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MORPHOLOGICAL AND FUNCTIONAL MODIFICATIONS DURING THE PROCESS OF AGEING: CHARACTERISTICS AND BENEFITS OF PHYSICAL ACTIVITY

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ABSTRACT

Ageing is a slow but dynamic process, which involves many internal and external influences. It is a complex multifactorial phenomenon characterized by progressive physiological, genetic, endocrinological and molecular changes, responsible for the increased risk of morbidity and death.

Because of an increase in life expectancy, the incidence of degenerative diseases, such as muscular and skeletal diseases will also increase.

The age-associated loss of skeletal muscle mass and strength (i.e. sarcopenia) seems to be an unavoidable part of the physical human decline. In fact, the relationship of ageing with impaired physical performance, frailty, loss of functional independence and increased risks of falls are well established in the literature. In addition, decreased muscle strength is also highly predictive of incident disability in the elderly. In particular, weakness and functional deficit have been considered hallmark predictors of age related morbidity and decreased autonomy. Research on ageing has traditionally been concerned with health, but recently the concept of functional capacity has also been attracting growing attention. Regular physical activity, including, muscle-strengthening activity such as resistance exercises, balance and flexibility exercises, aerobic activity, is essential to develop a strategy to delay ageing.

Keywords*: ageing, functional impairment, elderly, physical activity, functional ability, health*

MORFOLOŠKE IN FUNKCIONALNE SPREMEMBE V PROCESU STARANJA: ZNAČILNOSTI IN PREDNOSTI TELESNE AKTIVNOSTI

POVZETEK

Staranje je počasen, ampak dinamičen proces s številnimi notranjimi in zunanjimi vplivi. Je obenem kompleksen in večstranski pojav, ki ga označujejo progresivne fiziološke, genske, endokrinološke in molekularne spremembe, ki so razlog za povečano tveganje obolevnosti in smrti.

Zaradi zvišanja pričakovane življenjske dobe se ravno tako poveča tudi pojavnost degenerativnih bolezni, kot so bolezni mišic in skeleta.

Zdi se, da je s starostjo povezana izguba skeletne mišične mase in moči (tj. sarkopenija) neizogibni del fizičnega upada pri človeku. Opisi razmerja med staranjem in slabšo telesno uspešnostjo, krhkostjo, izgubo funkcionalne neodvisnosti in povečanim tveganjem za padce so dejansko dobro zastopani v literaturi. Poleg tega pa zmanjšana mišična moč zelo dobro napoveduje pojav invalidnosti pri starejših. Zlasti šibkost in upad funkcionalnosti se upoštevata kot znamenji s starostjo povezane obolevnosti in zmanjšane samostojnosti. Raziskave staranja so se tradicionalno ukvarjale z zdravjem, vendar se v zadnjem času vedno bolj osredotočajo na pojem funkcionalne sposobnosti. Redna telesna aktivnost vključno z dejavnostmi krepitve mišic, kot so vaje za moč, ravnotežje in gibkost ter aerobne aktivnosti, so bistvenega pomena za razvoj strategije za zaviranje staranja.

Ključne besede*: staranje, funkcionalne okvare, starejši, telesna aktivnost, funkcionalna sposobnost, zdravje*

INTRODUCTION

Manifestations of ageing appear in all body systems and tissues, the ones in the neuromuscular system have an essential role as they have a direct impact on mobility and physical independence. Indeed, Gersten (1991) reported that muscular strength decreases significatively beyond forty years of age and at the age of seventy-four 28 % of men and 66 % of women are unable to handle an object weighting more than 4.5 kg. With ageing, muscles become weaker for many reasons. First, muscle fibre size decreases which results in a reduction of the cross-sectional area. Second, the number of fast muscle fibres decreases which itself causes a strength loss. In addition, there is evidence that the ability to activate motor units reduces itself with age, so that even the fibres that remain in the muscle are not used (Lieber, 1992).

Muscle modifications consist of atrophy decreased II type fibre diameter, a disruption of sarcomere structure and an increased percentage of intramuscular connective tissue and intermuscular adipose tissue.

