

## Efeitos “antiaging” do exercício nos sistemas biológicos: uma breve revisão narrativa.

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## ABSTRACT

Aging is characterized by a progressive decline in function and morphological aspects of biological tissues, with especial regards to cardiovascular and musculoskeletal systems. In this sense, exercise has been shown to strongly counteract these aging-induced detrimental effects. Endurance exercise (EE) has been shown to reduce the rate of decline of factors related to cardiorespiratory fitness. In addition, the adoption of resistance training (RT) may also induce relevant adaptations, especially related to increased muscle strength and power levels, that have shown to positively influence functional aspects as improved balance and reduced risk of falls in the elderly population. Then, the aim of the present study is to briefly review the exercise literature regarding its mechanisms that could potentially present “antiaging” effects.

**Keywords:** elderly; training; endurance; muscle strength.

## RESUMO

O envelhecimento é caracterizado pelo declínio progressivo da função e dos aspectos morfológicos dos tecidos biológicos, principalmente no que diz respeito aos sistemas cardiovascular e musculoesquelético. Nesse sentido, foi demonstrado que o exercício neutraliza fortemente esses efeitos prejudiciais induzidos pelo envelhecimento. O exercício de resistência (EE) demonstrou reduzir a taxa de declínio de fatores relacionados à aptidão cardiorrespiratória. Além disso, a adoção do treinamento resistido (TR) também pode induzir adaptações relevantes, principalmente relacionadas ao aumento da força muscular e dos níveis de potência, que se mostraram influenciar positivamente em aspectos funcionais como melhora do equilíbrio e redução do risco de quedas na população idosa. Em seguida, o objetivo do presente estudo é fazer uma breve revisão da literatura sobre exercícios quanto aos seus mecanismos que podem apresentar efeitos “antienvhecimento”.

**Palavras-chave:** idoso; Treinamento; resistência; força muscular.

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## INTRODUCTION

It is worldwide estimated that, nearby the 2050 year, the number of people above 60 years old may triplicate, with the oldest group (>85 years) presenting the larger expansions<sup>1</sup>. Among the different physiological alterations usually observed during the aging process, the ones that affect the cardiovascular and muscular systems seem to strongly influence physical fitness, inducing relevant implications in functional and independence-related parameters. In this sense, the aim of the present study is to briefly review these alterations and to describe an eventual “antiaging” effect of the exercise in the mentioned biological systems, with especial regards to resistance training.

### Theories of aging

Why and how to we get old? To obtain an assertive answer to those questions is extremely difficult. Aging is usually defined as a function and/or morphological deterioration of the human organism that occurs after the completion of maturation process, with a progressive character through the time<sup>2,3</sup>. Although the exact mechanisms related to the aging process are not completely elucidated, many theories regarding its central causes have been proposed. The most common refers to perturbations that occur on biological systems, as neuroendocrine and immunological, as so cells mutations, free radicals and cell loss<sup>3</sup>.

Briefly, the immunological theory is based on two main findings. First, during chronological aging process, the capacity of the immune system to produce antibodies seems to progressively decline<sup>4</sup>. Second, as this occurs, self-immune manifestations are increasingly with aging, leading the immune system to reduce its capacity to discriminate external agents. In addition, a reduction in lymphoid cells’ activity has been also described<sup>5</sup>.

Even though one can suggest that the immunological theory of aging is quite plausible, it must be considered that the immune system is directly regulated by the neuroendocrine system. Then, it is still not completely clear in which extent the declines in immune function that are observed with aging reflect eventual neuroendocrine dysfunctions. Indeed, functions of the majority of human tissues are subjected to a refined neuroendocrine control, which may also suggest that eventual perturbations in this system would induce general and relevant physiological effects. In this context, several aging-related hormonal alterations might be explained by a reduced number of receptors and also disturbs regarding hormonal regulation that would induce a progressive increase in adaptive latency of enzymes<sup>6</sup>.

The free-radicals’ theory is also usually adopted to explain the aging process since there seems to be a strong association between chronological aging and reactive oxygen species (ROS)<sup>7,8</sup>. Additionally, mitochondrial function

also seems to be affected by aging, which would potentiate ROS production<sup>9</sup>. It is also noteworthy that several aging-related diseases are associated with a progressive oxidative stress<sup>10</sup>. However, the free-radicals’ theory does not seem to solely explain the aging process, since deleterious effects in the lifespan of rodents receiving antioxidants doses and the existence of longevous species with increased ROS production and elevated oxidative damage have been previously described<sup>10-13</sup>. Then, additional studies must be addressed in order to further elucidate the effects of free-radicals in the aging process.

