Ameliorative Effect of Exercise Training on Age-Related Vascular and Biochemical Changes in Rats

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Abstract

Background: Physical exercise is suggested as a life style modification to improve the age related patho-physiologic heamodynamic alterations.

Aim of Study: The present study was designed to evaluate the possible ameliorating role of aerobic exercise training in improving age associated vascular dysfunction and hemodynamic disturbance.

Material and Methods: Thirty male albino rats of local strain were used for this study. Rats were divided into three main groups: The young control (aged 3-4 months, weighing 150-200gm) (n=10), aged sedentary (aged 22-24 months, weighing 300-400gm) (n=10) and aged exercised group (aged 22-24 months, weighing 300-400gm) (n=10). Rats in the aged exercised group practiced moderate intensity treadmill exercise for 5 days/week for 6 weeks. After 6 weeks rats were subjected for rat tail-measurement of SBP. Then, fasting retro-orbital blood samples were collected for measuring serum lipid profile (TC, HDL-C, LDL-C, VLDL-C and TGs) and inflammatory cytokine (TNF-a). Lastly, rats were sacrificed and abdominal aorta was exposed for assessing MNV and RP using Doppler ultrasound.

Results: In aged sedentary group, there were significant increase in SBP, RP, serum (TC, LDL-C, HDL-C) and serum TNF-a associated with significant decrement in MNV when compared to the corresponding values in the young control ones. Exercise training for six weeks significantly restored age-related vascular and biochemical changes except for HDL-C and TC there was insignificant difference when compared to the corresponding values in aged sedentary group.

Conclusion: Regular exercise training in aging has a beneficial effect on the cardiovascular functions by accelerating blood flow and decreasing resistance to blood flow, also it has an additive beneficial effect on the associated dyslipidemia and chronic inflammatory state in aging.

Key Words: Exercise – Aging – Doppler U/S – Rats.

Introduction

BIOLOGICAL aging is associated with reduction in the reparative and regenerative potential in tissues and organs. This reduction manifests as a decreased of physiological reserve in response to stress and a time-dependent failure of complex molecular mechanisms that cumulatively create disorder [1].

The most important determinant of cardiovascular health is a person’s age. By 2030, approximately 20% of the population will be aged 65 or older. In this age group, Cardiovascular Diseases (CVD) will result in 40% of all deaths and rank as the leading cause. Furthermore, the cost to treat cardiovascular disease will triple in that time. Hence, it remains vital that we understand why age is such a critical component of CVD etiology [2].

Aging is associated with increased levels of circulating cytokines and pro-inflammatory markers. Aged-related changes in the immune system, known as immune senescence, and increased se-cretion of cytokines by adipose tissue, represent the major causes of chronic inflammation. This phenomenon is known as “inflamm-aging”. High levels of tumor necrosis factor-a, and C-reactive protein are associated in the older subject with increased risk of morbidity and mortality [3].

Clinical studies show a significant relationship between ageing and increased blood pressure, with advancing age being a major non-modifiable risk factor in the development of hypertension [4]. Ageing is associated with functional, structural and mechanical changes. These changes that occur in the vasculature, including endothelial dysfunc-
ness, inflammation, atherosclerosis, calcification and increased stiffness [5].

Aging is associated with multiple systemic dysfunctions of the body accompanied by lipid metabolism disorder and chronic inflammatory state which contribute to atherosclerotic CVD [6]. Dyslipidemia is characterized by increased Triglyceride (TG) and/or Low-Density Lipoprotein (LDL) levels, and also declined High-Density Lipoprotein (HDL) levels. Such an atherogenic lipid profile often predisposes risk to cardio-vascular diseases [7].

Habitual physical activity is proving to strongly benefit health and longevity in humans, including a reduced risk CVDs. Aerobic exercise training has been reported to ameliorate age-associated reductions in both central and peripheral cardiovascular function. For example, cardiac output, stroke volume, and maximal aerobic capacity are increased as a result of exercise training [8].

Furthermore, exercise confers anti-inflammatory actions; exercise suppresses TNF-alpha, and thereby may offer protection against TNF-alpha induced vascular impairment. Regular exercise also promotes mitochondrial health, induces mitochondrial biogenesis, activates mitochondrial antioxidant systems, decreases fat content and attenuates of hyperlipidemia [9].

