led to structural brain and neurocognitive changes with stress reducing positive modulations. In few cases, it was also noted that some of these specific changes were interdependent on an entire pool of hormones, while others were completely independent [42, 56, 79, 82–84]. Neurotrophins, brain-derived neurotrophic factor, insulin-like growth factor-1, and vascular endothelial growth factor showed significant improvement with long years of regular training, which clearly indicates the habitual benefits of exercise not just for physical health but for overall improvement of mental health as well [62, 63, 68, 78, 81].

Findings and discussion on exercise and neuromodulators

Neuromodulator class of neurochemicals was no exception. They showed significant enhancement with exercise of various grades and types. Exponential improvements were depicted with practice of intensity-dependent acute exercises in peripheral levels of endogenous opioids. Positive changes in hypothalamic–pituitary–adrenal (HPA) axis hormones, mood upliftment and peripheral endocannabinoids were proved by Schwarz and Kindermann (1989) and similar results were seen in studies conducted many years later [22, 48].

Pooled evidence of exercise-induced beta endorphins, enkephalins and endocannabinoids has been collectively represented in Table 3. A total of eleven studies have been summarized here on 102 male and 37 female subjects. Graded exercise and acute aerobic exercise seemed to show significant spike in β -endorphin levels among female subjects [101, 106], and strength resistance training showed similar spike among male subjects [107]. In another group of women, testing exercise interventions coincided with their early follicular phase results showed exercise acted as physiological stimulus for the rise in β -endorphin and enkephalin initially, but later the levels declined [102]. In a review conducted by Schwarz et al. 1992, an exercise-induced surge in

the peripheral beta-endorphin concentration was reported. This was the most significant one and evident with anaerobic exercise and the vulnerable substrate was lactate [114]. However, the trend shifted with time and studies performed a decade later found aerobic and endurance activity of acute nature to release significantly higher amount of endorphins and other endocannabinoids. These neuromodulators inhibit pain signals with release and are known to elevate neuro-synaptic transmission which leads to a euphoric state with acute intensity of exercise. The condition commonly called the runners high [115].

Acute aerobic exercise in the present study clearly indicated exponential rise in endocannabinoid system of neurochemicals in most of the pooled data highlighting the psychophysiological role of exercise in development of mental wellbeing and cognition [71, 109, 110].

Limitations of the study and future direction of research

The present study takes forth a vast and heterogeneous under survey, and subsequently the mechanistic viewpoints have been focused on more deeply along with certain overall limitations. The segregations of the neurochemical secretions in each study under consideration were not conducted according to their release levels meaning brain or periphery. Exercise-mediated physiological and cognitive events are so diverse that further research is required to understand the substrate effects and the inhibition and excitation relations among the neurochemicals and exercise. A critical appraisal of the studies through the bias assessment tools was refrained as this was a comprehensive pooling in light of the type of neurochemical released based on the type and grade of exercise performed. The heterogeneous pattern of the studies and their research designs, if put into the bias rubric the essence of this elaborate study, would be diminished. However, the prospective path of research to perform specific critical review of each neurochemical separately would of course make such assessments mandatory to improve transparency in the findings.

Conclusion

Numerous neurobiological hypotheses put forward an array of observed responses to exercise which were compiled, to conclude that adhering to a habitual exercise program appears to enhance neurogenesis, angiogenesis, and memory functions which induce cognition and thinking. After-effects of acute bout of exercise were also considered with utmost importance, the reason being that chronic exercise is ultimately the result of regular bouts of acute exercise.

All the three neurochemicals under review showed positive changes in brain neuro-cognition neurogenesis and mental well-being. Duration, intensity and grading of exercise patternology played a pertinent role along with age and gender in developing the psychophysiological set-up of the body and mind. Studies on female and adolescent age group can be further investigated as studies in these groups of the population are few.

However, understanding brain function takes more than just one sequence of experiments. It involves many precursor and predecessor neurochemicals—both excitatory and inhibitory with several complexities—yet we have tried to summarize these effects. This review magnifies that aerobic exercise of moderate intensity when performed in a regular and right way adhering to scientific methods can positively improve all three classes of neurochemicals under review, and modulate mental health and cognitive wellness. Vigorous exercise and high-intensity exercise have also given positive results, but the former reaping more significant outcomes. Thus, it arbitrates the frequently used saying sound mind in a sound body of the past into the present with a realistic meaning.

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Data availability This is a Review Paper and the data has been made available in the Tables as pooled evidence. There is no other data that has to be made available. All the data has been made available.

Declarations

Competing interests The authors declare no competing interests.

Conflict of interest The authors declare no competing interests.

Ethical approval This is a Review Article thus there is no Research involving Human Participants and/or Animals.

Informed consent Thus no Informed consent is required.

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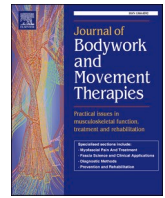
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A comparative assessment of yogasana and karate training on cardio-autonomic function in adolescents: An empirical study

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ABSTRACT

Introduction: Scientific findings reveal regular practice of traditional mind body exercises may reduce the invasion of chronic stressors and regain psychophysiological balance. This neuroautonomic relationship is assessed through several electrophysiological tools Heart Rate Variability (HRV) being one such measure. The present study compares the long-term cardio autonomic effects of yogasana – the physical aspect of yoga and another eminent but unexplored mind-body martial art form– karate.

Method: 90 male school going subjects - 30 experienced yoga (age: 15.5 ± 1.83 yrs); 30 karate (age: 15.23 ± 2.07 yrs) practitioners and 30 active age-gender matched controls (age: 15.46 ± 1.77 yrs) were conveniently sampled, after effect size calculation. Time and frequency domain HRV was compared using One-way ANOVA followed by LSD Post Hoc Test after normality distribution of the data was checked.

Results: High frequency power normalized unit (HF nu) showed significantly higher values among yoga practitioners (45.18 ± 16.00 nu) followed by karate practitioners (43.21 ± 18.14 nu) compared to the active control group (32.90 ± 15.76). The Low frequency normalized unit (LF nu) was at (53.90 ± 18.64 nu) and LF/HF Ratio at (1.40 ± 1.10) in the yoga group showed significantly lowest values.

Conclusions: Yogasana maintains stable parasympathetic dominance through its postures and steady breathing patternology, while karate practitioners being stress resilient show low sympathetic-vagal tone with a steady heart brain wellbeing.

1. Introduction

The central autonomic nervous system with its vagal and sympathetic branches plays a synchronous role in maintaining the overall health of an individual (Cerritelli et al., 2021). In fact, better cardio autonomic functioning results in a stress-free mind and superior bodily functions.

Physical activity and exercise should be incorporated in one's daily life cycle from the very young age as this supports effectual physiological working of the body, especially heart and brain health. World Health Organization recommends a minimum of 60 min of moderately intense activity per day for children and adolescents worldwide, which is unmet in most cases (World Health Organization, 2020). Empirical research clearly indicates that regular patterned physical exercise always has a definite progressive impact on autonomic physiology and cardiac conditioning (Carter et al., 2003; Chen et al., 2022; Flatt et al.,

2017; Wadden et al., 2018).

Practice of traditional mind body exercises like yoga and martial arts over the years have shown potential health benefits on cardiovascular functioning and working of the brain. Different stressors, emotional challenges, academic stress, mental overload, sedentary lifestyle, pressure situations and the environment hamper the psychophysiological homeostasis of the body and mind (Maulik, 2017; Olver et al., 2015). Cardiac and cognitive disorders and diseases have become a common finding among all ages and even prevalent in children and adolescents these days (Shaddy et al., 2018). In fact, a major cause of pre-mature mortality these days (Montes et al., 2023).

