Effects of Different Intensity Aerobic Exercise on Circulating levels of Neurotrophic Factor in Healthy and Hyperlipidemic Adults in a Local Population

Ghulam Mustafa[1], Muhammad Irfan[2], Nosheen Wasee[3], Nuvair Zia[4], Adil Ramzan[5], Nargis Anjum[5]

Abstract

Objective: The present study was to compare the pre and post serum brain derived neurotrophic factor (BDNF) levels in healthy and hyperlipidemic population at baseline and post 12 weeks of exercise and to correlate the pre and post serum BDNF levels in healthy and hyperlipidemic population at baseline and post 12 weeks of exercise.

Methods: Two arm follow up non-blinded randomized controlled trial (RCT) conducted at Physiology department, Basic Medical Sceines Institute. A total 258 participants of any age were divided into two groups: 129 participants in one of the two groups, Group-1 adult hyperlipidemic group and Group-2 healthy adults' group. Both groups were additionally divided into 3 subgroups with different exercise intensity i.e., light, moderate and high intensity exercise. To evaluate the health status of participants, graded exercise test by using Bruce protocol and the HRmax was performed and given a specific exercise program for 12 weeks. The test was a conducted as per Bruce protocol 25 using a treadmill with heart rate monitoring and ECG monitor. Blood sample had been taken for the analysis of total cholesterol and serum levels of BDNF.

Results: Mean levels of brain derived neurotropic factor (BDNF) of healthy and hyperlipidemic participants in all three different intensity exercise group (A, B, and C) at baseline and three follow-ups shown no statistically significant ($p>0.05$) difference inlight intensity exercise group (LIEG) on BDNF level from baseline (day zero) till three consecutive follow-ups. While, in moderate and high intensity participants significant ($p<0.05$) and highly significant ($p<0.01$) increase in BDNF levels respectively were demonstrated from day 0 to day 90.

Conclusion: In light of our findings, we conclude that 12 weeks of moderate to high intensity exerciseprogress cognitive function, serum BDNF levels, and improved lipid profile parameters, while low intensity exercise showed no significant mean difference for healthy participants.

Keywords: BDNF, Cognitive functioning, Diabetes mellitus.

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Introduction

Daily brisk walking or exercise is one of the useful factors for reducing a threat of cardiovascular illnesses, Diabetes Mellitus, and hyperlipidemia[1]. It helps in upgrading angiogenesis and neuronal development by expression of some neurotrophic factors. Cerebrum determined neurotrophic factor called BDNF, which is a protein from neurotrophic family. Basically it is present around 70-80% in CNS and in tissues like skeletal muscle, heart, liver, and fat cells[1,2]. BDNF expressionin exercises and during work out increases and it is an autocrine and paracrine hormone that is released inside the muscle and increases fat oxidation. Actually, exercise is firmly identified with the course of cell and sub-atomic cycles that advance angiogenesis,

1 Department of Physiology, Basic Medical Sciences Institute
2 Department of Physiology, Jinnah Postgraduate Medical Center
3,6 Department of Physiology, Karachi Medical and Dental College
4 House Officer, Karachi Medical and Dental College
5 Deaprtemnt of Medicine, Karachi Medical and Dental College

Correspondence: Dr. Muhammad Irfan
Department of Physiology, Jinnah Postgraduate Medical Center
Email: irfanbmsi17@gmail.com
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synaptogenesis and neurogenesis, hence improving learning, memory, intellectual capacity and protection from injury. An instrument to represent the progressions in mind pliancy is through the developmental factors[3]. It has been known for more than twenty years that active work on neuron growth and neuronal movement extraordinarily upgrades BDNF quality expression in the cerebrum. BDNF additionally decreases craving for food through hypothalamic control and improve the digestion. Additionally, it has been hypothesized that increased activity of skeletal muscles also increases the capacity of using lipids rather than glycogen, subsequently prompting decreased plasma lipid levels, however, familial hyperlipidemia is the most common type and sedentary lifestyle[4,5]. The inactive lifestyle, high fat eating habit in turns causes further falling apart wellbeing boundaries. Brain Derived Neurotrophic Factor (BDNF) assumes a basic part in the synaptic movement and versatility of mature neurons and manages the development and upkeep of memory. Moreover, human and mouse BDNF levels were observed to be changed in mental illnesses[3,6]. In reality, BDNF affects into the pathophysiology of sorrow and in remedial impacts of antidepressants. Additionally, BDNF was demonstrated to be upgraded under certain dietary conditions[7].