During ageing, there is a true muscle remodelling. Some authors (Longo et al.; Vago et al., 2014) have seen that ageing changes both the length of muscle fibre fascicles and the angle of pennation.

Thom et al. (2007) have analyzed the changes in muscle in elderly people (aged from 69 to 82) and also in younger men (aged from 19 to 35). The analysis showed that there is a decrease in fascicle length, which leads to a loss of sarcomeres in series, which implies a loss of muscle shortening velocity, as a decrease in pennation angle reflects a loss of sarcomeres in parallel, therefore, in muscle cross sectional area and in muscle force.

The remodeling of muscles occurs due to atrophy. Occasionally, as seen before, with atrophy the muscle tissue is lost, the packing of contractile tissue along the tendon aponeuroses decrease. (Narici & Maffulli, 2010).

The reduction of sarcomeres in parallel (decrement in pennation angle and muscle cross sectional area) and in series (decrease in length fascicle) is due to the decrease in protein synthesis that occurs with ageing and disuse.

The age-related loss of muscle mass, affects > 50 % of the population aged seventy-five and over and is the main cause of impaired physical performance and reduced mobility. Amongst several factors contributing to loss of muscle mass, neuroendocrine changes are regarded as primary drivers of this condition (Narici & Maffulli, 2010) and are responsible for alpha-motor neurons and neuromuscular junction degeneration, since muscle fibre denervation, also fuelled by mitochondrial dysfunction and oxidative damage, leads to the loss of motor units and muscle weakness. One of the major functional characteristics of ageing is the disproportionate loss of muscle strength: at the age of eighty the loss of muscle strength is about four-fold greater than that of muscle size. This intrinsic muscle weakness, also known as deterioration in 'muscle quality', has traditionally been reconducted to a decrease in fibre specific tension, reduced excitation-contraction coupling and reduced neural drive. However, new evidence suggests that this disproportionate loss of force also arises from changes in the extracellular matrix and of associated proteins, leading to a decrease in lateral force transmission (Zhang & Gao, 2014) which in young muscle normally contributes to > 50 % of muscle force output (Huijing, 1998).

Age-related atrophy is often paralleled with increases in inflammation, metabolic syndrome, arterial stiffness and glucose intolerance (Ershler & Keller, 2000).

Muscular changes also affect the respiratory system as shown by alterations in inspiratory and expiratory volumes and pressures. In addition, the cardiovascular system (fundamental for independence) undergoes age-related changes associated with ageing. Since 1938, when Robinson Sid first reported a reduction of VO_{2max} (maximal oxygen uptake) with ageing, numerous studies have addressed the impact of ageing on cardiorespiratory function. For example, vigorous exercise may increase longevity while a moderate physical activity may improve cardiac function in octogenarian individuals

(Shepard, 1994). Fleg et al. (2005) reported that age contributes to the decline in performance and that a decrease in physical activity and muscle mass worsens the process. They also showed that VO_{2max} drastically declines with advancing age, as a result of a decrease in maximal heart rate, stroke volume and oxygen extraction by working muscles. Untrained men and women reach their highest aerobic capacity at the age of approximately twenty-five, women's aerobic capacity being about 20 per cent below men's. While growing older, men lose about 10 per cent of their aerobic capacity per decade, whilst women lose approximately 7 per cent. Therefore, at around seventy-five years of age, the gender difference in aerobic capacity is almost nullified (Wieser & Haber, 2007).

The ageing process is also characterized by difficulties in ensuring balance control, especially in the condition of reduced or conflicting sensory information, leading to an increased risk of falling. The balance modifications can alter the gait action: shorter stride length and increased double support time are often observed in elderly people. For many of them, ageing process adversely affects balance control resulting in a restriction in their ability to move independently, to maintain various positions or to react to external disturbances, such as a moving bus or to walk on an uneven surface or in shadowy light (Buatois et al., 2007).

