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Review

Exercise and longevity

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A B S T R A C T

Aging is a natural and complex physiological process influenced by many factors, some of which are modifiable. As the number of older individuals continues to increase, it is important to develop interventions that can be easily implemented and contribute to "successful aging". In addition to a healthy diet and psychosocial well-being, the benefits of regular exercise on mortality, and the prevention and control of chronic disease affecting both life expectancy and quality of life are well established. We summarize the benefits of regular exercise on longevity, present the current knowledge regarding potential mechanisms, and outline the main recommendations. Exercise can partially reverse the effects of the aging process on physiological functions and preserve functional reserve in the elderly. Numerous studies have shown that maintaining a minimum quantity and quality of exercise decreases the risk of death, prevents the development of certain cancers, lowers the risk of osteoporosis and increases longevity. Training programs should include exercises aimed at improving cardiorespiratory fitness and muscle function, as well as flexibility and balance. Though the benefits of physical activity appear to be directly linked to the notion of training volume and intensity, further research is required in the elderly, in order to develop more precise recommendations, bearing in mind that the main aim is to foster long-term adherence to physical activity in this growing population.

Contents

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1. Introduction

Aging is a natural and complex physiological complex process influenced by many factors that can be broadly classified as intrinsic (related to genetic factors), extrinsic (related to psychosocial and environmental factors) and related to the effects of disease [1,2]. Biologically, the nature of this phenomenon and the mechanisms involved remain unknown. While no intervention has been shown to increase overall longevity, certain ones have been shown to influence the aging process. Among these, physical activity (PA) is fundamental, in addition to a healthy diet and psychosocial well-being. After briefly reviewing the various profiles of aging, we will review the reported effects of exercise, and then sum up the latest recommendations.

2. Profiles of aging

Three types of aging can be discerned [3] and help to understand the effects of exercise on longevity and life expectancy, especially in subjects without disability.

2.1. Regular or normal aging

Refers to a gene-related decline in physiological functions and processes. Aging can lead to frailty when the body's physiological reserve can no longer adapt to environmental challenges. The most important physiological processes with respect to this topic include changes in cardiorespiratory fitness and skeletal muscle function, due to their substantial influence on quality of life, functional independence and mortality. Aerobic fitness decreases by 5–10% per decade in untrained individuals and implies changes in the O_2 carrying capacity of the cardiovascular system. Importantly, the rate of decline in aerobic capacity does not appear to be linear, but rather accelerates dramatically with advancing decades [4–8].

Sarcopenia refers to the age-related decline in muscle mass and strength. It is characterized by a decrease in contractile protein content, and its replacement by intra- and extracellular lipids and structural proteins [9]. Sarcopenia is also characterized by a preferential decrease in type II fibers (fast-twitch fibers), which affects the strength and speed of movements. Decreases in muscle tissue quantity and quality may begin to occur before the fourth decade [10] and gradually worsen throughout the later stages of adulthood. There is considerable variation in muscular atrophy and weakness among aging adults, which is thought to be related to peak muscle mass and strength attained earlier in life [11,12]. Numerous investigations have identified a disparate decline in strength and muscle mass, suggesting that these age-related phenomena are to some extent, independent [13,14]. Thus, muscle strength may be a superior indicator of muscular dysfunction, as longitudinal data suggest that it is a robust predictor of functional decline that may occur during aging [15,16].

In addition to the changes in cardiovascular and muscle systems noted above, data also suggest that the skeletal response to exercise is altered with age [17]. Mechanical loading forces become less effective in eliciting an osteogenic effect with increasing age, suggesting a progressive loss of bone sensitivity to chemical and physical signals [18].

The decrease in PA that comes with aging accompanies the changes in physiological parameters that govern a person's physical capabilities as noted above. The effects on muscle function and cardiorespiratory fitness interact with the decrease in PA to create a "vicious cycle" (Fig. 1).