Previous studies have uncovered an important cross talk between inflammatory processes and generation of ROS in the pathogenesis of cardiovascular aging [10]. Therefore, the present study was conducted to investigate the therapeutic effects and underlying mechanisms of aerobic exercise training on age-related biochemical and vascular haemodynamic changes in aged male rats.

Material and Methods

The study protocol was approved by the Ethical Committee of Faculty of Medicine, Menoufia University, and was carried out in strict accordance with the recommendations in the guide for the care and use of laboratory animals of the Egyptian Universities. This study followed a randomized controlled animal experimental design, and was carried out at Medical Physiology Department, Faculty of Medicine, Menoufia University, Egypt from 8th of November 2017 till 1st of March 2018.

Animals:

Thirty male wistar albino rats of local strain were used in this study. Rats were housed in spacious wire mesh, fully ventilated cages (80 X 40 X 30cm) in a temperature-controlled room (25 ± 1°C) and maintained on a 12:12 hour light: Dark cycle with free access to water and food throughout the study period. Strewment was changed every 4 days, and the same person handled the rats throughout the study. Male rats were used to avoid variability caused by hormonal cycles in females as well as because of their more similar homeostatic adaptation (negative energy balance) to exercise in humans compared with female rats [11,12]. Rats were acclimatized for 10 days before the start of the study then randomly divided into the following groups, each of 10 animals.

Young control group:
Ten adult male albino rats (age 3-4 months old, weighing 150-220gm) were fed a standard laboratory chow diet for 6 weeks. Rats were left on the treadmill without running for the same time period as the exercise group to reduce the handling stress on the day of sacrifice.

Aged sedentary group:
Ten aged male albino rats (age 22-24 month, weighing 300-400gm) maintained under sedentary conditions (untrained) for 6 weeks [13]. Rats were left on the treadmill without running as young control group for the same time period as the exercised group.

Aged exercised group
Ten aged male albino rats (age 22-24 month, weighing 300-400gm) were exposed to a moderate running exercise program for 6 weeks [13] as the following:

Exercise training protocol:
Treadmill training began with familiarization of rats with the apparatus for 4 days by placing them on the motorized-driven treadmill. Training group was given exercise training for 5 days/week for 6 weeks. Rats were exercised on the treadmill at a speed of 10m/min. The angle of inclination was 0% gradient and the running time was 15min/day. This condition corresponded to a moderate intensity of about 65% of maximal oxygen consumption [13]. The animals were not exercised for 24h prior to sacrifice [14].

Systolic blood pressure measurement and blood sampling for biochemical assays:
At the end of the experimental period (after 6 weeks), rats were subjected for measurement of systolic BP (SBPmmHg) by Pneumatic pulse transducer (Harvard apparatus Ltd, Aden Berge, England) [15]. Then, animals were fasted overnight and biochemical measurements were performed using
Detection of abdominal aorta blood flow using doppler ultrasound:

Blood flow velocity was measured in the rat abdominal aorta by using Bi-directional blood flow meter with FFT-Analysis (HADICO, Japan). The technique for use the probe and application of the flow meter was according to the method described by Ruan et al., [16]. The end diastolic blood flow velocity and the end systolic blood flow velocity were measured and the Resistance Parameter (RP) was calculated [17].

Statistical analysis:

The data collected were tabulated and analyzed using statistical package for the social sciences (SPSS, Version 20; SPSS Inc., Chicago, Illinois, USA) software, on an IBM compatible computer. The results were expressed as mean ± Standard Deviation (SD). The significance of differences between groups was determined by one-way analysis of variance (ANOVA) and post-hoc Turkey test was done. p-values ≤0.05 were considered statistically significant.

Results

The presented (Table 1) demonstrate the means ± SD of (SBP), (MNV), (RP) and serum TNF-α values of the different experimental groups.

The mean value of SBP in the aged sedentary group was significantly higher (p<0.001) when compared to the corresponding value in the control group (163.1±20.23 vs 104.0±8.48mmHg) respectively. While the mean value of SBP in the aged exercised group (109.9±6.80mmHg) was significantly lower (p<0.001) when compared to the corresponding value in the aged sedentary group but it was still significantly higher (p<0.05) when compared to the corresponding value in the young control group (Fig. 1).

