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Physiology of Detraining in Older Population: Pandemic Time Considerations

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Abstract

With population aging, physical activity is among the factors that determine quality of life. A considerable numberof elders do not meet the minimum requirements for physical activity or are sedentary. Moreover, adults who were physically active can decrease their activity due to diseases or even the confinement generated by the SARS-CoV-2 pandemic. Therefore, it is important to describe the characteristics of detraining in the elderly populationto determine how detraining impacts the biological systems of human body, and the deleterious effects that converge with aging per se, making it difficult to determine the influence of each in the physical health of individuals.

It is remarkable how quickly the deleterious effects of detraining occur, which shows the importance of maintaining a physically active life at the appropriate intensity throughout life. The aim of this review is to describe the effects of training cessation on the cardiovascular, pulmonary, metabolic, and musculoskeletal systems.

Key words: *Exercise, aging, longevity, physical fitness.*

Introduction

According to the World Health Organization, population older than 60 years would duplicate by 2050, with an increase from 900 million in 2015 to 2 billion elders worldwide(1). Aging is a natural and complex process with decline in physiological and cognitive functions, the velocity of establishment depends on intrinsic (genetics) and extrinsic (environment and lifestyles) factors. It also depends largely by the burden of chronic diseases throughout life (2, 3).

The benefits of physical activity and exercise include pulmonary, cardiovascular, hematopoietic, neurophysiologic, metabolic, and musculoskeletal adaptations. Which protect against chronic diseases and along with a healthy diet and mental well-being, contribute to successful aging (2, 4, 5). Physical activity is associated with reduction in all-cause mortality and mortality of cardiovascular causes by 33% and 35% respectively, extending lifespan by one to two years (6-8)

Detraining refers to total or partial loss of exercise induced adaptations in response to a lack or reduction in training stimulus (9, 10). Its effects depend to an important extent on age, clinical conditions, type and intensity of previous training (9-11). The loss of adaptations also depends on timeof detraining(9-13).

In the past decades there has been a demographic shift with inversion of the population pyramid, this has expanded the number of adults over 65 years, among whom physical inactivity is frequent. With increasing age, a vicious circle is generated between deconditioning, perception of loss of functionality, physical inactivity, and sedentary lifestyle. Thus, in older adults where the burden of chronic diseases is higher, knowledge of detraining becomes as

important as knowing the benefits and adaptations of physical activity, because it regulates the time frame of protective effects loss, and will be associated with greater fragility, morbidity and mortality typical of this age group(2, 14-16).

Cardiovascular System

There is a strong association between cardiovascular effects of exercise and reduction in mortality(6-8). Explained by enhanced endothelial function, greater coronary flow reserve, autonomic modulation, greater capillary density, reduction in blood pressure and arterial stiffness (17, 18). Additionally there is an increase in plasma volume, end diastolic volume, systolic volume and improvement in cardiac output (17, 18), that along with additional adaptations, improves maximal oxygen uptake (19).

These changes in volume and pressure will eventually lead to cardiac structural changes due to long-term adaptations, like increased heart size, increased cavity volume and wall thickness (17, 20). Regarding vascular adaptations, there is an increase in endothelial turnover with a decrease in pressor responses to sympathetic activity, an increase in angiogenesis at both the peripheral (muscular) and central (cardiopulmonary) levels (18, 19, 21).

Additionally, the reduction of cardiovascular risk, seems to be associated with improvement of endothelial function that leads to the stabilization of atheromatous plaques, reducing the risk of coronary ischemic event, as well as sudden death by the improvement of autonomic control (8, 18, 21).

Cardiovascular effects of detraining are inversely related to the time and adaptations previously obtained (9, 10). Thus, the longer the time of cessation of physical activity and the lower previous fitness, the cardiovascular consequences of detraining will be greater and earlier (9-12). The decrease in blood volume is the earliest modification of detraining and will be partly responsible for thedecrease in oxygen consumption. 10 days after the suspension of the training stimulus, it has been described a decrease between 9% to 12% after 2 weeks in endurance athletes, associated to diminished plasma proteins and red blood cells (9, 22, 23).