Stress coping and self-regulatory mechanism are a part and parcel of mind-body training like yoga, karate, taichi and qigong (Hagen et al., 2023; Li et al., 2022; Qi et al., 2022). The muscle stretch with slow breath control and mediated movements which improve neurocognition are practiced time and again by these practitioners which regulate their

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muscle memory, rewiring their neuro signaling, cognitive behaviour and heart health. Several studies have depicted these positive changes by assessing the cognitive processing time, biofeedback dispensation, magnetic resonance, EEG measurements, EVP Measurements etc. (Boaventura et al., 2022; Desai et al., 2015; Bhattacharya et al., 2022). Heart Rate Variability (HRV) is also one such precise non-invasive marker which has been assessed to realize cardiac activity and neuro-autonomic modulation. There are studies on mind body exercises like qigong, karate, taekwondo and pranayama a segment of yoga or combined yogic activity which point out the attainment of sympatho-vagal balance and improvement in vagally mediated HRV (Jiayuan et al., 2022; Zou et al., 2018; Lin et al., 2015; Bhattacharya et al., 2023).

The present study thus, attempts to investigate the long-term effects of yogasana and karate training on their practitioners, focusing on the cardiac-cognitive relationship through Heart Rate Variability (HRV) assessment. To our knowledge, this is the first attempt to compare yogasana, a specific aspect of yoga, with karate as long-term interventions evaluated using HRV. Yogasana and karate share several commonalities, including postural similarities, the use of breath and balance, and energy circulation through various body plexuses. Similar to the heart and brain's indissoluble link, yogasana and karate are closely connected, which has been analyzed using the cardiac vagal tone indicator, HRV.

1.1. Objective of the study

To compare cardio-autonomic regulation through Heart Rate

Variability among yogasana and karate practitioners along with their active control counterparts.

To compare the effects of yogasana and karate practice on cardio-autonomic regulation, as measured by Heart Rate Variability (HRV), in practitioners of these disciplines and their active control counterparts.

2. Method

2.1. Study design

The study was performed at the Exercise and Sports Physiology Laboratory, Department of Physical Education, of the University. This comparative study is a sub group analysis within the ongoing observational trail registered with the Clinical Trial Registry of India (CTRI). Regn. No: CTRI/2021/06/034,483 to assess and compare the effects of neurocognitive variables between karate and yoga practitioners. This study compared the cardio-autonomic dominance among three groups based on Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (2023).(von Elm et al., 2014) The research protocol and design were approved by the Institutional Ethics Committee for Human Research, of the University and the Independent Ethics Committee under the affiliation of Central Drugs Standard Control Organization (CDSCO), Ministry of Health and Family Welfare, Government of India. The inception and pre administration of the study began in November 2020, data collection and testing occurred between December 2020 and April 2021. The data recording protocol for the study was in accordance with under the National Ethical Guidelines for Biomedical and Health Research involving Human Participants for

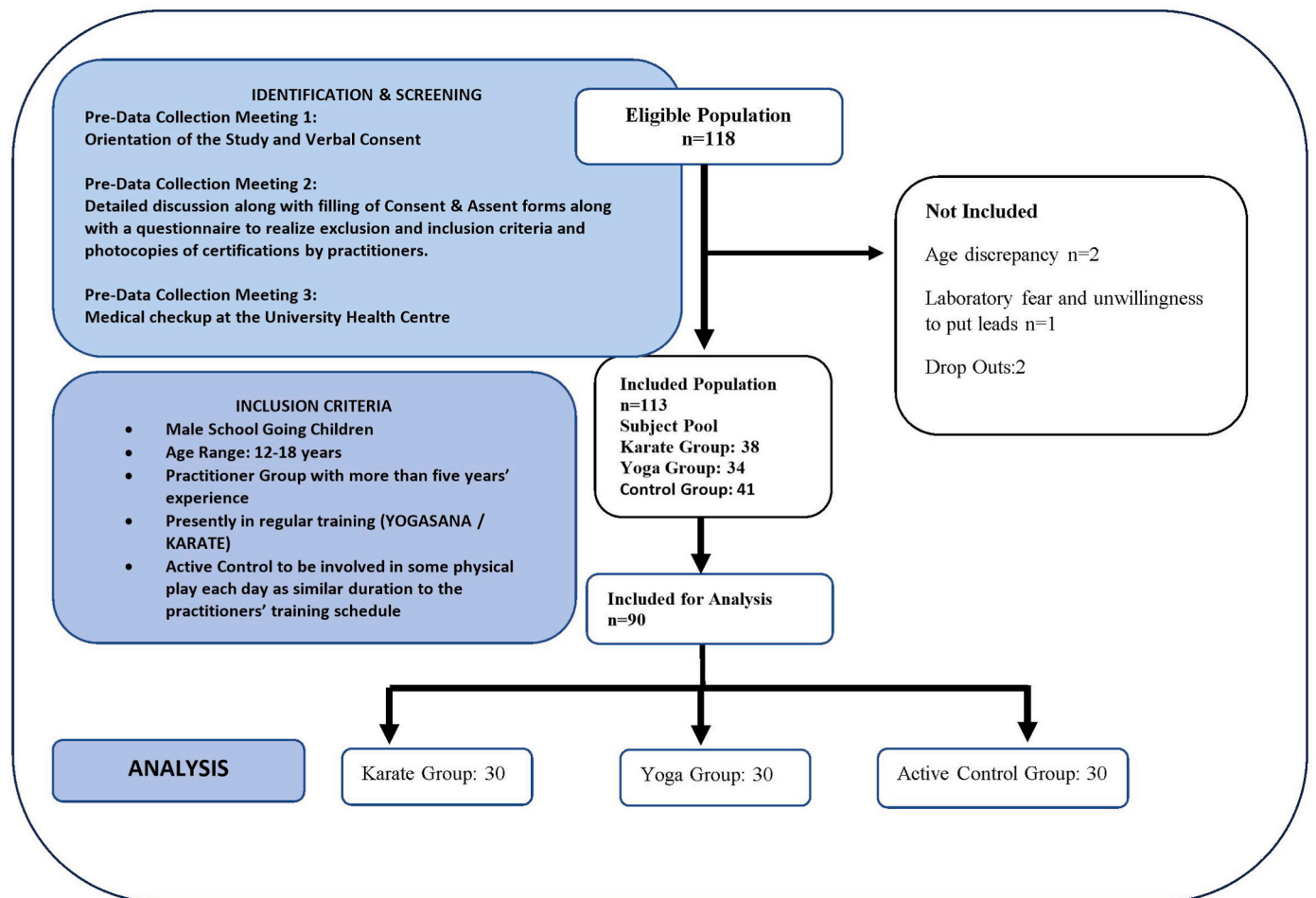


Fig. 1. Strobe flow diagram of the present empirical study.

mature minors framed by the Indian Council of Medical Research ICMR (National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, 2017; National Ethical Guidelines for Bio-Medical Research Involving Children, 2018). The legal representatives that are, the parents, elders, teachers and coaches along with the mature minor subjects were guided throughout the procedure while assent and consent forms were duly signed by them.

2.2. Determination of sample size

A priori sample size was determined using G*Power version 3.1.9.4 for Windows (2020); University of Keil, Franz Faul, Germany (Faul et al., 2007). The analysis determined that ninety participants be considered sufficient for the present study for an error probability of .05 and power of .84, with an effect size of .35. Thus, a total of ninety male school going subjects aged 12–18 years (n = 90) were selected through convenient sampling method under three groups; the Karate group (K; n = 30); the Yoga group (Y; n = 30) and the ages – gender matched Active Control group (C; n = 30).