It has been observed that the privately delivered skeletal muscle BDNF doesn't enter in course and works in autocrine or paracrine design in the muscle subsequently managing fat oxidation. CNS inferred BDNF, acts as a great factor in administrative systems for nerve development, and discovered to be associated with neuro-degeneration, upgrading the protection of nerve injury, hippocampal neural pliancy, memory, and learning[8,9]. Commitment in daily episodes of activity gives various constructive outcomes on cerebrum wellbeing across the life expectancy[10]. Intense episodes of activity briefly work on intellectual capacity; further develop cerebrum capacity, and helps in fighting off neurological illness. The activity of neurotrophic factor BDNF is an important component for consideration in the activity of mind wellbeing. It is grounded that intense exercise increases the BDNF and various examinations have looked to depict this reaction to further develop cerebrum wellbeing[11]. Sub-atomic proof shows that this neurotrophin through tyrosine kinase b receptor (TrkB) causes neurogenesis, axonal development, and synaptogenesis. Other than the neighborhood impact of BDNF in the mind, a few creators propose that the cerebrum is the significant wellspring of flowing BDNF which vary with activity and during exercise[12]. In the fringe, concentrates acted in rat and human tissues have uncovered that BDNF manages other physiological pathways like glucose digestion, and fat oxidation. BDNF potentiate its physiological activities by enhancing intermembrane tropomyosin-related kinase Type-B-receptor (TrkB). The same BDNF, TrkB both were broadly communicated in different sensory system regions. Its appearance has been recorded in non-neuronal tissues like atherosclerotic vessels, vascular smooth muscle. An expansion of BDNF is related with an increment in hippocampal size and an improvement in the presentation of activity like memory and learning. BDNF and TrkB articulation in the hippocampus and cerebral cortex decline throughout the life, expanding the danger of experiencing diverse neurodegenerative pathologies[11,13]. It is generally realized that exercise can successfully improve the BDNF combination in the brain. Concerning the effect of the exercise on expanding BDNF in cerebrum, distinctive atomic systems have been proposed to clarify how exercise upgrades BDNF expression in neurons. The study postulated and gathering information that exercise expands the intracellular Ca2+ levels in neuronal cells This particle initiates BDNF by implication; and this kinase builds the MAP-K pathway, phosphorylate CRE-restricting protein and actuate the BDNF expression, and subsequently BDNF expression[14,15].

BDNF has been discovered to be profoundly communicated in regions like ventromedial cores (VMH) of nerve center that manage food admission, consequently; it manages hunger and digestion through hypothalamic control. Different examinations have meant the job of activity in expanding BDNF levels in CNS and furthermore affirmed the

effect of activity on metabolic result, altogether fat oxidation[16]. Past examinations showed that intense or persistent exercise appears to increase fat oxidation in fatty people. There is effect ofdifferentstrength and duration of activity have been shown in past investigations[17,18].

Pakistan is not the special case affected overall by the pandemic of hyperlipidemia influencing people alike. Regular practice is the main intend to decrease hyperlipidemia and statins are very famous in the clinical practice. The positive results of activity impacts wellbeing in a complete manner. Exercise help in cultivating cardio metabolic function, support psychological execution, and practically aid the avoidance and treatment of different medical conditions, identified with CVS, CNS, and digestion.

Our present study was planned to compare the pre and post serum brain derived neurotrophic factor (BDNF) levels in healthy and hyperlipidemic population with 12 weeks of exercise and to correlate the pre and post serum BDNF levels in healthy and hyperlipidemic population from baseline to post 12 weeks of exercise.