Table 1: Systolic Blood Pressure (SBP), Doppler ultrasound parameters (mean value of blood velocity (MNV) and Resistance Parameter (RP), and tumor necrosis factor-α (TNF-α) values in the young control, aged sedentary and aged exercised groups.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Young control</td>
<td></td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>104.0±8.48</td>
<td></td>
</tr>
<tr>
<td>MNV (cm/s)</td>
<td>2.28±0.85</td>
<td></td>
</tr>
<tr>
<td>RP</td>
<td>0.65±0.10</td>
<td></td>
</tr>
<tr>
<td>TNF-α (pg/ml)</td>
<td>10.87±0.72</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Aged sedentary</td>
<td></td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>163.1±20.23*</td>
<td>&lt;0.001 *</td>
</tr>
<tr>
<td>MNV (cm/s)</td>
<td>0.65±0.16</td>
<td>&lt;0.001 *</td>
</tr>
<tr>
<td>RP</td>
<td>1.47±0.22</td>
<td>&lt;0.001 *</td>
</tr>
<tr>
<td>TNF-α (pg/ml)</td>
<td>13.60±0.50*</td>
<td>&lt;0.001 *</td>
</tr>
<tr>
<td></td>
<td>Aged exercised</td>
<td></td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>109.9±6.80</td>
<td></td>
</tr>
<tr>
<td>MNV (cm/s)</td>
<td>1.53±0.61</td>
<td></td>
</tr>
<tr>
<td>RP</td>
<td>0.82±0.13</td>
<td></td>
</tr>
<tr>
<td>TNF-α (pg/ml)</td>
<td>6.37±0.46</td>
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</table>

Results are expressed as mean ± SD (n=10). Significance was considered when p-values <0.05.

The marks * and • indicate that values are significantly different when compared to the corresponding values in the control and the aged sedentary groups respectively.

Regarding the doppler findings; (MNV) in the aged sedentary group was significantly lower (p<0.001) when compared to the corresponding value in the young control group (0.65±0.16 vs 2.28±0.85cm/s) respectively. While the mean value of MNV in the aged exercised group (1.53±0.61 cm/s) was significantly higher (p<0.05) when compared to the corresponding value in the aged sedentary group but, it was still significantly lower (p<0.05) when compared to the corresponding value in the young control group [Fig. (2), panel A]. The mean value of RP in the aged sedentary group was significantly higher (p<0.001) when compared to the corresponding value in the control
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The mean value of RP in the aged exercised group (0.82 ± 0.13) was significantly lower (p<0.05) when compared to the corresponding value in the young control group [Fig. (2), panel B].

The mean value of TNF-α in the aged sedentary group was significantly higher (p<0.001) when compared to the corresponding value in the young control group (13.60 ± 0.50 vs. 10.87 ± 0.72 pg/ml) respectively. On the other hand, the mean value of TNF-α in the aged exercised group (6.37 ± 0.46 pg/ml) was significantly lower (p<0.001) when compared to the corresponding values in both the young control and the aged sedentary groups Fig. (3).

The presented (Table 2) demonstrate the means ± SD of the fasting serum lipid profile (TC, HDL-C, LDL-C, VLDL-C and TGs) in the young control, aged sedentary and aged exercised groups.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Young control</th>
<th>Aged sedentary</th>
<th>Aged exercised</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC (mg/dl)</td>
<td>53.98 ± 16.96</td>
<td>73.10 ± 18.30</td>
<td>62.44 ± 16.78</td>
<td>0.055*</td>
</tr>
<tr>
<td>HDL-C (mg/dl)</td>
<td>13.21 ± 4.23</td>
<td>21.20 ± 8.44*</td>
<td>23.40 ± 12.60</td>
<td>0.072</td>
</tr>
<tr>
<td>LDL-C (mg/dl)</td>
<td>32.59 ± 14.43</td>
<td>45.11 ± 12.21*</td>
<td>31.64 ± 6.53*</td>
<td>0.020*</td>
</tr>
<tr>
<td>VLDL-C (mg/dl)</td>
<td>8.17 ± 1.26</td>
<td>7.38 ± 2.02</td>
<td>7.39 ± 2.06</td>
<td>0.547</td>
</tr>
<tr>
<td>TGs (mg/dl)</td>
<td>40.88 ± 6.31</td>
<td>36.95 ± 10.13</td>
<td>37.05 ± 10.34</td>
<td>0.555</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± SD (n=10). Significance was considered when p-values <0.05.