Regarding heart rate, there is no significant increase in heart rate at rest with acute detraining (10 days), however, changes of 5-10% are noted in maximal and submaximal intensities. Returning to baseline can take months, it has even been described that in highly trained subjects the maximum heart rate may not return to baseline(9-13).

Systolic volume can be reduced by 10-17% over a period of 12 days to 8 weeks, with a 12% reduction in end-diastolic ventricular dimensions by one month. (9-13, 24). In relation to cardiac output (CO), the increase in heart rate does not completely offset the decrease in plasma volume, which ultimately results in a decrease in cardiac output, approximately 8% and 10% in a period of 21 and 90 days of inactivity respectively (9-13).

The cardiac structural changes takelonger and will be reflected in a decrease in cardiac mass and size of the cavities, as well as reduction inthickness of the left ventricular wall. Significant changes have been described in periods longer than 8 weeks with a return to baselineafter 4 months of detraining(9, 13, 25).

In older adults there is a higher prevalence of chronic diseases associated with vascular impairment, oxidative stress, and reduced antioxidant capacity. These variations are associated with disruption of endothelial function, increased risk of atherosclerosis and cardiovascular disease(26, 27). Endothelial progenitor cells (EPC) and vascular endothelial growth factor (VEGF) help maintain vascular integrity; therefore their reduction is associated with endothelial disfunction, coronary ischemic events and death from cardiovascular disease(28-32).

EPC are sensitive to changes in redox potential and have a high expression of antioxidant enzymes, therefore interruptions in the redox state can negatively affect their function (27, 32, 33). Low-density lipoproteins (LDL) have an atherogenic potential and additionally decrease the number of EPC, their proliferative capacity, migration and adhesion (32, 34).

Exercise can increase the number and function of EPC by enhancing redox and antioxidant capacity (26, 27, 29, 30). In the short term, an increase in EPC has been described in response to exercise both in healthy older adults and in older adults with risk factors or already established cardiovascular disease (32, 35, 36). In the long term, increase in EPC has been described in elders with cardiovascular disease but not healthy elders (32, 35, 37, 38). Detraining relates to loss of the antioxidant capacity within a time frame that depends

on the intensity and mode of the previous training (27). Witkowski et al. studied healthy older adults with a history of more than 30 years of moderate to high exercise intensity, and found after 10 days of detraining, a significant decrease in the vascular endothelial growth factor receptor (VEGFR2) and EPC. This reflects that alterations of oxidative stress in detraining in older adults may be related to loss of the cardiovascular protective mechanism(32).

Respiratory System

In the respiratory system detraining changes can be described according to the time of cessation of stimuli, in short (4 weeks) or long term (more than 4 weeks)(9, 11, 12). Regarding the maximal oxygen consumption (VO_2max), it has been described decreases with periods of cessation of training as short as 2 weeks, and it seems, that at higher previous values of VO_2max, greater is the decline with detraining (11, 39). It is estimated that the change ranges between 4 and 14%, in highly trained athletes. However, for recently trained people, this decrease is less noticeable, hovering between 4% and 6% after 4 weeks of detraining (11). For highly trained individuals, prolonged cessation of training results in a progressive decrease in VO_2 during the first 8 weeks with subsequent stabilization, still reporting higher values than sedentary people. Recently trained individuals with prolonged detraining results in the total loss of the gains obtained in VO2max(12, 39).

Among the most characteristic changes with detraining are the decrease in ventilatory function measured by the decrease in the values of the maximum ventilatory volume, decrease in the oxygen pulse and a secondary increase in the ventilatory equivalent of oxygen (11). Decreases of up to 14% in maximum ventilatory volume have been reported in highly trained individuals during prolonged periods of detraining, along with a marked increase in the respiratory equivalent for oxygen during submaximal exercise and decrease in the oxygen pulse(12). Similar effects are described on ventilatory function in recently trained individuals with long term detraining.