2.2. Pathological aging

Refers to accelerated aging that is caused by various conditions including disease processes that occur during the life course. These may include but are not limited to cardiovascular disease, metabolic abnormalities, cancer, dementia, depression, impaired locomotion, and sensory disturbances. These conditions are frequently associated with undernutrition and malnutrition, which in itself are associated with poorer prognosis among the elderly [19].

2.3. Successful aging

Refers to the maintenance of physical and mental well-being and functional independence in the absence of chronic disease, the ability to adapt to change, and the ability to compensate for limitations. The capacity to age successfully is highly variable from one individual to another. This fact is reflected in data from the European SHARE study, which showed that successful aging represents 1.6–21% of the noninstitutionalized population aged over 50 years[20].

Taking these concepts into account, the promotion of regular exercise is one of the main non-pharmacological measures that should be promoted in older subjects, especially regarding a preventive approach for successful aging.

3. Main effects of exercise

3.1. Definition of exercise

Physical activity is defined as "any situation employing the skeletal muscles, whatever the aim, accompanied by an increase in energy expenditure compared with the resting state" [21]. It usually includes both activities of daily living, leisure-time and recreationnal PA, as well as sport, this latter being defined as "a subset of PA, specialized and organized, in the form of exercises and/or

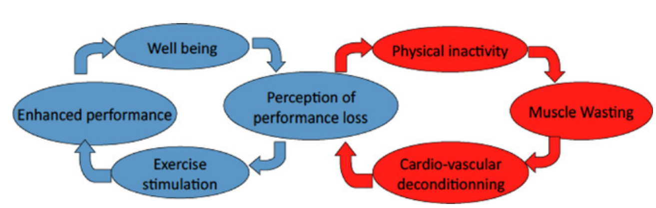

Fig. 1. "Vicious circle" of inactivity and positive effects of the regular physical activity.

competitions, facilitated by sports organizations" [21]. The term "exercise" is more specifically used in order to describe PA that is planned, structured and repetitive, that is performed in order to maintain or improve health and fitness.

3.2. Effects of exercise on life expectancy and mortality

A large and growing body of epidemiological data have studied and confirmed the benefits of physical activity on longevity. Recent meta-analyses would indicate that regular physical activity is associated with a 30% reduction in the risk of both all-cause and CV mortality in subjects free of CV disease [22], with similar results observed in subjects with CV disease [23,24]. This risk reduction corresponds to 1–2 years of additional life attributable to adequate exercise relative to individuals who engage in little or no physical activity [25,26].

Meta-analyses also demonstrate a clear positive dose-response relationship with respect to physical activity and longevity [27,28]. Larger training volume (exercise duration × intensity) is associated with greater mortality benefits. Furthermore, for a given training volume, engaging in higher intensity physical activity provides additional benefit [28]. Extreme examples of the benefits of high exercise volume and/or intensity come from data on competitive athletes. For example, among 2 675 Finnish endurance ex-athletes having participated in the Olympics games between 1920 and 1965, longevity was greater by 5.5 years (75. vs. 69.9 years) relative to an age-matched sedentary cohort [29]. Similar results have been observed in cross-country skiers [30] and former participants of the Tour de France [31].

The development of simple tools such as step counting devices (accelerometers and pedometers) offers an opportunity to economically and objectively quantify ambulatory activity on a daily basis in the real world setting [32]. In the ongoing Japanese Nakanojo Study among elderly individuals, substantial associations between overall health and the year-averaged daily step count were observed [33]. The threshold for improved physical health was found to be >8000 steps/day, and >4000 steps/day for better mental health. However, no studies to date have evaluated hard outcomes including mortality using such technologies at this time [34].

3.3. Protective effects of exercise: mechanistic considerations

Regular physical activity has unequivocally been shown to reduce the risk of cardiovascular disease, stroke, hypertension, type 2 diabetes, osteoporosis, obesity, colon cancer, breast cancer, anxiety, and depression [7]. Moreover, exercise reduces the risk of falls and injuries from falls [7]. Clinical practice guidelines also identify a role for exercise in the comprehensive management of depression and anxiety disorders, dementia, chronic pain, congestive heart failure, stroke survivors, prophylaxis of venous thromboembolism, low back pain, and constipation. Finally, there is some evidence that physical activity prevents or delays cognitive impairment and improves sleep [7,21].