2.3. Study participants

Pre-data collection meetings were conducted with the subject population and their legal representatives who matched the inclusion criteria and gave positive consent regarding their student’s participation in the study from their respective training organizations, schools, etc. All required information about the study was shared, and any additional queries were cleared. Subsequently, a subject pool was formulated, and a convenience sample of 90 subjects was selected from this pool, with 30 subjects in each group. The study’s trail profile with inclusion criteria is illustrated in Fig. 1. The karate group (K) and yoga group (Y) comprised male practitioners with an overall training age of five years and above (6.633 ± 1.449 years), practicing four days a week for one and a half hours each day at reputed karate or yoga training organizations. Healthy, age-gender matched male children, free from disease and engaged in regular physical activity, formed the third group. The active control group had no training or skill acquaintance with yogasana or karate. While both karate and yogasana are art forms, they are currently represented as sports. All subjects have at least state-level positions or participation in either karate or yogasana, justifying their practical applicability. Sedentary and female children were excluded from the study. Female subjects couldn’t be included as their regular practice was most affected post-pandemic, and there was more fear and restraint from their parents in sending them to the laboratory compared to boys. The core team and experts involved in the data collection and extraction process had received training from system experts and were well

qualified for the laboratory equipment handling and all good clinical practices were followed in order to avoid any kind of bias or personal discrepancy.

2.4. Variables assessed

Anthropometric variables were measured, and subjects were rested for 30 min in a calm environment. Data was recorded by seating participants comfortably in chairs, cleaning the skin at electrode sites with alcohol spirit, applying gel, and attaching electrode pegs. Jewelry and electronic gadgets were removed. The RMS Polyrite (RMS, India) poly-graph was set and run for 2 min, followed by 5 min of data collection. Electrode impedance was checked and kept below 5 KΩ. Leads were checked for proper attachment to cables, ECG amplifier, and data acquisition unit. Extracted data was examined for artifacts or noise and graphically projected on the RMS Physiograph D version 5.0.6. The data collection was carried out on two successive days and the best trial was taken for assessment. All the sessions were conducted in the morning before lunch between 8:00 a.m. and 12:00 noon. Linear analysis was extracted from the RMS Vagus HRV software report on both the time and the frequency domains to realize the cardio autonomic activity in the participants.

2.5. Statistical analysis

Kolmogorov-Smirnov test showed the data was normally distributed. Mean and standard deviation was performed as descriptive statistics, while HRV variables of both time and frequency domains were compared using One Way ANOVA. SPSS 20.0 software for Windows; for the comparative analysis of the data. Least Significant Difference (LSD) Post Hoc Test was used to find out the

Inter group significance. Measurement data were expressed as Mean ± SD and the significant level was set at .05 levels (P < 0.05).

3. Results

3.1. Participant characteristics

After three detailed Pre-Data Collection meetings a subject pool with a total of 113 subjects was formulated, followed by rigorous screening, application of inclusion and exclusion criteria and effect size calculation criteria, 90 children were selected as the subjects for the present study (30 in each group; K = 30, Y = 30 and C = 30).

The anthropometric variables age, height, weight, body mass index (BMI) and waist hip ratio (WHR) along with training age were measured and compared among all the three groups. The mean age of the three

Table 1
One way ANOVA and LSD post hoc test for selected demographic variables.

Demographic Variables	Groups	N	Mean ± SD	Groups	Sum of Squares	df	Mean Square	F	Sig.	Dependent Variable	Mean Difference (I-J)	Std. Error	Sig.	
BMI	Karate	30	19.737 ± 3.455	Between Groups	185.215	2	92.607	9.822	.000	K Yoga Control	.530	.793	.506	
	Yoga	30	19.207 ± 2.196	Within Groups	820.276	87	9.428				Y Karate Control	-.274333*	.793	.001
	Control	30	22.480 ± 3.395	Total	1005.491	89					C Karate Control	-.327333*	.793	.000
	Total	90	20.474 ± 3.361							Karate Control	-.274333*	.793	.001	
										Yoga Control	-.327333*	.793	.000	
WHR	Karate	30	.862 ± .047	Between Groups	.013	2	.006	3.633	.031	K Yoga Control	-.017	.011	.126	
	Yoga	30	.879 ± .027	Within Groups	338.467	87	3.890				Y Karate Control	-.02900*	.011	.009
	Control	30	.891 ± .048	Total	355.956	89					C Karate Control	-.017	.011	.011
	Total	90	.878 ± .043							Karate Control	-.02900*	.011	.009	
										Yoga Control	-.012	.011	.257	

(*The mean difference is significant at the .05 level).

Table 2
Comparison of Mean ± SD, Analysis of Variance and Post Hoc Analysis of the Time domain HRV Variable among the three groups;
 Table Abbreviations: K: Karate, Y: Yoga and C: Controls, Tot: Total.

Variables & Groups	N	Mean	Std. Error	Groups	Sum of Squares	df	Mean Square	F	Sig.	Dependent Variable	Mean Difference (I-J)	Std. Error	Sig.		
Mean RR	K	30	.71 ± .10	.02	Between Groups	.06	2	.029	2.829	.065	K	Yoga	.023	.026	.380
											K	Control	-.039	.026	.145
	Y	30	.68 ± .09	.02	Within Groups	.96	87	.010			Y	Karate	-.023	.026	.380
											Y	Control	-.061,933*	.026	.021
	C	30	.75 ± .11	.02	Total	.90	89				C	Karate	.039	.026	.145
											C	Yoga	.061,933*	.026	.021
Mean HR	Tot	90	.71 ± .10	.01											
	K	30	85.23 ± 11.97	2.18	Between Groups	139.62	2	69.811	.456	.635	K	Yoga	-1.800	3.195	.575
											K	Control	1.233	3.195	.700
	Y	30	87.03 ± 11.60	2.12	Within Groups	13,461.96	87	153.130			Y	Karate	1.800	3.195	.575
											Y	Control	3.033	3.195	.345
	C	30	84.00 ± 13.48	2.46	Total	13,322.33	89				C	Karate	-1.233	3.195	.700
										C	Yoga	-3.033	3.195	.345	
SDNN	Tot	90	85.42 ± 12.30	1.30											
	K	30	54.55 ± 22.84	4.17	Between Groups	1056.64	2	528.320	1.255	.290	K	Yoga	7.990	5.298	.135
											K	Control	1.771	5.298	.739
	Y	30	46.56 ± 14.90	2.72	Within Groups	36,634.95	87	421.091			Y	Karate	-7.990	5.298	.135
											Y	Control	-6.220	5.298	.244
	C	30	52.78 ± 22.80	4.16	Total	37,691.59	89				C	Karate	-1.771	5.298	.739
										C	Yoga	6.220	5.298	.244	
RMSSD	Tot	90	51.30 ± 20.58	2.17											
	K	30	34.70 ± 13.28	2.42	Between Groups	190.78	2	95.391	.550	.579	K	Yoga	-2.376	3.400	.486
											K	Control	1.115	3.400	.744
	Y	30	37.08 ± 14.51	2.65	Within Groups	15,081.51	87	173.351			Y	Karate	2.376	3.400	.486
											Y	Control	-3.491	3.400	.307
	C	30	33.59 ± 11.54	2.11	Total	15,272.29	89				C	Karate	2.376	3.400	.744
										C	Yoga	3.491	3.400	.307	
NN50 pNN50	Tot	90	35.12 ± 11.54	1.38											
	K	30	69.33 ± 43.78	7.99	Between Groups	7638.42	2	3819.211	1.198	.307	K	Yoga	-8.833	14.577	.546
											K	Control	-22.400	14.577	.128
	Y	30	78.17 ± 55.65	10.16	Within Groups	277,298.70	87	3187.341			Y	Karate	8.833	14.577	.546
											Y	Control	-13.567	14.577	.355
	C	30	91.73 ± 67.44	12.31	Total	284,937.12	89				C	Karate	22.400	14.577	.128
										C	Yoga	13.567	14.577	.355	
pNN50	Tot	90	79.74 ± 56.58	5.96											
	K	30	18.50 ± 14.03	2.56	Between Groups	349.33	2	174.663	.789	.458	K	Yoga	2.182	3.842	.572
											K	Control	-2.637	3.842	.494
	Y	30	16.32 ± 14.24	2.60	Within Groups	19,261.99	87	221.402			Y	Karate	-2.182	3.842	.572
											Y	Control	-4.819	3.842	.213
	C	30	21.14 ± 16.27	2.97	Total	19,611.31	89				C	Karate	2.637	3.842	.494
										C	Yoga	4.819	3.842	.213	

(*The mean difference is significant at the .05 level).