THEORETICAL APPROACHES, MAIN QUESTIONS AND METHODS

Years ago, Heikkinen (1998) observed that as the musculoskeletal system deteriorates in old age, increasing mobility problems. An elderly person's range of movement is seriously decreased with inactivity or a sedentary lifestyle. Decreasing mobility and the age-related decline in balance lead to a decrease in gait skills, gait speed and cause more falls. Indeed, most causes of fall-related injuries in elderly are correlated to falls on stairs (normally an automatic skill). Mian et al. (2007), in a study conducted on 34 adults (69–82 years old) and 23 young adults (20–29 years old), all capable of descending stairs, observed that the deficit of physiological age-related functions can produce a negative effect in descending stairs. Moreover, an increasing body of evidence has been suggesting gait speed as a possible important vital sign in older people. Gait speed has been associated with clinical (e.g. comorbidities) as well as subclinical conditions (e.g. atherosclerosis or inflammatory status) and is able to predict several health- related events and even unrelated events to physical function (e.g. cognitive impairment, hospitalization, institutionalization). Gait speed may thus serve as a marker of physiological reserve and potentially it could quantify an overall health status. In other words, gait speed may represent the key-screening instrument to distinguish older (i.e. chronologically aged) from geriatric (i.e. biologically aged) patients and drive the subsequent clinical decision (Cesari, 2012).

Sedentariness, fatigue, poor muscle strength and slow and usual gait speed pose the old person in a state of increased vulnerability with high risk of major negative health-related events, including disability.

Therefore, a crucial role of physical activity becomes evident if these conditions are taken into account: all daily activities are affected. Indeed, the degree of effort depends on maintenance of sufficient aerobic capacity and the strength to deal with daily activities even if the elderly need, also, support in occupational adaptation process and in fluctuating day-to-day abilities using holistic strategies and client-centred interventions (Norberg et al., 2014).

Physical activity preserves the functional capability above that of sedentary individuals. Indeed, it can be concluded that movement could have a positive impact on all body functions, because this is both primary and secondary prevention. Warburton et al. (2006) reported that being fit or active was associated with a 50 % reduction in premature death. Besides, an increase of energy expenditure leads to a decrease of almost 20 % of cardiovascular deaths, with increased longevity (Lee & Paffberger, 2000). The regular physical activity increases cardiovascular efficiency, reduces hypertension and thromboembolic stroke and has a substantial therapeutic role in coronary heart disease as well as peripheral vascular disease (Nelson et al., 2007). In particular, regular low physical activity intensity (< 3 METs) that uses large muscle groups could attenuate or reverse the disease process in patients with cardiovascular disease, considering peripherals adjustments like increased capilarization (Pollok et al., 1998).

Age-related decline in insulin sensitivity appears progressively, which significantly contributes to the increased incidence of type 2 diabetes mellitus in older people. Aerobic and resistance activity (at least walking for 2 hours per week) should have benefits on glycaemic control and should also decrease the incidence of premature death for cardiovascular cause ─ related with diabetes (Warburton et al., 2006). Other investigations confirmed that aerobic exercise (with 500 Kcal in energy expenditure per week) decrease the incidence (6 %) of diabetes in high risk people and adding life-style modifications (in 3 to 4 years) as people could reduce the risk for between 40 % and 60 %.

A life-style based on a correctly carried out and controlled systematic training could, in advance, support people to manifest low level of depressive symptoms especially when the body mass index is in a norm weight range (Dugan et al., 2014). Indeed, the High Intensity Training (based on 15 minutes of exercise) could reduce the cardio metabolic disease risk (Kessler et al., 2012), the metabolic syndrome (Tjønna et al., 2008) and increase the insulin sensitivity (Gibala et al., 2012).

RESULTS OF THE APPROACHES IN AVAILABLE STUDIES

In an interesting review on cancer and its correlation with physical activity, there is evidence of a decrease in the incidence of colon (from 30 to 40 %) and breast cancer (from 20 to 30 %) in active people. (Warburton et al., 2006) while after the diagnosis

it becomes important to follow the guidelines for physical activity with encouragement: unprepared or less disposed categories of people, often, need motivational support (Hair et al., 2014).

Regular physical activity and weight loss can improve the risk factors that contribute to heart disease in women. Exercise of sufficient quality and quantity improves blood lipids, reduces insulin resistance, and promotes weight loss or weight maintenance, and attenuate abdominal fat gains in premenopausal and postmenopausal women (Mosca et al., 2007).