The mean value of TC in the aged sedentary group was significantly higher (p<0.05) when compared to the corresponding value in the control group (73.10 ± 18.30 vs. 53.98 ± 16.96 mg/dl) respectively. While the mean value of TC in the aged exercised group (62.44 ± 16.78 mg/dl) was insignificantly different (p>0.05) when compared to the corresponding values in both young control and the aged sedentary groups [Fig. (4), panel A].
The mean value of HDL-C in the aged sedentary group was significantly higher ($p<0.05$) when compared to the corresponding value in the young control group (21.20±8.44 vs. 13.21±4.23mg/dl) respectively. While the mean value of HDL-C in the aged exercised group (23.40±12.60 23mg/dl) was insignificantly different ($p>0.05$) when compared to the corresponding values in both the young control and the aged sedentary groups [Fig. (4), panel B].

The mean value of LDL-C in the aged sedentary group was significantly higher ($p<0.05$) when compared to the corresponding value in the young control group (45.11±12.21 vs. 32.59±14.43mg/dl) respectively. While the mean value of LDL-C in the aged exercised group (31.64±6.53mg/dl) was significantly lower ($p<0.05$) when compared to the corresponding value in the aged sedentary group but, there was insignificant difference ($p>0.05$) in the mean value of LDL-C between the aged exercised and the young control groups [Fig. (4), panel C].

There was insignificant difference ($p>0.05$) in the mean values of VLDL-C between the young control, the aged sedentary and the aged exercised groups (8.17±1.26, 7.38±2.02 and 7.39±2.06mg/dl) respectively. Also, there was insignificant difference ($p>0.05$) in the mean value of TGs between the young control, aged sedentary and aged exercised groups (40.88±6.31, 36.95±10.13 and 37.05±10.34 mg/dl) respectively.

There was insignificant difference ($p>0.05$) in the mean values of VLDL-C between the young control, the aged sedentary and the aged exercised groups (8.17±1.26, 7.38±2.02 and 7.39±2.06mg/dl) respectively. Also, there was insignificant difference ($p>0.05$) in the mean value of TGs between the young control, aged sedentary and aged exercised groups (40.88±6.31, 36.95±10.13 and 37.05±10.34 mg/dl) respectively.

**Discussion**

Ageing is associated with functional, structural and mechanical changes in arteries that closely resemble the vascular alterations in hypertension which include endothelial dysfunction, vascular remodeling, inflammation, calcification and increased stiffness. The mechanisms underlying vascular alterations in ageing and hypertension are common and include dyslipidemia, oxidative stress and activation of pro inflammatory and pro-fibrotic transcription factors [18]. Exercise training has been reported to ameliorate age-associated reductions in both central and peripheral cardiovascular function. Also, it reverses old age-associated reductions in endothelium dependent vasodilatation in humans [19]. Therefore, physical activity has been recommended as a non-pharmacological approach for the treatment and control of age-induced vascular disorders [20].

The present study was conducted to evaluate the impact of regular exercise for 6 weeks on systolic blood pressure, blood velocity, vascular
resistance and lipid profile in aged rats. Also, we investigated the impact of exercise on pro-inflammatory cytokines in these aged rats.

In the current study, the mean value of SBP was significantly higher in the aged sedentary rats when compared to the corresponding value in the young control ones. This result was in agreement with the previous reported researches [4,18]. Hypertension with advancing age may be caused by the changes that occur in the vasculature, including endothelial dysfunction, vascular remodelling, increased vascular stiffness and inflammation [5]. In addition, aging is further associated with endothelial cell production of vasoconstricting growth factors such as angiotensin II and endothelin, whereas vasodilatory factors such as nitric oxide, prostacyclin are reduced [21].

The present study clearly demonstrated that, moderate exercise training resulted in significant decrement in the mean value of SBP when compared to the corresponding value in the aged sedentary animals; however, it was still significantly higher when compared to the young control ones. The attenuating effect of exercise on age-induced hypertension was in agreement with the reports of many researchers that stated that, regular aerobic exercise decreased systolic blood pressure by 3.84 mmHg and diastolic blood pressure by 2.58mmHg [22]. The ameliorating effect of regular exercise training on SBP may be due to enhancement of the expression of genes associated with local vasodilatory signaling [23]. Also regular aerobic exercise protects against age-dependent elastic arterial stiffness and vascular endothelial dysfunction by modulating structural proteins, reducing oxidative stress, decreasing inflammatory mediators, and restoring nitric oxide bioavailability [24].