Mean RR: Mean Inter beat interval.

Mean HR: Mean Heart Rate.

RMSSD: Root mean square of the successive differences.

SDNN: Standard deviation of the NN (R–R) intervals.

NN50: The number of pairs of successive NN (R–R) intervals that differ by more than 50 ms.

PNN50: The proportion of NN50 divided by the total number of NN (R–R) intervals.

Table 3Comparison of Mean \pm SD, Analysis of Variance and Post Hoc Analysis of Frequency Domain HRV Variable among the three groups; Table Abbreviations: K: Karate, Y: Yoga and C: Controls, Tot: Total.

Variables & Groups		N	Mean \pm SD	Std. Error	Groups	Sum of Squares	df	Mean Square	F	Sig.	Dependent Variable	Mean Difference (I-J)	Std. Error	Sig.	
VLF (nu)	K	30	49.81 \pm 18.51	3.38	Between Groups	154.85	2	77.423	.282	.755	K	Yoga	-3.204	4.276	.456
												Control	-1.807	4.276	.674
	Y	30	53.01 \pm 14.49	2.65	Within Groups	23,856.55	87	274.213			Y	Karate	3.204	4.276	.456
												Control	1.397	4.276	.745
	C	30	51.61 \pm 16.43	3.00	Total	24,011.40	89				C	Karate	1.807	4.276	.674
												Yoga	-1.397	4.276	.745
VLF (ms ²)	Tot	90	51.48 \pm 16.43	1.73											
	K	30	472.38 \pm 393.94	71.92	Between Groups	80,339.18	2	40,169.592	.258	.773	K	Yoga	-5.228	101.878	.959
												Control	-65.832	101.878	.520
	Y	30	477.61 \pm 341.00	62.26	Within Groups	13,544,826.71	87	155,687.663			Y	Karate	5.228	101.878	.959
												Control	-60.603	101.878	.553
LF Power (%)	C	30	538.21 \pm 442.26	80.75	Total	13,625,165.90	89				C	Karate	65.832	101.878	.520
												Yoga	60.603	101.878	.553
	Tot	90	496.06 \pm 391.27	41.24											
	K	30	35.56 \pm 13.03	2.38	Between Groups	779.04	2	389.522	2.059	.134	K	Yoga	5.053	3.552	.158
												Control	6.977	3.552	.053
LF Power (nu)	Y	30	30.50 \pm 14.69	2.68	Within Groups	16,462.25	87	189.221			Y	Karate	-5.053	3.552	.158
												Control	1.924	3.552	.589
	C	30	28.58 \pm 13.50	2.26	Total	17,241.30	89				C	Karate	-6.977	3.552	.053
												Yoga	-1.924	3.552	.589
	Tot	90	31.55 \pm 13.92	1.47											
LF Power (ms ²)	K	30	59.96 \pm 16.51	3.01	Between Groups	1900.59	2	950.296	3.488	.035	K	Yoga	6.059	4.262	.159
												Control	-5.186	4.262	.227
	Y	30	53.90 \pm 18.64	3.40	Within Groups	23,703.96	87	272.459			Y	Karate	-6.059	4.262	.159
												Control	-11.245100*	4.262	.010
	C	30	65.15 \pm 14.05	2.56	Total	25,604.55	89				C	Karate	5.186	4.262	.227
												Yoga	11.245100*	4.262	.010
HF Power (%)	Tot	90	59.67 \pm 16.96	1.79											
	K	30	259.77 \pm 129.16	23.58	Between Groups	13,588.21	2	6794.104	.311	.733	K	Yoga	29.919	38.149	.435
												Control	12.124	38.149	.751
	Y	30	229.85 \pm 147.98	27.02	Within Groups	1,899,220.01	87	21,830.115			Y	Karate	-29.919	38.149	.435
												Control	-17.795	38.149	.642
HF Power (nu)	C	30	247.64 \pm 164.04	29.95	Total	1,912,808.22	89				C	Karate	-12.124	38.149	.751
												Yoga	17.795	38.149	.642
	Tot	90	245.75 \pm 146.60	15.45											
	K	30	17.67 \pm 13.83	2.52	Between Groups	282.27	2	141.133	.898	.411	K	Yoga	-4.338	3.238	.184
												Control	-2.177	3.238	.503
HF Power (ms ²)	Y	30	22.01 \pm 12.25	2.24	Within Groups	13,680.74	87	157.250			Y	Karate	4.338	3.238	.184
												Control	2.161	3.238	.506
	C	30	19.85 \pm 11.43	2.09	Total	13,963.01	89				C	Karate	2.177	3.238	.503
												Yoga	-2.161	3.238	.506
	Tot	90	19.84 \pm 12.53	1.32											
HF Power (nu)	K	30	43.21 \pm 18.14	3.31	Between Groups	2610.72	2	1305.361	4.699	.012	K	Yoga	-1.975	4.303	.647
												Control	10.308967*	4.303	.019
	Y	30	45.18 \pm 16.00	2.92	Within Groups	24,166.32	87	277.774			Y	Karate	1.975	4.303	.647
												Control	12.284000*	4.303	.005
	C	30	32.90 \pm 15.76	2.88	Total	26,777.04	89				C	Karate	-10.308967*	4.303	.019
												Yoga	-12.284000*	4.303	.005
HF Power (ms ²)	Tot	90	40.43 \pm 17.35	1.83											
	K	30	141.94 \pm 96.27	17.58	Between Groups	68,024.93	2	34,012.467	1.563	.215	K	Yoga	-62.444	38.094	.105
												Control	-53.058	38.094	.167
	Y	30	204.38 \pm 153.82	28.08	Within Groups	1,893,713.96	87	21,766.827			Y	Karate	62.444	38.094	.105
												Control	9.385	38.094	.806
HF Power (ms ²)	C	30	194.99 \pm 179.92	32.85	Total	1,961,738.89	89				C	Karate	53.058	38.094	.167

(continued on next page)

Table 3 (continued)

Variables & Groups	N	Mean ±SD	Std. Error	Groups	Sum of Squares	df	Mean Square	F	Sig.	Dependent Variable	Mean Difference (I-J)	Std. Error	Sig.
Total	90	180.44 ± 148.47	15.65							Yoga	-9.385	38.094	.806
LF/HF Ratio	30	1.91 ± 1.18	.22	Between Groups	10.20	2	5.099	4.476	.014	Yoga	.519	.276	.063
	30	1.40 ± 1.02	.19	Within Groups	99.11	87	1.139			Control	-.295	.276	.288
	30	2.21 ± .99	.18	Total	109.31	89				Karate	-.519	.276	.063
	90	1.84 ± 1.11	.12							Control	-.814,300*	.276	.004
										Karate	.295	.276	.288
										Yoga	.814,300*	.276	.004

(*The mean difference is significant at the .05 level).

VLF: Very low frequency.
 LF: Low Frequency.
 HF: High Frequency.
 Units Abbreviation.
 Nu: normalized unit.
 Ms²: square milli second.
 %: percentage.

groups was 15.8 ± 1.886 years, inter group comparison showed no significant difference in age among the three groups ($Y = 16 \pm 1.8$; $K = 15.6 \pm 2.08$; $C = 15.5 \pm 1.78$). The mean height and weight for the three groups was 160.99 ± 10.13 cm and 53.433 ± 10.58 kg respectively. Inter group comparison for height and weight also showed no significant difference on comparison ($Y = 159 \pm 8.69$ cms; $K = 162.5 \pm 10.86$ cms; $C = 160.99 \pm 10.13$ cms) ($Y = 48.4 \pm 6.468$ kgs; $K = 52.8 \pm 12.54$ kgs; $C = 59.1 \pm 12.76$ kgs). The mean training age for the practitioner group was 6.50 ± 1.183 yrs which was well within the criteria for inclusion while the respective training age for the Yoga group (Y) was $6.366 \pm .927$ yrs and for the Karate group (K) it was 6.633 ± 1.449 yrs.