It is important to contrast the changes in lung parameters triggered with aging, since both detraining and aging, can have deleterious effects on lung function and structure. The most relevant changes in lung function linked to the aging process are decrease in vital capacity, forced vital capacity and forced expiratory volume in the first second (FEV1) (40, 41). Additionally, decrease in residual volume and functional reserve have been reported in healthy adults in relation to increasing age(40, 42).

Changes in the composition of lung tissue and remodeling have been related to a decrease in lung elastic recoil, which can be expressed as a measure of high compliance, similar to that of an emphysematous lung (40, 43, 44). Many conclusions on aging and changes in lung function have been made on research in animals (mainly mice). Schulte et al. (40), carried out an important investigation with mice, finding changes in lung physiology at different moments of life. They were able to determine structural changes in older mice, given by increased lung volume and widening of the alveolar ducts. An additional effect was the development of late alveolarization,accompanied by a reduction in alveolar size. The lungs do not express homogeneous mechanical responses to changes in air volumes (45). This may correspond to the variations of specific compartments (airway, parenchyma, blood vessels) and their functional needs (45-47).

Sicard et al. demonstrated greater stiffness in the vascular and pulmonary parenchyma compartments by increasing the elastic modulus, a capacity related to the resistance of a material to be elastically deformed during an applied tension (41, 45, 48). These results support that changes in lung architecture play a determining role in the increase in compliance with aging (40, 45, 49).

Stiffness of the pulmonary vessels, increased pressures in the pulmonary circulation, and increased resistance of the pulmonary vascular bed have been frequently associated with normal aging in healthy adults. However, these changes do not seem to limit the capacity of older adults to exercise, it is compensated by a pulmonary vascular expansion and an effective recruitment of the capillary and alveolus surface (50,51).

Coffman et al. (51) stipulate that in aging there is a decrease the pulmonary diffusion capacity of carbon monoxide (DLCO), related to a decrease in the pulmonary capillary surface area. Following this reasoning, a reduced response in lung diffusion capacity should be expected during exercise in older adults. However, age-related decline in lung

function does not appear to affect the response of the pulmonary capillary network during exercise in healthy individuals, regardless of age or cardiorespiratory fitness. Therefore, pulmonary responses to exercise such as pulmonary capillary distention and recruitment results in an adequate expansion of the capillary surface area, which allows an adequate diffusion capacity for the metabolic demands of exercise, independent of fitness or age (51, 52).

In addition, the researchers showed that highly trained elderly had a higher (DLCO) and greater conductance of the alveolar-capillary membrane during maximal exercise compared to results of untrained elderly (51). Further studies are needed to understand the influence of better cardiorespiratory fitness in elders and pulmonary function due to aging, and the impact of detraining.

Musculoskeletal System

Loss of muscle mass and functionality is an important characteristic of aging, which is associated with high risk of falls(53, 54), it is estimated that one third of people over 65 years suffer a fall annually (55). These events can be mitigated through exercise, especially focused on balance and strength, because they improve postural control and physical function (56).

Additionally, in older adults, there is atrophy of type IIa and IIx fibers, as well as reduction in the number of myofibrils (57, 58). Exercise has been associated with maintenance of these fibers, better muscle quality (54) and maintenance of mitochondrial function(59). With detraining, the acquired distribution is lost and IIa fibers are transformed into IIa, in addition there is a decrease in size and muscle strength, changes observed in periods greater than 4 weeks of cessation of physical stimuli(9, 10, 22).

Preserving muscle mass requires mechanical stimuli for anabolism, if it stops, the protein turnover, given by the difference between synthesis and degradation, tends to be negative (60). A study in young people showed that the disuse of one leg for 3 weeks, resulted in muscle loss of 5% after 10 days and 10% after 21 days (61). Just as decrease in muscle protein synthesis in immobilization has been described in young people, this phenomenon has also been described in the elderly, and is called “anabolic resistance” (54).

Aging is associated with changes in the properties of the motor units, as well as their loss, this is relevant because the force produced in muscle contractions depends on the rate of discharge of the action potentials and the recruitment of motor units. Exercise becomes important as it protects against muscle denervation associated with aging (57, 60).