In the present study, our results demonstrated that, the mean value of MNV was significantly lower while the mean value of RP was significantly higher in the aged sedentary rats when compared to the corresponding values in the young control ones. These results were in agreement with previous studies by [25,26]. On the other hand, in the aged exercised group, the mean value of MNV was significantly higher and RP was significantly lower when compared to the corresponding values in the aged sedentary rats. These results were in agreement with previous studies by [27,28].

The effect of aging on MNV and RP may be explained by that; the aged vessels are exposed to less hemodynamic stress due to reduced blood flow caused by decline in heart function; in addition, endothelial cells become less responsive to shear stress, resulting in a decline in the protective vasodilator NO [26]. Also, the aging of the vasculature leads to increase arterial thickening and stiffness as well as dysfunctional endothelium. Clinically, these changes result in increased systolic pressure and present major risk factors for development of atherosclerosis and hypertension [29]. This vascular dysfunction leads to loss of adequate tissue perfusion (resulting in diminished blood flow), insufficient vascular growth or regression (resulting in hypertension) [25].

The ameliorative effect of exercise on MNV and RP was reported by Prior and Green et al., who found that there was a relationship between increased shear stress on the endothelium and increased nitric oxide and prostacyclin release which leads to increase in the caliber of the large conduit vessels consequently increased blood flow through the vessel lumen in exercise training since vessel resistance is a function of the radius [27,30]. Also, the reduction in muscle tissue oxygen tension in the exercising muscle is associated with reduction in vascular resistance [31]. Furthermore, metabolically linked vasodilatation in exercising skeletal muscle is associated with reduced response to adrenergically mediated vasoconstrictor mechanisms [32]. The fact that vascular resistance falls in spite of increased vasomotor tone caused by sympathetic stimulation is further evidence of the sympatholytic nature of the vasodilatation in exercising skeletal muscle [33]. Also, regular exercise training resulted in decreased blood viscosity and consequently reduction in the systemic peripheral resistance [34].

Dyslipidemia is a well-established risk factor for cardiovascular disease in elderly and is estimated to account for more than half of the global cases of coronary artery disease [35]. Physical exercise is an important strategy to avert many of the observed age-related physiological decrements on the traditional risk factors as (blood lipids, hypertension, diabetes etc.) [36,37].

In our hands, the mean value of TC, HDL-C and LDL-C were significantly higher in the aged sedentary rats when compared to the corresponding values in young control ones. These results were in agreement with previous studies by [38-41]. While in the aged exercise group, the mean value of LDL-C was significantly lower, but there was insignificant difference in the mean values of HDL-C & TC when compared to the corresponding values in the aged sedentary rats, these results were consistent with the published studies [42-44]. Also, there were insignificant change in the mean values
of VLDL-C and TGs among the experimental groups.

The increased level of TC in the aged sedentary group may be caused by the age-related gradual reduction in the capacity for plasma cholesterol clearance through Reverse Cholesterol Transport (RCT), which is a biologic process transferring cholesterol to bile acid through the liver [45], also, a decline in the activity of the bile acid biosynthesis by cholesterol 7 hydroxylase, confirmed in the aging rat [46]. An interesting theory suggests that the relative deficiency in Growth Hormone (GH), occurring with normal aging in both humans and rats [47] brings about the development of the age-related hypercholesterolemia, as GH exerts several important effects on lipid metabolism in adult humans and animals [38]. GH secretion declines by 14% on the average with each decade in normal adults after 20 years old [48].