However, the next two variables, Body Mass Index (BMI) and Waist to Hip Ratio (WHR) showed significant variation in the One Way ANOVA and so LSD Post hoc test was conducted to realize the intergroup differences. BMI of the karate and yoga group measured significantly lower values than the control group ($Y = 19.207 \pm 2.196$; $K = 19.737 \pm 3.455$; $C = 22.48 \pm 3.395$). While WHR of the karate practitioners was significantly lower in comparison to the control group ($Y = .879 \pm .27$; $K = .862 \pm .047$; $C = .891 \pm .048$). These significant results for the anthropometric variables are tabulated in Table 1.

3.2. Heart Rate Variability

Time Domain and Frequency Domain measures of Heart Rate Variability were calculated and tabulated in Tables 2 and 3. The time domain variables showed no significant changes among the three groups. However, results for the frequency domain variables showed significant differences in three components, which were high frequency normalized unit (HF nu) component which depicted significantly highest value for the yoga group (45.18 ± 16.00 nu) followed by the karate practitioners (43.21 ± 18.14 nu) in comparison to the active control group (32.90 ± 15.76 nu). Low frequency normalized unit (LF nu) depicted significantly lower values in the yoga group (53.90 ± 18.64 nu) when compared to the karate and control group and the LF-HF Ratio showed also measured significantly lower ratio values in the yoga group in comparison to the other two groups at (1.40 ± 1.10). The significance level was $P < .05$.

3.3. Discussion on participant characteristics

The participants' characteristics that are-age, height, weight, training age, body mass index (BMI) and waist hip ratio (WHR) were compared among all the three groups. BMI among karate and yoga practitioners measured significantly lower values than the control group. Similar results were commonly reported in previous studies on healthy adults' which measured improvements in BMI with habitual yoga practice (Chauhan et al., 2017; Madanmohan et al., 2008); as well as in patients after yogic intervention (Telles et al., 2019; Taneja, 2014). Karate, like yogasana involves equal and opposite movements involving muscle stretch and contemplation of the mind with balanced actions involving both dominant and non-dominant sides of the body. These types of movements are synchronized with slow and fast breathing activity, and have recorded to reduce the BMI and WHR in previous studies on martial artists as well (Schwartz et al., 2015; de Souza et al., 2020).

The control group comprised of active male school going children who were associated with regular physical activity however, with no acquaintance with karate or yogasana. There is a supposition that the higher BMI and WHR in the control group could be because of the involvement of this group in an unsupervised physical activity that was not under any training programme, nor guided by any training personnel or expert. There are reported documentations that predict that unguided physical activity alone cannot reduce BMI or obesity (Kesavachandran et al., 2009; Raustorp et al., 2004). This could have been the case in this study too, as the practitioner groups were involved in rigorous guided mind body practices since a young age.

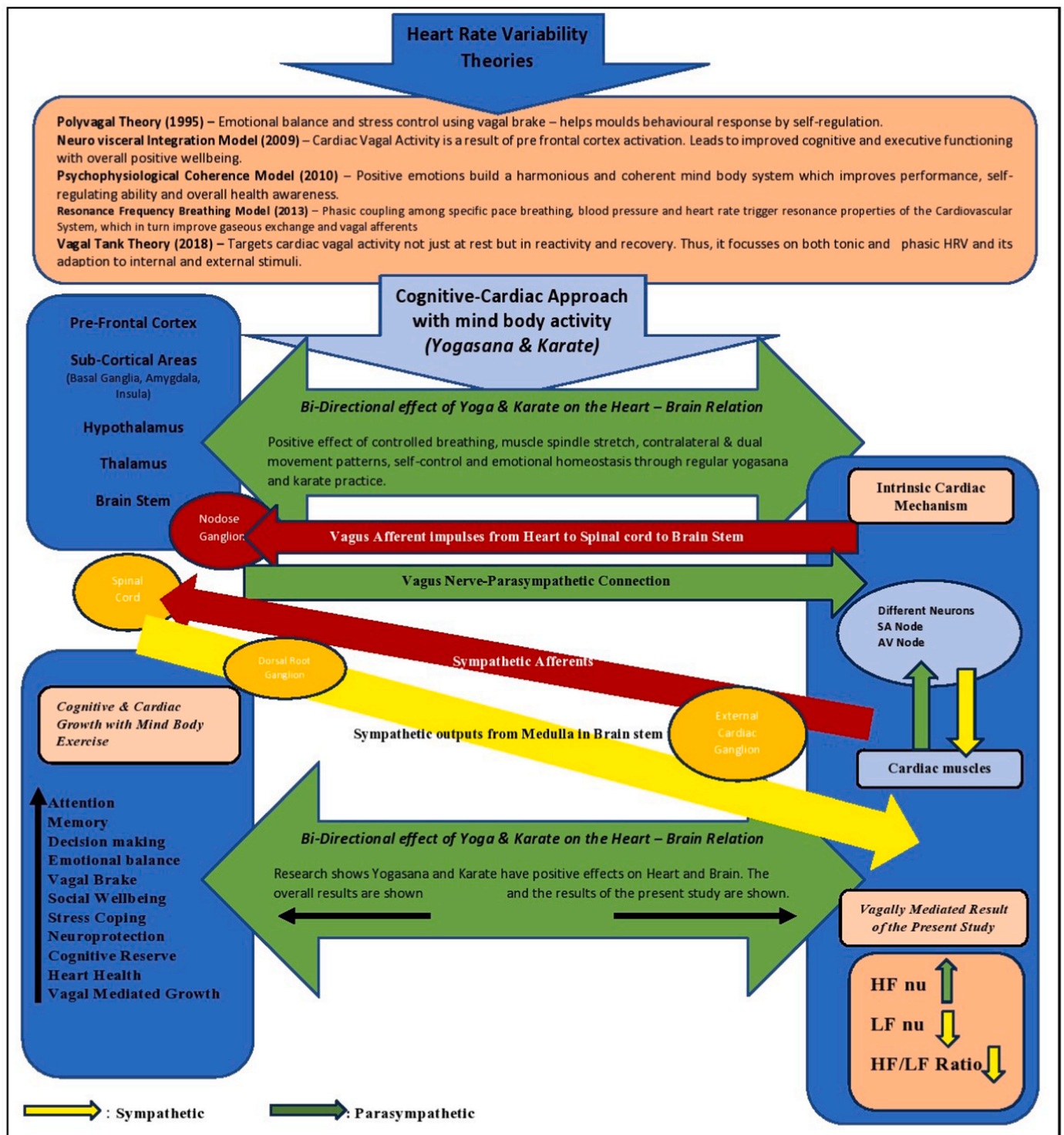


Fig. 2. Cardiac-Cognitive Approach with Bidirectional effect of Yoga and Karate on Heart and Brain.

3.4. Discussion on Heart Rate Variability

The autonomic nervous system plays a basic role in regulating several organs of the body. Heart-brain interactions being one of them, this systemic interplay was first experimented in the 1970's by John and Beatrice Lacey, the forerunner to suggest a causal role of the heart in moderating cognitive functions (Lacey and Lacey, 1974). Heart brain neural interactions and their dynamic cardiac-cognitive connection are being researched and reviewed even today (Arakaki et al., 2023).

The present study emphasizes on this very same connection between the vagal and cortical areas and the influence of two mind body practices – yogasana and karate on these regions in boys. The interpretation of the impact has been backed by renowned Heart Rate Variability Theories (HRV) which have been compounded over the years by various remarkable psychophysicologists to express cardio-autonomic behaviours. Both yogasana and karate involve bilateral and contralateral movements, focus and concentration and engage in stress coping activity in order to train their practitioners to face mental and physical stressors.