In addition to the aforementioned theories, genetic-related factors have been studied in order to better explain the aging process. However, such theme is beyond the scope of the present study. In this sense, readers are invited to consult the review studies from Hayflick<sup>3</sup> and Perls et al.<sup>14</sup>, where the aging process is further detailed from a genetic perspective.

### **Aging of the cardiovascular system**

Biological aging is usually described as a process with relevant declines in the function and auto regulating process of the organic systems<sup>15</sup>. Classic alterations regarding the cardiovascular system have been previously described. For example, cardiac mass increases 1 to 1.5 grams per year between 30 and 90 years<sup>16</sup>. In addition, a thickening in the interventricular septum and its relation to a higher arterial stiffness are also reported. Indeed, these alterations are explained

by an increased collagen storage in the left ventricle<sup>17</sup>.

As for the function, heart pump does not seem to be compromised during rest, presenting, then, a similarity with the young heart. However, with an increased effort, aged heart presents an impaired work capacity (cardiac output, heart rate, ejection fraction) compared to the young one<sup>16</sup>. This is usually justified by impairments in the sympathetic response that seems to occur due to changes in the production of neurotransmitters that bound to adrenergic receptors. Then, through a lower neural activation, relevant alterations are observed in heart- contractile properties, which reflects a decline in cardiac output and maximal oxygen uptake (VO<sub>2</sub>max) during chronological aging.

Although some variability between studies has been observed, the rate of reduction in VO<sub>2</sub>max with aging is around 10% per each decade, being mainly explained by the aforementioned central factors as for a reduced arteriovenous difference (3% per decade)<sup>17,18</sup>. Additionally, local factors as an impaired oxidative capacity, lower muscle capillaries density and reduced muscle blood flow help to explain why older people’s muscle normally presents an impaired capacity to uptake and use oxygen to produce energy in the aerobic pathway<sup>19,20</sup>.

### **Skeletal muscle aging**

Skeletal muscle corresponds to the larger tissue mass in human body, presenting an important

plastic capacity when adapting its function/form according to the different mechanical, metabolic, neural and hormonal demands. With the chronological aging, muscles are affected by several morphological and functional alterations. Among them, the sarcopenia process, that primarily refers to reductions in muscle mass observed in aging people, and its causes, have been widely investigated. These declines in muscle mass usually begin after 20-30 years, with reductions around 40% until the 80th decade of life<sup>21,22</sup>. Reductions in the number and, especially, in the size (cross sectional area [CSA]) of the muscle fibers are the main mechanisms explaining this process. Indeed, between 20-80 years, a 40% reduction seems to occur in the number of muscle fibers, with the larger values around 60 years old<sup>22,23</sup>. For muscle fiber size, the type 2 seems to be largely affected when compared to the type 1 (20-50% vs 1-25% of reduction, respectively)<sup>24</sup>. This phenomenon, in turn, may be explained by neural factors, as a reduction in the number of the larger motor units and impairments in the velocity of the nerve impulse conduction. In fact, the loss of the alpha motoneurons has been pointed as strongly influencing the sarcopenic process<sup>25</sup>.

Molecular, immunological, hormonal and nutritional aspects also seem to influence the reductions in muscle mass that affect the elderly. Generally, these factors may shift net protein balance, in which reduced muscle protein synthesis and/or increases in muscle protein breakdown values chronically modulate the

amount of muscle mass in this population. In addition, reduced physical activity levels also help to explain the sarcopenia process, since it has been shown that sedentary elderly usually present lower levels of muscle mass compared to their active counterparts<sup>26</sup>.

As aforementioned, the term sarcopenia was originally created to denote aging related-reductions in muscle mass. However, it is of great relevance to highlight that defining sarcopenia as an exclusively morphological process may be somewhat mistaken. In this sense, in order to provide an accurate diagnostic, it is important that, in addition to the amount of appendicular muscle mass, functional factors (as gait speed and muscle strength) must be assessed<sup>27</sup>.

Several studies investigating changes in muscle strength within chronological aging have described a plateau until the 4th decade of life. More specifically, after 65 years, muscle mass decrements are accompanied by significant reductions in muscle strength (dynamic and static) about 25%<sup>28,29</sup>. Basically, the reduction in fiber size and neural impairments previously mentioned explain the lower muscle strength values in older compared to the younger adults.

Regarding the different manifestations of muscle strength, maximal strength and muscle power seem to be more affected by the aging process compared to strength endurance. Importantly, the annual rate of muscle power decline seems to be higher than the usually reported for maximal strength (3.5% vs 1.5%

per year, respectively) in 65-84 years subjects<sup>30</sup>. This reduced workload rate of older adults is also observed through an impaired rate of force development, which described one’s capacity to elevate the strength production for a given amount of time<sup>30</sup>.