4. Mechanisms underlying the positive effects of exercise on aging process

4.1. Cardioprotective mechanisms

The mortality benefits of exercise appear to be related to multiple cardioprotective mechanisms, including effects on endothelial function, autonomic tone, inflammation and improved risk factor control [21,35] (Table 1). The final common pathways of risk reduction presumably operate through improved endothelial function leading to plaque passivation thereby reducing the risk of new or recurrent ischemic events, as well as effects on autonomic control of cardiovascular function leading to a reduced risk of sudden cardiac death. Future work will be required to enhance our understanding particularly of the anti-thrombotic potential of exercise training which at this time remains unclear.

Table 1
Physiological mechanisms underlying the positive effects of exercise training on the aging process.

	Protective mechanisms of exercise training
1	Improved endothelial function and passivation of atherosclerotic plaques
2	Reduction in systemic inflammation
3	Beneficial effects on the autonomic regulation of cardiovascular function
4	Improvement in cardiovascular risk factor control • Increase in HDL-cholesterol concentrations • Reduction in triglyceride and LDL-cholesterol • Reduction in blood pressure • Reduction in body fat mass • Reduction in insulin resistance and improvement in glucose metabolism
5	Potential anti-thrombotic and anti-platelet effects
6	Heart intrinsic mechanisms • Ischemic preconditioning with reduced myocardial damage during prolonged ischemia • Prevention of reperfusion-induced ventricular arrhythmias
7	Improvement in maximal oxygen uptake ($VO_{2\,max}$) • Reduced all-cause and cardiovascular mortality • Improved functional capacity, QoL and ADL performance • Improved pulmonary function • Improved central hemodynamics (cardiac output/stroke volume) • Improved skeletal muscle metabolism (muscle blood flow, O_2 utilization, mitochondrial function)
8	Improvement in skeletal muscle function (resistance training) • Improved muscle mass and strength developed by muscle groups • Improved muscle power (force generation at high contraction speed) • Improved muscle quality, muscle recruitment and connective tissue • Reduction of functional deficits and disease co-morbidity • Improved QoL and IADL performance
9	Improvements in bone mineral density and ultrastructure
10	Improvement of chromosomal function • Improved telomerase enzyme activity • Less reduction in telomerase length
11	Improvement in cognitive function (aerobic and resistance training)

QoL indicates quality of life; ADL: activities of daily living; IADL: independent activites of daily living.

4.2. Effects on cardiorespiratory fitness

Aerobic fitness, objectively measured during cardiopulmonary exercise testing and expressed as maximal total body oxygen consumption or $VO_{2\,max}$, is one of the strongest predictors of all-cause mortality, CVD, health status and functional capacity in older people [36]. $VO_{2\,max}$ declines during the aging process and a value of 15–18 ml/kg/min is generally required to maintain instrumental activities of daily living [37]. $VO_{2\,max}$ in endurance-trained older subjects has been reported to be similar to $VO_{2\,max}$ in sedentary young subjects [38], and regular exercise can partially counteract the 5–10% decrease of $VO_{2\,max}$ per decade [39]. Nevertheless, the rate of $VO_{2\,max}$ decline with aging in both trained and sedentary individuals remains a matter of debate [9]. Data support the benefits of endurance training for improving $VO_{2\,max}$ among elderly people, however published studies have generally been limited by small sample-size and potential recruitment bias [37]. Indeed, study participants were generally fit, without significant orthopedic conditions or comorbidities and able to participate in a high intensity endurance program, with $VO_{2\,max}$ improving by approximately 15% [37]. Older subjects with a lower baseline $VO_{2\,max}$ generally appear to experience the greatest improvement in $VO_{2\,max}$ after training [40].