Regarding the increased serum level of HDL-C in aged sedentary group, astudy by Le Couteur et al., reported that, elevated HDL-C level in elderly men may be due to age-related changes in the ultrastructure of the liver sinusoidal endothelial cells which associated with an increased expression of von Willebrand's factor (vWF, a capillary marker) in all species and laminin and collagen in rats leading to dyslipidemia in old age, including lipoprotein disposition, reduction in endocytosis and decrease of hepatic blood flow in addition to the structural changes of pseudocapillarization might impair the hepatic uptake of lipoproteins including HDL-C thus contributing to age-related increase in HDL-C in the elderly [49]. In contrary to our result, walter et al reported that, the decrement of HDL plasma concentrations with age may be due to hormonal changes, inflammatory processes, and diabetes mellitus [39] as insulin resistance and impaired lipolysis are more frequent at advanced age and may impair RCT which is the major determinant of HDL [50]. Inflammatory processes in aged people may cause low HDL cholesterol by physical replacement of apolipoprotein A-I with the acute-phase reactant Serum Amyloid A (SAA) and various cytokine-induced changes [51]. HDL metabolism is influenced by hormones that change with age. In aging men, a low testosterone level show a positive correlation with HDL concentration. As testosterone decline itself may impair lipoprotein lipase activity and RCT that impair HDL formation [52].

Concerning the increased level of LDL-C in the aged sedentary rats Liu and Li reported that aging is associated with increase in the release of FFAs from adipocytes and a decrease in the mass of metabolically active tissue combined with a decrease in the oxidative capacity of tissues, the net effect of these cellular changes is increased blood levels of FFA which results in hyperinsulinemia with insulin resistance and an inflow of fatty acids from the adipose tissue to the liver, leading to gluconeogenesis and an increase in the production of LDL [41].

On the other side, the lowering effect of regular exercise training on LDL-C could be explained by the preference of muscle tissue for fatty acids and carbohydrates for the production of muscle energy which increase adipose tissue lipolysis [53] and cause a significant decrease in LDL-C [54].

A traditional understanding of “inflamm-aging” suggests that low-grade inflammation increases during aging and can be measured by levels of proinflammatory markers [55]. Our results showed that the mean value of serum TNF-alpha was significantly higher in aged sedentary group when compared to the corresponding value in the young control group. This result was in agreement with previous study [56], however, in aged exercised group the mean value of TNF-alpha was significantly lower when compared to the corresponding values in both the aged sedentary and young control groups, this result was consistent with other reported results [56,57].

The increased inflammatory markers in aged sedentary rats in the present investigation can be attributed to the increase in the total and visceral adiposity with age also declining levels of sex hormones have been proposed for mechanisms to increase pro inflammatory cytokines [55]. Adipose tissue acts as an active endocrine organ, capable of secreting several cytokines and adipokines, including IL-6 and TNF-alpha [58]. Increased oxidative stress with aging may also contribute to the development of chronic inflammation and disease. It was well established that aging is associated with high level of Reactive Oxygen Species (ROS), as well as low level in antioxidant capacity [59]. ROS activation of toll-like receptors on a variety of immune cells play an important role in activating the inflammatory cascade [60].

Our results in the aged exercised group obviously indicate that, exercise training effectively counteracts some of the disrupting inflammatory effects seen in the aged sedentary rats. This effect of exercise may be ascribed to that, regular exercise reduces fat mass and adipose tissue which is known to contribute to systemic inflammation because,
TNF-alpha is produced in adipose tissue [61] and A recent clinical trial demonstrated that anti TNF-alpha treatment enhanced high-density lipoprotein without influencing low-density lipoprotein, indicating that TNF-alpha causes a risk lipid profile [63]. Another possibility is that, regular exercise reduces oxidative stress by up-regulating endogenous anti-oxidant defense systems [64]. Moreover, a study by Harbuz, et al., reported that exercise training activates the hypothalamic-pituitary-adrenal axis and sympathetic nervous systems. Cortisol is known to have potent anti-inflammatory effects, and catecholamines can inhibit pro-inflammatory cytokine production [65]. Exercise training might reduce systemic inflammation in the elderly because it increases muscle production of IL-6 [66]. Starkie et al., reported that exercise and IL-6 infusion could inhibit endotoxin-induced production of TNF-a in humans circumstantially suggesting that IL-6 can act in an anti-inflammatory fashion [67].

Conclusion:

Regular exercise offers protection against aged induced vascular dysfunction primarily by improving dyslipidemia and indirectly offers protection against the disturbance in laminar blood flow by augmenting the blood velocity and decreasing the vascular resistance. Also it decreases the inflammatory status in aging by inhibiting the production of the pro-inflammatory cytokine (TNF-alpha) and hence suppresses the systemic low-grade inflammation.

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