Studies comparing changes in strength have been developed in different age groups with detraining. Lemmer, et al (10) described loss of 8% strength in people between 20-30 years, compared to loss of 14% in people between 65-75 years, after 31 weeks of detraining. Additionally, Toreman and Ayceman, described that performance and flexibility are more affected in people between 74-86 years than in people between 60 - 73 years. Which would imply differences by age group among the elderly (10).

Handgrip strength is an indicator of fragility, propensity to fall and physical functionality. A study evaluated the impact on quality of life and handgrip strength after 3 months of detraining in individuals with a mean age of 75 years, previously physically active. The authors describe a decrease in most dimensions of the SF-36 quality of life questionnaire after detraining, especially in women, with no change in handgrip strength (55).

At the capillary level, training adaptations optimizes the distribution, uptake and use of oxygen by increasing the capillary density and increasing myoglobin (18). These effects regress with detraining, with no evidence of decrease in muscle myoglobin levels (9, 62-64).

Endocrine System

The adaptations related to training are a set of modifications in different body systems. The endocrine system is one of them, with changes in catecholamine levels during and after exercise, as well as growth hormone levels, cortisol, thyroxine, testosterone, insulin, glucagon and renin-angiotensin-aldosterone system (18, 65, 67).

The effects of training on metabolism are well known and are related to optimization of physiological processes and improvement on performance (18, 65). The metabolic changes that training entails are closely related to the type of exercise, because of specific metabolic needs, especially the dependence or not of

oxygen. This generates specific changes in the type of muscle fibers, capillary supply, myoglobin content, mitochondrial function, oxidative enzymes, storage and use of metabolic substrates (18, 65).

Regarding the optimization of oxygen-dependent metabolic processes, the most relevant changes occur at the mitochondrial level, with an increase in the number and size of these organelles, increased enzyme activity (18, 65) and oxidative capacity.

Another important aspect is the storage capacity and use of energy sources during exercise. Among the most prominent considerations is a greater glycogen reserve with slower depletion, thanks to a greater efficiency in fat oxidation (18, 65). Likewise, in strength training metabolic adaptations are also generated. One to highlight is the increase in adenosine triphosphate-phosphocreatine (ATP-PC) and glycolytic enzymes (18, 66).

Baker et al. In two studies published in 2003 and 2010, showed performance declines with increasing age, clarifying that some attributes tend to decrease with greater speed(68, 69). Such effects are explained by the physiological changes of aging (14, 15, 70). The impact of aging on performance is given by a deterioration in VO2 max. (68-70). The metabolic and endocrine factors that contribute to the decrease in VO2 max are due to structural muscular changes, and a decrease of lean mass (14), this translates into a lower oxygen uptake by the active muscles, in addition to a decrease in the sympathetic response and maximum heart rate (70, 71).

Although VO2max is one of the most studied factors of the deterioration in performance, there are other metabolic and endocrine changes associated as decreased levels of testosterone, growth hormone, Insulin-like growth factors and dehydroepiandro sterone (DHEA) (54, 72, 73); hormones that change concentrations during and after exercise, as an acute and adaptive response to this stimulus (18, 65, 67).

It can be understood that detraining in the elderly population has special considerations, among them, a greater impact on the physical fitness, especially aerobic endurance (74). With detraining there is a decrease in mitochondrial mass, increase in respiratory exchange ratio and changes in lactate concentration(9, 10, 13). Decreasing in mitochondrial mass is reflected in decreased oxidative enzyme activity in the first 8 weeks of inactivity (10, 75). R. Wibom et al. also demonstrated that the rate of mitochondrial production of ATP improves with training but decreases rapidly with the loss of this stimulus (76). More recent studies such as the one carried out by C Granata et al. show that the decrease in training volume has an impact in reversing adaptive mitochondrial effects (77).

The use of metabolic substrates alsochanges, withdecreased oxidative activity, lipid metabolism is reduced, increasing dependence on glycolytic metabolism. This change explains an increase in the respiratory quotient, that can be observed between 2 to 4 weeks of inactivity (9, 10, 13, 75, 78). Consequently, lactate concentrations tend to increase with lower intensities and the lactate threshold decreases progressively from the first 7 days of cessation (9, 10, 13, 75, 78).