In parallel with the overall increasing proportion of older adults in the general population, the number of middle-aged and older ('masters') endurance athletes has increased as well [41]. Masters athletes reflect individuals with extreme training volumes. Among the masters category, the influence of beginning exercise training early in life versus later in life (i.e. after 40 years age) is not known. However, some elderly individuals express a highly unique physiological phenotype that has been termed 'exceptionally successful aging' [42]. Such individuals may improve upon their performance achieved at a younger age. In addition, the peak exercise performance of masters athletes continues to increase each year. For example, during the last three decades, NewYork marathon running times of master runners have significantly decreased for males older than 64 years and females older than 44 years, respectively [41]. The exponential increase in participation of masters athletes, particularly females, in sporting events such as a marathon running should lead to a re-evaluation of the aging process and how it relates to athletic performance. Further investigations are required in order to understand the age-related physiological changes and the potential slowing of some of the aging processes through athletic training.

4.3. Effects on sarcopenia

Resistance training increases both muscle mass and, to a greater extent, the force developed by a group of muscles [43–45]. Specific interventions have also been shown to improve muscle power, i.e. the ability to generate force at a high speed of contraction; muscle power appears to be even more important than maximal force to preserve functional independence and quality of life among elderly subjects [46,47]. A recent meta-analysis confirmed the significant association between resistance exercise and upper and lower body strength improvement among older individuals [48]. As strength decline is highly related with functional deficits [15,16]and disease comorbidity, it is likely that improvements in strength would help to maintain independence, health, and overall well-being.

Older adults show similar gains in power and isometric and dynamic strength in response to strength training relative to younger individuals [49]. These improvements appear to be related to improved quality of muscle, muscle recruitment and connective tissue given that muscle size does not increase substantially in the elderly despite a similar degree of protein synthesis [50–52].

4.4. Effects on bone mass and mineral density

The mechanical loading of bone through exercise has been investigated thoroughly for its potential to positively alter bone structure, including bone mass [53]. These effects have been attributed to strain, defined as the fractional changes in the dimension of a bone, in response to a changing load [54]. Accumulating evidence suggests that high strain rates and unusual strain distributions are positively related to the osteogenic response [53]. In vitro and in vivo studies have shown that mechanical stimulation can inhibit osteoclast formation and activity by changing the osteoprotegerin (OPG)/receptor activator of the nuclear factor-κBligand (RANKL) ratio in favor of OPG [55,56]. OPG is known to have an osteoprotective role in humans, preventing excessive bone resorption by acting as a decoy receptor and binding RANKL, thereby inhibiting nuclear factor-κB in osteoclasts, a transcription factor for immune-related genes and a key regulator of inflammation and cell differentiation [57]. However, the impact of exercise on bone density and fall-related injuries is complex and unclear, especially with respect to the risk of fracture. Some authors even suggest a U-shaped relationship between physical activity and fracture risk, with an increased risk of falls with certain types of exercise [58]. Furthermore, bone mineral density (BMD) appears to increase only in the bones directly involved in performing a given type of exercise. A recent systematic review from the Cochrane collaboration [58] addressing the impact of exercise on osteoporosis in postmenopausal women reported a relatively small statistically significant and potentially clinically significant effect of exercise on BMD. Compared with controls, the most effective type of exercise for improving BMD of the femoral neck was noted to be non-weight bearing high-force resistance training of the lower limbs, while the most effective intervention for BMD at the spine was a combination exercise program (consisting of more than one type exercise). Exercise was not shown to reduce the risk of fracture however. Importantly, although dual energy X-ray absorbtiometry measurement (DXA) was the most widely used bone densitometric technique among the reported studies, the ability of new techniques such as peripheral quantitative computed tomography (pQCT) to assess bone geometric properties may prove advantageous in evaluating the effects of training on bone health. In some recent studies, changes in bone mass and geometry became evident by pQCT whenDXA measurements were unchanged [59]. Nevertheless, the large differences in type, intensity and duration of exercise training programs, the differences in age, sex and characteristics of the subjects (i.e. use of medications, baseline bone mass or coexistence of other pathologies),the skeletal sites studied, and the lack of dietarysupervision (i.e. calcium or vitaminD intake), are the main confounding factors which currently limit our ability to make firm conclusions about the exact effects of exercise on bone mass.