Patients and Methods

This randomized controlled trial (RCT), conducted in art center after the approval of Ethical Review Board. All 258 participants were inducted after taken informed consent, from the Art center of Physiology department. The duration of study was Jan. 2020 to Feb. 2021. All adult participants who are able to qualify pre-participation screening through the American Heart Association (AHA)/ American College of Sports Medicine (ACSM) health/fitness screening questionnaire (ACSM 2012) and cardio-respiratory fitness through graded treadmill exercise test (lee 2014), whereas,participants with cardiovascular, neurological, musculoskeletal, hepatic disease or any physical disability were excluded, longstanding illness renal failure, malignancy, diabetes mellitus, psychiatric illness were excluded, pregnant or lactating women who were taking drugs affecting serum lipid levels i.e., anti-hyperlipidemic drugs, estrogen were excluded. All study participants were separated into two groups, 129 each in the two groups 1) adult hyperlipidemic group and 2) healthy adults group. Each group was further divided into three subgroups for different intensity exercise i.e. light, moderate and high intensity exercise protocols. Each subgroup was having 43 participants, forming six (06) subgroups. To assess the health status of individuals a graded exercise test using Bruce protocol and the HRmax was performed before starting exercise-training program. All the participants included in the study was given a specific exercise program for 12 weeks. The test was conducted according to Bruce protocol, using a treadmill with heart rate monitoring and ECG monitor. According to this method, exercise level is uniformly increased, starting with a speed of 1.7 mph and 10% inclination, 3.4 mph and 14% inclination, 5.0 mph and 18% inclination, 6.0 mph at 22% inclination to continue until exhaustion (Shah, 2013). Pre-intervention venous blood samples were taken after 12 hours of fasting on the first day of exercise program. After the intervention, fasting blood samples were also obtained. Samples collected were analyzed for serum BDNF levels and lipid profile levels by using available ELISA kits. For data analysis, quantitative variables were expressed as mean and standard deviation, which was assessed by SPSS version 21 or above. Quantitative variables such as age, height, weight, BMI, Lipid levels, BDNF levels, was a presented as mean and standard deviation. Categorical variables were presented as absolute frequencies and proportion. Two-way analysis of variance (ANOVA) with post hoc (Tukey test) was a used for comparison between groups. Paired t-test was applied to compare the quantitative parameters before and after exercises within a group. Statistical significance was taken as p-value of ≤ 0.05.

Results

In both groups and three sub-groups A, B, C the parameters, mean age, height, weight, BMI, blood pressure, TG, LDL and HDL were not statistically significant ($p>0.05$) while mean of Total

Table 1. Baseline characteristics of adult hyperlipidemic participants

	Group A (n=43) Low intensity exercise Mean ± SD	Group B (n=43) Moderate intensity exercise Mean ± SD	Group C (n=43) High intensity exercise Mean ± SD	P-value
Age (yrs)	42.0 ± 1.02	41.2 ± 0.99	41.7 ± 1.14	0.843
Height (m)	1.70 ± 0.02	1.67 ± 0.01	1.71 ± 0.02	0.107
Weight (kg)	75.4 ± 1.95	76.3 ± 1.54	75.1 ± 1.61	0.925
BMI (kg/m2)	26.5 ± 0.95	28.9 ± 0.63	25.6 ± 0.38	0.127
B.P. (mm Hg)	130.5 ± 2.25	133.2 ± 2.29	129.8 ± 1.93	0.690
B.P. (mm Hg)	85.2 ± 1.19	85.0 ± 1.04	85.0 ± 1.17	0.692
Total Cholesterol (mg/dl)	227.8 ± 3.08	236.7 ± 4.65	241.9 ± 5.51	0.054
Triglycerides(mg/dl)	197.5 ± 10.11	211.0 ± 8.04	214.6 ± 8.62	0.641
LDL (mg/dl)	183.4 ± 3.25	185.2 ± 5.64	190.5 ± 8.41	0.780
HDL(mg/dl)	34.5 ± 0.75	36.2 ± 0.61	35.9 ± 0.77	0.316

Table 2. Baseline characteristics of adult healthy participants

	Group A (n=43) Low intensity exercise Mean ± SD	Group B (n=43) Moderate intensity exercise Mean ± SD	Group C (n=43) High intensity exercise Mean ± SD	P-value
Age (yrs)	41.0 ± 1.1	42.1 ± 1.0	41.8 ± 1.16	0.72
Height (m)	1.65 ± 0.03	1.67 ± 0.02	1.70 ± 0.02	0.105
Weight (kg)	74.9 ± 1.96	75.3 ± 1.45	75.0 ± 1.51	0.915
BMI (kg/m2)	26.5 ± 0.95	28.9 ± 0.63	25.6 ± 0.38	0.127
B.P. (mm Hg)	129.1 ± 2.05	130.2 ± 2.09	128.8 ± 1.99	0.684
B.P. (mm Hg)	86.2 ± 1.21	86.0 ± 1.14	85.9 ± 1.19	0.530
Total Cholesterol (mg/dl)	157.1 ± 3.18	165.4 ± 3.65	161.9 ± 3.51	0.184
Triglycerides(mg/dl)	117.5 ± 5.1	111.0 ± 5.44	114.6 ± 5.62	0.459
LDL (mg/dl)	103.1 ± 5.20	105.2 ± 5.84	109.5 ± 5.41	0.415
HDL(mg/dl)	46.5 ± 0.55	46.2 ± 0.61	48.9 ± 0.67	0.531