In women, ageing and the endocrine/neuroendocrine changes induced by menopausal transition, are at the basis of the many signals that occur together with the onset of many of the climacteric symptoms. The lack of oestrogens amplifies the progression of all age-related decaying processes and definitively induces the so called "frailty syndrome" of older age. This syndrome is the combination of the hypo function of many homeostatic systems and organs such as the metabolic system, the cardiovascular system, the endocrine and neuroendocrine systems and the central nervous system. The results of this is a perfect mixture of subnormal functions that induces a specific decay of many biological and vital functions, exposing the human being to a lot of potential risks such as cardiovascular risks, depression, anxiety, cognitive problems and more. Women in menopause, with hormonal disequilibrium, have a high probability of osteopenia/osteoporosis with low bone resistance and more probability of fractures. A regular activity that stresses body districts with external load prevents waste in body density (Carter et al., 2001) but a stress in all districts is necessary because its benefits affect only the involved areas.

Controversial evidence exists regarding the relations between physical exercise and mental health. Baldwin, R. C. (2010) suggested that moderate regular physical activity is necessary to prevent depression in later life. Elderly people with low mental health must be encouraged to keep up as much activity and exercise as possible, perhaps resorting to a short `programme` to encourage structure and purpose. A recent and fascinating report shows how physical activity in older adults changes the structure and functional capabilities of the brain and, conversely, the mechanisms by which the brain integrates metabolic, cardiovascular and behavioural responses to exercise (Benedict et al., 2013). Moreover, *brain-derived neurotrophic factor* (BDNF) plays a key-role as a mediator of the effects of exercise on the brain, regulating metabolic and cardiovascular responses to exercise (Mattson, 2012). At the same time, another fundamental role of physical exercise consists in the prevention and reduction of depression, stress, muscle tensions and anxiety, increasing self-esteem and feeling of life gratification (Dunn et al., 2005).

Ferris et al. (2005) reports also the benefits of 6 months of resistance exercise on sleep quality. Insomnia has notable consequences, the crucial point is the compromising of functions during the vigil times. Sleep disorders that are very common in the population, such as chronic insomnia, restless legs syndrome, obstructive apnoea may promote ageing, are co-factors of many age-related diseases. Sleep disturbances that characterize the aging process would also be an important co-factor of cognitive disor-

ders of various degrees, of immunosenescence and inflammaging. Sleep disorders promote ageing and age-related diseases generate a global psyconeuroendocrineimmune imbalancement. Inflammaging or low-grade chronic inflammation is one of the main players of this imbalancement that binds sleep disorders to ageing process. (Polimeni, 2012). Oxidative gets damaged with ageing, which further invokes an inflammatory response, it may be another mechanism leading to an increase in the level of inflammatory cytokines. The physiological alteration of sleep architecture that characterizes ageing process and age-related sleep disorders are considered an important pathogenic factor of inflammaging. The exact mechanism for the increase of inflammatory cytokines with age has not been fully understood. Some proposed mechanisms include the known increase in total and visceral adiposity with age (fat mass produces about 15 %–30 % of Interleukin-6), the declining levels of sex hormones, disnutrition, subclinical chronic infection, chronic stress, chronic pain disease and physical inactivity (Polimeni, A., 2012).

Reducing the secretion of inflammatory cascade in elderly, by administration of sex steroids, decreasing fat through diet and specific exercise, improving night-time sleep, and controlling adequately chronic pain and inflammation, may improve sleep, daytime alertness and performance and decrease of the risk of common old-age ailments, e.g. metabolic and cardiovascular problems, cognitive disorders and osteoporosis. Thus, improvements in sleep quality are related to life quality.

Furthermore, mobility is crucial to maintain independence. Activity focused on muscular flexibility and articular mobility could help subjects to preserve their range of movement.