4.5. Novel mechanisms

Chromosal telomere length is known to be associated with life expectancy. With age, the activity of the telomerase enzyme decreases and telomeres shorten. Their length is thus considered as a biological indicator of youth. Recent data suggest that PA helps to preserve telomere length [60]. Participants who were less physically active during their leisure time were shown to have shorter telomere lengths relative to subjects performing regular exercise. The average difference in length between exercisers and non-exercisers was 200 nucleotides, which corresponds approximatively to ten years.

Cognitive function is known to be an independent predictor of morbidity and mortality in the elderly [61,62]. There is growing evidence that exercise training improves cognition in this population, both acutely and chronically [63,64]. As little as 60 min of aerobic exercise, 3 times per week for 6 weeks was sufficient to improve certain cognitive parameters according to one recent study [64]. Future studies are required in order to confirm the beneficial effects of aerobic exercise training on cognitive function and to identify the optimal training strategy for improving cognition.

5. Exercise prescription recommendations

In 2007, the American College of Sports Medicine (ACSM) and the American Heart Association published the first physical activity recommendations to improve and maintain health in older subjects [7]. Similar recommendations have since been published by other bodies and organizations [21]. Without specifically addressing the “very elderly”, “frail elderly”, older subjects in nursing homes as well as older subjects with disability or major chronic conditions, global recommendations have been produced. In summary, current guidelines recommend a minimum of 30 min of moderate-intensity aerobic exercise 5 days/week, or 20 min of vigorous intensity aerobic activity 3 days/week. Furthermore, muscle strength training should be performed ≥2 days/week, flexibility training ≥2 days/week for at least 10 min, in addition to balance exercises, particularly for individuals at high risk for falls. Importantly, although a minimum of 30 min of moderate-intensity activity on most days of the week is recommended, a recent very large observational study showed that even a smaller amount of leisure-time physical activity (15 min/day, 6 days/week) reduced total mortality, mortality from cardiovascular disease, and mortality from cancer [65]. These data should encourage many more individuals to incorporate a small amount of physical activity into their daily lives [66].

Aerobic exercises that target cardiorespiratory fitness may consist of walking, cycling or swimming, or any dynamic activity that requires a large muscle mass, that can be maintained continuously, and that stays within the aerobic range. However, a significant proportion of elderly individuals are frail and possess comorbidities including cognitive impairment, malnutrition, functional limitations (e.g. arthritis) or poor psychosocial conditions, which make the aforementioned exercises difficult or impossible. In such instances, the primary aim of physical activity is to improve muscle strength, prevent/limit disability and maintain independent living through progressive endurance and resistance training, flexibility exercises and balance training. In debilitated patients, aerobic interval training may also be a useful adjunct to improve physical fitness. This training modality consists of exercise intervals interspersed by recovery (rest) intervals of similar or equal duration. Data from our own laboratory has shown that interval training employing very short (15–30 s) intervals with passive recovery intervals of equal duration is safe, well-tolerated and subjectively easier among subjects with coronary heart disease or chronic heart failure (refs). Certainly, when safety is at all a concern with respect to a particular individual, a supervised training program is recommended. Furthermore, a thorough clinical evaluation and exercise stress test should be performed prior to commencing an exercise training program with activites individualized according to functional limitations and co-morbidities.

6. Conclusion

Exercise can help “add years to life”, and above all, “add life to years”, by partially counteracting the effects of aging on physiological functions and preserving functional reserve in elderly. Numerous studies have shown that maintaining a minimal quantity and quality of exercise decreases the risk of cardiovascular mortality, prevents the development of some cancers, lowers the risk of osteoporosis and increases longevity. Training programs should include aerobic and resistance exercises to improve cardiorespiratory fitness and muscle function, as well as exercises targeting flexibility and balance. Though the benefits seem to be directly linked to the notion of training volume and intensity, exercise prescription still needs to be clarified to enable the scientific community to develop even more precise recommendations, bearing in mind that the main aim is to foster long-term adherence to physical activity in this growing population.

Contributors

All contributed equally to this manuscript.

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None.

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