Studies have found changes in the concentrations of lipoprotein lipase (LPL) in adipose and muscular tissue as a consequence of detraining (9, 13), RB Simsolo et al. found decreased activity of LPL in muscle and increased adipose tissue, in healthy athletes after a detraining period of 2 weeks. This favors the accumulation of adipose tissue and therefore alteration of the lipid profile with especially increased low-density lipoproteins and triglycerides (9, 79, 80).

These metabolic changes occur simultaneously to endocrine modifications, with multiple studies showing a decrease in insulin sensitivity (13, 79), marked increase in plasma insulin levels and blood glucose levels unchanged (79, 81). The decrease in insulin sensitivity is mainly mediated by changes in the number of receptors to this hormone (13). A clear example of this is the return to baseline in the number of GLUT4 after detraining periods (9, 13, 79, 82) as demonstrated by Michael McCoy et al. who found a decrease in the number of these proteins from the 10th day of inactivity in trained men (83).

As mentioned above there are several physiological changes related to aging as there are to training and detraining. The table 1 summarizes the effects of detraining previously described.

Table 1. *Effects of detraining in the different systems*

HUMAN BODY SYSTEMS	EFFECTS OF DETRAINING	CLINICAL IMPACT
CARDIOVASCULAR	Decreased blood volume: diminished plasma proteins and red blood cells.	Decrease in oxygen consumption, Loss of the cardiovascular protective mechanisms.
	Increased heart rate: First in maximal and submaximal exercise.	
	Reduced systolic volume.	
	Decreased cardiac output.	
	Decrease in cardiac mass, cavity sizes, and thickness of the left ventricular wall.	
	Decreased redox and antioxidant capacity (by decrease in VEGFR2 and EPC).	
RESPIRATORY	Reduced maximum ventilatory volume.	Decrease in oxygen consumption (stabilization after 8 weeks approx.). Decrease in ventilatory function.
	Decrease in DLCO and conductance of the alveolar-capillary membrane during maximal exercise.	
	Decreased oxygen pulse.	
	Increased ventilatory equivalent of oxygen.	
MUSCULOSKELETAL	Atrophy of type IIa and IIx fibers, reduction in the number of myofibrils	Loss of muscle mass and functionality. High risk of falls.
	Decreased muscle size, strength, and flexibility.	
	Decreased muscle protein synthesis ("anabolic resistance").	
	Decreased muscle capillary density (less uptake and use of oxygen).	
METABOLIC	Diminished mitochondrial mass. (decreased oxidative enzyme activity).	Change in the use of metabolic substrates. Accumulation of adipose tissue and alteration of the lipid profile (increased LDL and triglycerides). Increased risk of chronic diseases as diabetes, high blood pressure, dyslipidemia, etc.
	Changes in lactate concentration (increases with lower intensities and lactate threshold decreases).	
	Reduced lipid metabolism, increasing dependence on glycolytic metabolism: Increase in the respiratory quotient.	
	Decreased activity of LPL in muscle and increased adipose tissue.	
	Decrease in insulin sensitivity (by changes in the number of hormone receptors, eg. Reduction in the number of GLUT4)	

VEGFR2: vascular endothelial growth factor receptor, EPC: Endothelial progenitor cells, DLCO: pulmonary diffusion capacity of carbon monoxide, LPL lipoprotein lipase. LDL: low-density lipoproteins. *The exact chronology of these events in older adults is limited, much of the evidence is based on the general population and not exclusively on the mature population.

Conclusions

Time periods in which the loss of the adaptations occur have been analyzed in multiple studies, however, evidence regarding chronology of events in older adults is limited. Adaptations generated by different types of training are reversible and can be influenced by multiple factors. Within these, age should be considered, the physiological changes associated suggest this population may have earlier and greater changes. Evidence regarding this point is limited, therefore more studies are needed to clarify the impact of detraining in this age group.

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