Karate and yogasana equally develop a mindful relationship between the cardiorespiratory functioning, autonomicity and behavioural response mechanism among its practitioners. The link between HRV and neurocognition has been discussed below in reference to the HRV theories and the results of the present study depicted in Fig. 2.

3.4.1. HRV and yoga

Mind body practices cultivate interoception, proprioception, mental resilience, adaptability, regulation and somatic awareness which appraise their real-life activity (Cramer et al., 2013; Bhattacharya et al., 2021; Bittencourt et al., 2015). Polyvagal theory recognizes this neural exercising in order to foster such adaptive responses through its vagal brake and behavioural response (Porges et al., 1996).

According to the neuro-visceral model there is a deep integration between the prefrontal cortex, sub cortical areas, hypothalamus and the brainstem. It is the brain stem nuclei as shown in Fig. 2, which are influenced by the vagally mediated and sympathetic nerve supply from the cardiac intrinsic system (Thayer and Lane, 2009) Regular and prolonged yogasana training which involves stretching of the musculo-skeletal system and controlled breathing patterns improve cardiac functions and cognitive outcomes which are evident in previous (Pitale et al., 2014; Rathore et al., 2021; De et al., 2019; Shobana et al., 2022); as well the present study.

The results of the present study also reiterate the psychophysiological coherence model and the resonance breathing model which pointed out that specific breathing patterns improves gaseous exchange and vagal afferents which help better reactivity and recovery (McCraty and Childre, 2010); similar results were seen in experimental models of research on yoga protocols with breathing in previous works (Chaitanya et al., 2022; Alaguvani and Devaki, 2021).

Research endorses that HRV, particularly High Frequency (HF) dominated parameters are often reflecting parasympathetic activity and among them HF Power (nu) is found to dominate and is related to active cognitive and executive functional development among yoga practitioners. On the other hand LF Power (nu) and LF/HF ratio seem to drop down among them (Tyagi and Cohen, 2016; Kuppusamy et al., 2020). As in previous research RMSSD from the time domain variable was correlated to HF nu as it was not affected by respiratory coordinates. It showed significantly higher values after yogic breathing protocols; here too we found RMSSD among practitioner group to be higher than the controls but it did not yield significant results, sample size could have been a limitation (Kuppusamy et al., 2020). There are arguments on this as well but further investigation is required (Mosley and Laborde, 2022).

3.4.2. HRV and karate

Martial art research in this area is quite scarce and thus the results are dispersed; Pooled evidence measuring effects of Qigong through HRV variables showed improvement in parasympathetic parameters and stress resilience among its practitioners (Ramos et al., 2017) Judo and Muay-Thai practitioner adolescents showed higher RMSSD and SD1 post training values and considered martial art training appropriate for improving efficiency of cardiovascular functioning (Suetake et al., 2018). Only one case study on elite karate athletes and HRV, which reported no signs of fatigue accumulation which was indicative of a steady HRV and low sympathetic tone (Nakamura et al., 2016). In the present study too, karate practitioners showed better vagally mediated HRV and it echoed the same outcomes as previous studies, but it further suggests karate as an evident mind body exercise along with its multifaceted benefits as a self-defense practice and a stress regulator. Karate practitioners are trained and simulated to face stimuli which create a fight or flight response but prevent sympathetic over activation to the particular stimulus. Such that they can adapt to a threatening environment with least disturbance in homeostasis. This resonates the vagal tank approach which states the adaptation to internal and external stimuli through autonomic functional improvements by striking a balance between sympathetic and parasympathetic tension (Lacey and

Lacey, 1974).

4. Conclusion

The current study orchestrates an integrative perspective between the theoretical and practical modulates of HRV and mind body practitioners from two areas yogasana and karate. It realizes positive cardio autonomic feedback on such practitioners when compared to their active control equivalents. Thus, such practitioners may have developed a better brain-heart coupling mechanism and may adapt better to the changing environment, have an enhanced physiological profile which positively correlates better cardiovascular efficiency and neurocognitive balance. The present research also concluded in its results that the practitioner groups i.e. yogasana and karate practitioners showed overall vagally mediated physiological oscillations in HRV. Thus, this may help in retention of a better overall cognitive reserve among our future population in this era of sedentarism.

CRedit authorship contribution statement

Bhattacharya Puneet: Writing – review & editing, Writing – original draft, Resources, Methodology, Investigation, Conceptualization. **Chatterjee Sridip:** Visualization, Validation, Supervision, Project administration, Conceptualization. **Dilip Roy:** Methodology, Investigation, Data curation. **Mondal Samiran:** Visualization, Supervision.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Original Research

Heart Rate Variability as a Neuroautonomic Marker to Assess the Impact of Karate Training - An Observational Pediatric Study

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ABSTRACT

International Journal of Exercise Science 16(2): 342-352, 2023. Habitual physical activity improves heart functions and parasympathetic tone; Karate training is considered as a moderate physical activity with rhythmical breathing patternology. Heart rate variability (HRV) is an electrophysiological tool which measures cardio autonomic homeostasis; is used in the present study as an indirect marker to measure neurocognitive development with karate training. The aim of the present study was to find out the impact of regular karate training on cardiac autonomic responses through Heart Rate Variability (HRV) between karate players and age-sex matched active controls. A total of 30 male school-going children were evaluated; fifteen were experienced male karate practitioners (9.5±1.26 years) and fifteen controls (10.6±1.57 years). The time and frequency domain measures of HRV were taken into account after check for normality distribution, followed by t-test for comparison of Mean±SD. Frequency domain measures; low frequency normalized unit (LF nu) and low frequency is to high frequency ratio (LF/HF ratio) both showed significant reduction in the karate group which quantified sympathetic disposition while High frequency normalized units (HF nu) reflected a significant rise and it predicted increase in parasympathetic tone. Karate practitioners show higher HRV measures and more involvement of the parasympathetic nervous system which help in stress resilience and improved recovery time. This training if performed regularly from an early age can improve cardiac health which is very pertinent in the present times.

KEY WORDS: Cardio autonomic homeostasis, moderate physical activity, parasympathetic tone, stress resilience, cardiac health

INTRODUCTION

Neurobiological mechanisms have been investigated in recent times and prove the interplay between cardiorespiratory fitness and cognitive enhancing benefits of physical exercise. Heart rate variability (HRV) is a reliable non-invasive index which measures the interactions between the autonomic nervous system and the cardiovascular system (1). Identified by a series of time and frequency domains it expresses bio signaling of the heart rhythms with changing

environmental situations. It expresses the dominance of the parasympathetic and sympathetic nervous systems of the brain indirectly affecting the heart through the vagal neural pathways (17).

HRV is an independent marker which circuitously reflects cognitive control, thus assesses the cardiac autonomic status of an individual. The dimensions of sustained and selective attention, memory, perception, behavioural inhibition, cognitive flexibility and loading can be viewed through its assessment (11). Hon and Lee in 1965 first recorded the significance of HRV clinically, which is the result of temporal oscillations between heart beats. In this study HRV has been measured through short term recordings of two areas; the time domain and frequency domain analysis, the complete detail of which are given in Table 1 below (13).

There is multiple evidence that psychophysiological stress negatively impacts the autonomic equilibrium and it results in various diseases and disorders (28, 5). This became even more pronounced with the strike of the pandemic especially in the younger generation (19, 20). HRV has proved to be a good clinical marker to echo these changes. On the other hand, various physical activity, aerobic exercises, mind body exercises have positively improved resilience to stress and enhanced the cardiac and brain health (2, 16, 18, 29). HRV has been measured in several studies previously on adults but documented evidence on children is minimal (24, 26).

Karate is a martial art form which involves slow and fast intermittent physical activity along with rhythmical breathing. Encompassing different levels of cognitive ability, focused attention, memory and methods to reduce stress and cope with it (4). This research paper is an effort to investigate the effects of karate training on neuro-autonomic modulation through HRV analysis. This analysis measures consecutive time intervals between the adjacent heart beats (RR intervals) and inter-beat measurement differences (NN intervals) from the sinus source providing information about the autonomic tone. Karate practitioners are compared with age sex matched active controls to understand the insights of neurocognition through the analysis of HRV.