This information may help health professionals when designing and implementing exercise programs aimed at the elderly. Periodizing training phases with predominance or combination of the distinct muscle strength manifestations may positively influence several factors related to performing daily tasks and quality of life in this population.

### **“Antiaging” effects of exercise on biological systems**

Effects of endurance exercise in cardiorespiratory fitness and cardiovascular diseases

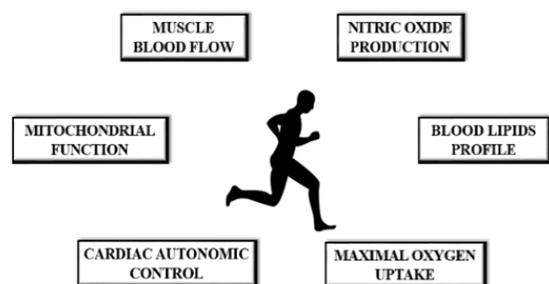
The regular practice of endurance exercise (EE), especially with moderate intensity (70% VO<sub>2</sub>max) and high demand of aerobic metabolism, plays an important role in attenuating deleterious effects of aging in cardiorespiratory fitness<sup>31</sup>. It is of great relevance to stress that EE seems to induce important adaptations on endothelial function, especially related to an increased nitric oxide (NO) production and augmented synthesis of new blood vessels (angiogenesis)<sup>32</sup>. Additionally, further benefits of exercise on endothelial health occur through the activation of peroxisome proliferator-activated

receptor (PPARc), a complex that seems to exert a relevant effect in controlling blood lipids levels<sup>33,34</sup>.

Other EE-induced adaptations are related to autonomic balance. Chronic elevated sympathetic activity in elderly people may represent deleterious effects on cardiovascular system, as a reduced blood flow, increased blood pressure and impaired baroreflex function. In this sense, EE has been shown to be a viable non-pharmacological alternative in attenuating autonomic imbalance. Trained older adults, for example, usually present similar baroreflex function compared to their active young counterparts<sup>35</sup>. Additionally, heart rate variability (HRV), a relevant marker of autonomic function, is increased in older adults submitted to EE-based training programs, which indicates a better cardiac autonomic control<sup>36</sup>.

The positive effects of EE in cardiorespiratory fitness may be experienced by older individuals even within short-time interventions. For example, 5 days of high-intensity training (90% Vo<sub>2</sub>max) induced significant increases in maximal oxygen uptake in previously sedentary elderly (65-71 years)<sup>37</sup>. Briefly, central adaptations especially related to ventricular function, may explain this adaptation. Moreover, despite the fact that the rate of reduction in VO<sub>2</sub>max that occurs during aging does not seem to be significantly influenced by the adoption of exercise training, endurance-trained older adults may present similar values of

Vo<sub>2</sub>max observed in the non-trained young ones<sup>38</sup>. Together, these data seem to corroborate the relevant effects of exercise, especially endurance-oriented, in attenuating the deleterious effects that occur within chronological aging in cardiorespiratory fitness.



**Figure 1.** Schematic review of the effects of endurance exercise on cardiorespiratory fitness-related outcomes.

Effects of resistance training on muscle function

Aging-related muscle atrophy is a multifactorial process, being result, basically, of a sustained negative net protein balance. In this sense, resistance training (RT) is a potent stimulus for inducing skeletal muscle hypertrophy, leading to adaptations mainly on type II muscle fibers, which seem to be more affected by the sarcopenia process than type I fibers<sup>39</sup>. When exposed to a RT program, older adults also present a shift in fiber type distribution (IIx towards IIa)<sup>40</sup>.

In addition to the reduced fiber size, it is also observed a relevant decrease in the number of muscle fibers during aging process<sup>39</sup>. Although methodological limitations must be addressed, there are no evidence that RT might induce an increase in muscle fibers' number (hyperplasia) in

humans<sup>41</sup>. Then, counteracting muscle atrophy in elderly is exclusively dependent of inducing muscle hypertrophy.

The effectiveness of RT in attenuating reductions in muscle function has been widely reported. Increases ranging from 25% to 35% in lower limbs strength<sup>42,43</sup>, assessed through one repetition-maximum test (1RM), and similar increments for upper limbs<sup>44,45</sup> have been observed in older adults submitted to moderate/high intensity RT-programs lasting 8-12 weeks<sup>46-48</sup>. Additionally, muscle strength and power increases are usually accompanied by improvements in balance<sup>49,50</sup> and reduced risk of falls, which in turn may lead to a reduced mortality in this population<sup>51</sup>.