Table 3. Comparison of levels of bdnf (ng/ml) amongs healthy participants in three exercise groups at baseline and subsequent three followups

	Baseline (Day Zero) Mean ± SD	Day 30TH Mean ± SD	Day 60TH Mean ± SD	Day 90TH Mean ± SD	P-value
LIEG	24.79 ± 5.77	25.0 ± 3.44	25.3 ± 3.42	25.05 ± 2.47	0.8941
MIEG	25.90 ± 6.59	26.0 ± 4.08	28.5 ± 4.65	29.71 ± 5.86	0.016
HIEG	25.24 ± 4.17	27.7 ± 3.87	28.1 ± 3.97	30.09 ± 4.00	0.009

Table 4. Comparison of BDNF levels (ng/ml) among hyperlipidemic adults in three exercise groups at baseline and subsequent three follow-ups

	Baseline (Day Zero) Mean ± SD	Day 30TH Mean ± SD	Day 60TH Mean ± SD	Day 90TH Mean ± SD	P-value
LIEG	21.22 ± 4.17	22.0 ± 3.90	22.3 ± 4.01	22.17 ± 3..64	0.6302
MIEG	22.40 ± 2.48	23.99 ± 4.03	24.2 ± 2.95	27.01 ± 3.54	0.044
HIEG	21.36 ± 3.56	26.0 ± 3.74	28.41 ± 3.86	32.01 ± 4.18	0.006

Cholesterolof all groups hadshown statistically significant difference ($p<0.05$). In light intensity exercise group (LIEG) the mean difference of brain derived neurotropic factor of healthy adults and hyperlipidemic adultsin all three different intensity exercise group (A, B, and C) shown no statistically significant mean difference on BDNF level from base linei.e day zero until three follow-ups ($p>0.05$). While in moderateintensity exercise group (MIEG) and high intensity exercisegroup (HIEG) participants demonstrated an escalation pattern in levels of BDNF at 90th day when it was compared at day zero($p<0.01$). Importantly, no significant mean difference had been observed at baseline ($p>0.05$), however a significant mean difference was found at day 30, 60 and 90.

Discussion

The correlation of levels of BDNF and exercise has been widely reported and play utmost role and CNS cognative activity. In our current study, we have investigated varying intensity of exercise programs and their physiological effects on BDNF expression in the body. Our study findings also indicated that the change in BDNF expression is dependent on the moderate and the high intensity physical exercise with strong association while the low intensity exercise has no such drastic effect on BDNF expression. The study conducted and were found no strong relationship of BDNF levels in light exercise while have shown strong and positive association with increased levels of BDNFwith moderate and high intensity exercise[19,20,21]. Another study conducted and they had exhibited that high impact exerciseabout 20% of the edge and at 55% of vo2 Max has not produced significant change in levels of the BDNF levels. In a similar analysis, they likewise have showed that just 10 % over the edge and 75% of vo2 Max has extremely dynamic, critical and very strong relation with levels of BDNF and exercise[19,22,23]. The accommodating impacts of actual activities, particularly the focused energy highimpact exercise are not restricted for a more limited length of span[24]. Truth be told, it has been accounted for that after long and intense exercise the BDNF levels in the serum remained high even though at the resting state. The high and escalating pattern of levels of BDNF increment can work on the entire cellular reaction of body which increases oxygen consuming activity inside the cell[17,25,26]. Additionally, BDNF levels were just altogether expanded in the MIEG and HIEG while no expansion has been seen in the LIEG. This relationship has been accounted for in different experimental studies and correlates it with different intensities of exercise and found significant relation of BDNF expression levels with exercise[27,28,29]. We had not noticed a reduction in body weight among our investigation members in the 12 weeks' study. Prior distributed proof proposes that weight reduction can be accomplished through actual exercise related to dietary changes[30,31,32,33]. Not withstanding, the after effects of our examination ought to be deciphered with alert since we didn't change or control the eating regimen of our investigation members, wellbeing profile of our investigation members like co morbidities, and gauge BMI.

Conclusion

Based on our current study we concluded that twelve weeks of moderate to high intensity exercise improves cognitive function, expression of BDNF levels and improve the borderline parameters of lipid profile. Current study has not found the relation of light intensity exercise with levels of BDNF.

Conflict of Interest

Authors have no conflict of interest and no grant/funding from any organization.

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