The purpose of the present observational study was to understand the impact of regular karate training towards cardiac autonomic function through Heart Rate Variability (HRV) analysis in the pediatric male population. To fulfil the purpose of the present study, the following objectives were elaborated:

- a. To compare the dominance of karate training on brain functions among karate practitioners and age-sex matched active controls using HRV parameters.
- b. To measure the effects of regular karate training on the time domain and frequency domain HRV measurements.
- c. To examine Heart Rate Variability as a neuroautonomic tool to understand the mechanism underlying the benefits of neurocognition through parasympathetic and sympathetic dominance.

Table 1. Details of Time Domain and Frequency Domain Variables which comprise HRV Measurements.

Time Domain Variables	Units	Description	Dominance	Time Measures
SDNN	milli seconds (ms)	Inter-beat interval between successive heart beats	Parasympathetic dominance	Standard deviation of all NN intervals.
RMSSD	milli seconds (ms)	The square root of the mean of the sum of the squares of differences between adjacent inter beats.	Parasympathetic dominance	Square root of the mean of the squared differences between successive NN intervals
NN50 Count	numbers	Adjacent NN intervals differing by more than 50 msec in the entire recording.	Parasympathetic dominance	Number of adjacent NN intervals that differ from each other by more than 50 msec
PNN50	percentage %	The percentage of differences between successive NN intervals	Parasympathetic dominance	NN50 count divided by the total number of all NN intervals.
Frequency Domain Variables	Units	Description	Dominance	Frequency Range
VLF power	square milliseconds (ms ²)	Power in very low frequency range	Parasympathetic dominance	^0-04 Hz
LF power	square milliseconds (ms ²)	Power in low frequency range	Parasympathetic dominance	0-04-0-15 Hz
LF norm	n.u.	LF power in normalized units LF/ (Total Power-VLF) x 100	Sympathetic dominance	0.04-0.15 Hz
HF power	square milliseconds (ms ²)	Power in high frequency range	Parasympathetic dominance	0-15-0-4 Hz
HF norm	n.u.	HF power in normalized units HF/ (Total Power-VLF) x 100	Parasympathetic dominance	0-15-0-4 Hz
LF/HF	%	Ratio LF [ms ²]/HF [ms ²]	Sympathetic dominance	-

METHODS

Participants

The study was conducted at the Exercise and Sports Physiology Laboratory, Department of Physical Education, Jadavpur University, Kolkata, India. A power analysis was conducted with G*POWER 3.1.9.7 for Windows (2020) determined that 30 participants were needed in the

present study for a power of 0.26, with an effect size of 0.5 and $\alpha=0.05$. Thus, a total of 30 male school going subjects aged 8-12 years ($n=30$) were selected through convenient sampling method under two groups; the Karate group (K; $n=15$) and the Control group (C; $n=15$).

Inclusion and Exclusion Criteria: The karate group comprised of male practitioners with a training age of minimum three years (3 ± 0.2 years), practicing four days a week for one hour each day, at a reputed karate training organization, while age-sex matched children from reputed schools in Kolkata, who participated in unorganized play for similar duration formulated the control group. This detail was obtained through a simple survey conducted during the pre-data collection meetings with the entire subject population. Thus, sedentary children were excluded from the study. These criteria were strictly adhered to as the study intended to measure the training effect on these young children. This research study was carried out fully in accordance to the ethical standards of the International Journal of Exercise Science (23).

Protocol

The complete recording protocol followed the ethical guidelines for Biomedical Research on Human Participants (Minors) formulated by the Indian Council of Medical Research ICMR (2017) (10, 22). The protocol was explained to the minor subjects, on their verbal affirmation the informed consent forms were filled by their legal representatives. Independent Ethics Committee under the affiliation of Central Drugs Standard Control Organization (CDSCO), Ministry of Health and Family Welfare Government of India and the Institutional Ethics Committee for Human Research, Visva-Bharati approved the protocol. The study was also approved by Clinical Trial Registry of India (CTRI). Regn. No: CTRI/2021/06/034483.

The demographic variables were then measured, following which the subjects were rested in a quiescent and calm environment with a constant temperature of 27-30°C for around thirty minutes. The data was then extracted by placing each one comfortably in a chair using the RMS Polyrite (RMS, India), the polygraph was set and run for two minutes after which data was collected for five minutes. Any jewelry near the electrode sites was removed and mobile phones kept away from the participants. The skin was then cleaned with alcohol spirit at the standard lead placement regions after which electrode gel was put on the electrode sponge pads and then attached to the skin. The electrode impedance was checked for resistance and kept below 5 K Ω ; surety was maintained that the leads are properly attached to the cables and the ECG amplifier and the data acquisition unit. Extracted data was checked for artefacts or noise and projected graphically on the RMS Physiograph D version 5.0.6. Five subjects were measured each day, after which the setting of the leads was checked. The data collection was carried out on two successive days and the best trial was taken for assessment. All the sessions were conducted in the morning before lunch between 8:00 am and 12:00 noon. The RMS Vagus HRV software, provided readings in its analysis report on both the time and the frequency axis to realize the cardio autonomic activity in the participants. Figure 1 provides the detailed Trail Profile with the particulars of the primary outcomes.

RESULTS

Descriptive statistics indicated the weight (34.50±5.04) and Body Mass Index (BMI) (18.53±1.20) of the Karate Group (k) to be significantly lower in comparison to the weight (49.20±9.69) and BMI (25.82±5.15) of the control group (c). Age and height showed no significant difference. HRV measuring both time and frequency domains were compared among the two groups as shown in Table 2. The t-test showed significant results in the frequency domain parameters HF nu, LF nu and the LF/ HF ratio. The LF nu better known as the Low frequency power in normalized units was found to be significantly lower in the karate group (57.149±12.899 nu) than the control group (69.704±3.997) also, the LF/HF ratio in the karate group (1.536±0.773) was significantly lower than the active controls (2.354±0.453). This explains reduction in the sympathetic modulations in the Karate group. On the other hand, HF nu better known as the High frequency power in normalized units was measured to be significantly higher in the karate group (42.852±12.899nu) than in the control group (30.296±3.997nu) this explicates parasympathetic dominance in the karate practitioners (P<0.05). Results have been given below in Table 2.

Table 2. Comparison of the karate group and control group- descriptive and inferential statistics.

Comparison of the Karate Group and Control Group- Descriptive and Inferential Statistics									
Descriptive Statistics - A Comparison of the Karate Group and the Control Group									
Variables	Groups	N	Mean & Std. Deviation	Std. Error Mean	df	Mean difference	St Error difference	t-ratio	Sig. (2 tailed) p value
Age	Karate Group	15	9.50±1.27	0.4	28	1.1	0.64	1.72	0.103
	Control Group	15	10.60±1.58	0.5					
Height	Karate Group	15	136.20±8.66	2.74	28	1.9	3.16	0.6	0.555
	Control Group	15	138.10±4.95	1.57					
Weight	Karate Group	15	34.50±5.04	1.59	28	14.7	3.45	4.26*	0
	Control Group	15	49.20±9.69	3.07					
BMI	Karate Group	15	18.53±1.20	0.38	28	7.29	1.67	4.36*	0
	Control Group	15	25.82±5.15	1.63					
Inferential Statistics - A Comparison of the Karate Group and the Control Group: Time Domain HRV Variables									
Min RR	Karate Group	15	0.796±0.172	0.054	28	0.064	0.063	1.016	.323
	Control Group	15	0.521±0.053	0.017					
Max/Min	Karate Group	15	1.591±0.163	0.051	28	0.074	0.080	0.917	.371
	Control Group	15	1.517±0.195	0.062					
Mean RR	Karate Group	15	0.678±0.082	0.026	28	0.042	0.043	0.976	.342
	Control Group	15	0.636±0.108	0.034					
Max HR	Karate Group	15	111.900±12.432	3.931	28	4.500	5.276	0.853	.405
	Control Group	15	116.400±11.128	3.519					
Min HR	Karate Group	15	70.800±8.804	2.784	28	7.700	5.745	1.340	.197
	Control Group	15	78.500±15.890	5.025					
Mean HR	Karate Group	15	89.700±11.206	3.544	28	7.100	6.112	1.162	.261
	Control Group	15	96.800±8.804	4.980					