Although it is well documented that RT is able to partially revert the muscle strength decrements even in very-old people (>80 years)<sup>52,53</sup>, the magnitude of these effects does not seem to be completely elucidated. Longitudinal studies as the one from Bassey and Harris<sup>54</sup> describe annual reductions of 3% and 5% in handgrip strength in men and women, respectively, during a period of 4 years. Similarly, decreases of 1% per year in the same variable were observed after a 27-year follow-up<sup>55</sup>.

A classic study from Klitgaard et al.<sup>56</sup> compared older adults that performed during 12 to 17 years, running, swimming or strength activities with sedentary older and young adults that served as a control group. When compared to the young-control, reduced strength values

were observed for knee extension (-44%) as for elbow flexion (-32%) in older-control. However, although runners and swimmer older adults presented similar values to the sedentary ones, no significant differences were observed in muscle strength and cross-sectional area between resistance-trained older adults and the young-control. Then, it can be suggested that RT-practice was able to revert the deleterious effects of aging in muscle function and morphology. This data was also corroborated in a 6-month intervention training program, in which a reduction (-21%) in lower limbs strength's difference between old and young adults was observed. In addition, mitochondrial impairments usually observed in the elderly was partially reversed in transcriptomic and phenotypic levels<sup>57</sup>.

In addition to the relevant effects of RT in the capacity of force production in the older adult, muscle power is also positively affected in this population. As aforementioned, elderly subjects usually present a reduced capacity to elevate force within a given period of time compared to the young adults, which help to explain, among other factors, a notably reduced velocity when performing daily activities as so a lower ability in resist to falls. However, it has been reported that the rate of force development of trained older subjects is four-fold higher than their sedentary counterparts<sup>58</sup>. Additionally, trained octogenarians present similar muscle power values compared to those normally observed in non-trained sexagenarians<sup>59</sup>, suggesting that RT

may be able to “rejuvenate” in 20 years the muscle power declines that affect the elderly population.

Muscle strength and power increments in the elderly induced by RT-programs might, especially in the initial phases, be explained by neural adaptations. For example, increases in electromyography amplitude signal (EMG) during maximal voluntary contractions have been described following a period of RT in older subjects, which suggests an increase in the magnitude of neuromuscular efferent activity<sup>30,60</sup>. In addition, RT may also increase the firing rate of motoneurons in this population, leading to relevant implications, especially regarding to the maximal muscle power produced and rate of force development<sup>61</sup>. Among several factors, the declines in muscle strength that affect the elderly are explained by an increased activation of antagonists muscle groups, as those observed during elbow flexion/extension movements<sup>62</sup>. In this sense, a classic and important RT-induced adaptation observed in older subjects is the reduction in the co-activation of the antagonists muscles, especially in those individuals in which the activation of these muscle groups is elevated to 20-25% of the agonists activity<sup>63</sup>.

Interestingly, RT is also able to induce important adaptations related to the central nervous system activation during movement in the elderly. Indeed, it seems to exist a high association between central activation and isometric maximal strength during knee

extension in very old subjects (>80 years old) <sup>64</sup>. In this sense, in addition to the classic peripheral adaptations previously mentioned, RT also seems to affect relevant central mechanisms, influencing the excitability of the efferent pathways and the amount of force produced.

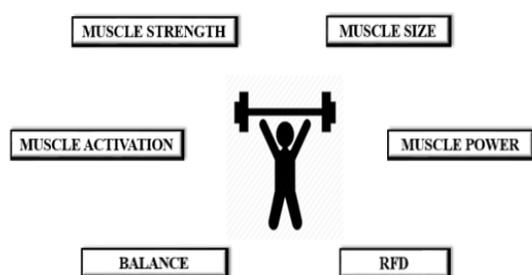
programs, especially RT, in the elderly population, bringing relevant improvements in daily activities performance and a reduced risk of mortality.

### Conflict of Interest

The Authors declare that there is no conflict of interest.

### Funding

This study received no grants.



**Figure 2.** Schematic review of the effects of resistance exercise on skeletal muscle function-related outcomes. RFD = rate of force development.

## CONCLUSION

Together, the data mentioned above bring important information regarding the relevance of an active life style, especially related to the adoption of EE and RT along the lifespan. Then, cardiorespiratory, muscle strength and morphological-related parameters might be maintained over the time, evidencing both training modalities as major components of exercise programs that aim to counteract the deleterious effects of aging on biological tissues. Moreover, the authors of the present study strongly recommend the use of the information here in raised aiming to implement exercise

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**OBSERVAÇÃO:** Os autores declaram não existir conflitos de interesse de qualquer natureza.