SDNN	Karate Group	15	59.196±23.060	7.292	28	11.570	10.485	1.103	.284
	Control Group	15	47.626±23.825	7.534					
RMSSD	Karate Group	15	39.907±11.623	3.676	28	8.097	6.500	1.246	.229
	Control Group	15	31.810±16.955	5.362					
NN50	Karate Group	15	89.800±64.480	20.391	28	27.900	28.563	0.977	.342
	Control Group	15	61.900±63.250	20.001					
pNN50	Karate Group	15	25.940±16.302	5.155	28	9.310	8.061	1.155	.263
	Control Group	15	16.630±19.598	6.197					

Continuation of Table 2. Comparison of the karate group and control group- descriptive and inferential statistics.

Inferential Statistics - A Comparison of the Karate Group and the Control Group: Frequency Domain HRV Variable									
VLF	Karate Group	15	54.576±22.381	7.078	28	2.864	9.884	0.290	.775
	Control Group	15	57.441±21.818	6.899					
VLF ms ²	Karate Group	15	485.163±488.485	154.472	28	190.708	317.274	0.601	.555
	Control Group	15	675.871±876.364	277.131					
LF Power	Karate Group	15	23.995±11.012	3.482	28	5.918	6.105	0.969	.345
	Control Group	15	29.913±15.857	5.014					
LF nu	Karate Group	15	57.149±12.899	4.079	28	12.555	4.270	2.940*	.009
	Control Group	15	69.704±3.997	1.264					
LF ms ²	Karate Group	15	172.481±130.167	41.162	28	53.536	71.783	0.746	.465
	Control Group	15	226.017±185.968	58.808					
HF Power	Karate Group	15	21.429±13.246	4.189	28	8.782	4.666	1.882	.076
	Control Group	15	12.646±6.501	2.056					
HF nu	Karate Group	15	42.852±12.899	4.079	28	12.555	4.270	2.940*	.009
	Control Group	15	30.296±3.997	1.264					
HF ms ²	Karate Group	15	133.914±102.383	32.376	28	37.640	40.346	0.933	.363
	Control Group	15	96.274±76.127	24.073					
LF/HF	Karate Group	15	1.536±0.773	0.245	28	0.818	0.283	2.886*	.010
	Control Group	15	2.354±0.453	0.143					

DISCUSSION

Physical activity positively influences heart rate variability and helps in reduction of stress for all age groups for the general population. The documented evidence of higher heart rate variability and stable autonomic innervations have been reported for the elderly and general adult community (12, 25). However, such studies on children and adolescents are restricted and around a score of studies were found in the past decade (7).

Karate is a kind of physical activity which influences the mind and the body through its slow and fast intermittent movements and synchronized breathing pattern. Moreover, in this pandemic situation sedentary routine has become a lifestyle especially among the younger generation having to stay indoors for safety. When all other physical activity is restricted karate is one such practice which can be continued even in home isolation. Moderate intensity actions

with rhythmical breath control and mental focusing through concentration development qualify this art form as a mind body practice to maintain physical and mental health.

HRV profiling has steadily evolved into an application tool in sports training and athletic conditioning (14, 8, 15). The shift from sympathetic to the vagal tone in various types of athletes have been researched on, but interestingly very few studies in the area of martial art have been reported on the same lines, (9, 26) with one on judo, jujitsu and mixed martial art (27, 21, 6). The judo, jujitsu and mixed martial art players in these three studies were between an age range of 18-45 years. Judo players were made to perform a strength training program for four weeks, mixed martial art players on the other hand were professionals and all jujitsu players had graduated from the white to black belt thus were experienced; no exercise intervention was incorporated on them. The present study is a first time attempt where long-term karate training has been considered an intervention as a comparative model among school going children. The mechanism indicative of such results has been shown in Figure 2.

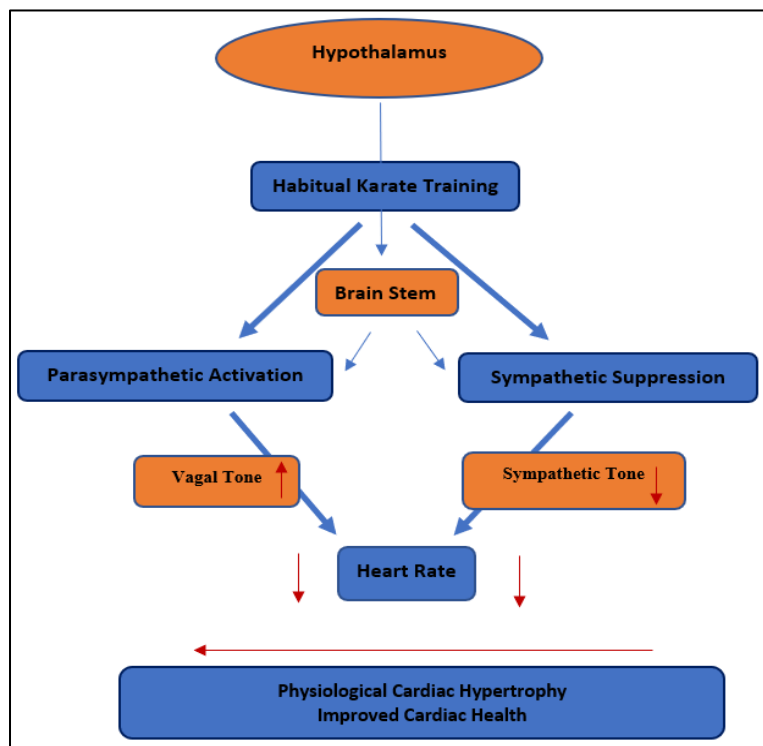


Figure 2. Dynamic Cardio Autonomic Relationship with Habitual Karate Training.

Hence, the present study intended to identify the effects of karate exercise and training on the young population as a habitual training. Previous research work on the immediate effects of karate exercise by the authors highlighted increase in heart rate and sympathetic systemic changes in the body (3). In the current study regular karate training of three years or more has been investigated and shown to produce prominent vagal tone. The parasympathetic dominance also significantly increased as seen through HRV quantification in the frequency domain parameters HF nu, LF nu and the LF/ HF ratio evident through the statistical results of

the study. While time domain aspects RMSS, SDNN and NN50 all showed positive improvement reflecting parasympathetic dominance in the karate group.

In fact, this research paper also clearly indicates a very pertinent aspect through its results, the active control group indulged in unorganized play for similar hours as the karate practitioners practiced their training protocols, nevertheless the BMI of the control group were significantly higher and so was their weight, which may indicate that there is a difference between a leisure play mind-set and a karate growth mind-set which may have caused this difference.

The findings in the present study through short term HRV time and frequency domain measurements clearly explain the intervention being provided to the karate practitioners strongly maintains a dynamic homeostasis between the stress, autonomic adaptations and cardiac fitness.

Positive and significant relations have been drawn within the limitations of this research study; between long term karate training and cardio autonomic modulation with HRV as the measurement tool. The physical activity comparison among both the groups could be quantified, to realize energy expenditure in the future. The study clearly signifies that simple karate movements through regular practice with very few requirements in terms of space and equipment, can do wonders to optimize cardiovascular fitness and autonomic functioning. Attention and focus are developed through this art form, not just to optimize oneself in a stressful environment but also to maintain a better psychophysiological homeostasis. However, the present study involved children with a training age of three years to the maximum, it could yield even better results among elite karate practitioners with a longer training span.

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