Regarding these aspects, many third-age physical activity programmes are proposed. Typically, most training protocols focus on improving limb and abdominal muscle strength but gait is the most important function to preserve in order to maintain independence in old persons. The positive effects are often underestimated and relegated only to psychological and social aspects while also in a homely protocol after 8 weeks of training (2 times per week, 1 hour each) physical improvements were evident (Merati et al., 2011). For example, the score obtained in Tinetti Test (1986) increased (at least for 1 point) with reductions in variability while in Chair Stand Test (Jones et al., 2000; Jones & Rikli, 2002, Rikli & Jones, 2007) all people increased their performance between 1 and 5 complete movements (Lovecchio et al., 2010). Also, during ‘8 Foot Up and Go Test’ (the measurement of speed gait and balance during changing direction, Jones & Rikli, 2000; Rikli & Jones, 2007) the performance time decreased, on average, till 1.7 sec (Lovecchio et al., 2010).

So, the stand-up capacity (strength), the capacity of stand up and walking with a change of direction (strength and balance), and gait capacity (balance) are easily improved during the course.

Other authors found positive results (Persch et al., 2009; Rogers et al., 2003; Rose et al., 2002) even with different scores. Within these differences there were no reports of negative training-related effects and suggested that muscle strength training (not isometric contraction) is the best way to improve both walking action and balance. From

a general point of view, Hunter et al. (2001) found, after six months of training (three sessions per week), low level of fatigue during carrying a load.

An interesting study published on Medicine and Science Sports Exercise (2011), has proved that strength training (e.g. resistance training) is effective for eliciting gains in lean body mass among older adults, particularly with higher volume programmes. Results suggest that resistance exercise participation earlier in life may provide superior effectiveness. (Peterson & Sen, 2011)

Thus, regular physical activity helps the elderly to maintain independence (the most important aim) and physiological function for a long-term period through a holistic training programme, focused on muscular strength, bone density, neuromuscular coordination, postural stability and gait performance (American College of Sports Medicine position stand, 2009).

CONCLUSIONS AND PERSPECTIVES

According to the reports from the World Health Organization (WHO, 2003), a systematic physical activity can be highly recommended in the elderly and the derived benefits are extensive. There is substantial evidence that regular activity reduces risk of injuries from falls, prevents or mitigates functional limitations and is an effective therapy for many chronic diseases. Physical activity prevents or delays cognitive impairment and helps to manage depression and anxiety disorders.

Physical activity and exercise should meet the real individual's need. The plan of intervention, preferably in consultation with a health care provider or fitness professional, should be tailored according to individual's ability or limitations, strategies for increasing activity gradually over time (for non-active older adults), behavioural strategies for adhering to regular physical activity.

A systematic resistance training could be very effective, it leads to a genuine increase in muscle mass and muscle strength in healthy old men and women beyond seventy years of age (Wieser & Haber, 2007). At this age, the pure muscle training can significantly increase the maximum oxygen uptake, due to an augmentation in muscle mass (fat free body mass).

Volume of training and age of participation are important determinants of effectiveness, suggesting that higher dosage results in greater adaptive-response, and that ageing individuals should consider starting a regimen of resistance exercise as early as possible, to optimize results. (Peterson et al., 2011).

Any improvements could help to motivate people to persist with physical activity behaviour change. This is important because increasing physical activity in middle-aged and young-old adults may help increase independence, improve health and reduce disability in later years.

Older people may need to be persuaded that age is no obstacle and that with regular exercise they will enjoy physical independence and interaction with others.

In conclusion, there is evidence that improvements in an upcoming field of science named 'bio gerontology' and the scientific understanding of ageing has made huge advances in recent years. One of the most important findings in *biogerontology* is that there are no specific genes for ageing, known as gerontogenes, and ageing is not controlled by a single mechanism. A promising and powerful approach is that of mild stress such as the well- documented beneficial effect of moderate exercise, which initially increases the production of free radicals, acid and aldehydes. The response to the stressor defends the organism against not only that particular stress, but also it overshoots, facilitates the removal of other molecular damages in cells and tissues. Mild stresses that have been reported to delay ageing and prolong longevity in cells and animals include temperature shock, irradiation, heavy metals, pro oxidants, alcohol, acetaldehyde, hyper gravity, mechanical stretching exercise and food restriction. (Rattan, 2012).

Future perspectives for the global management of age-related disorders predict that structural and functional genomics and proteomics may help to search for reliable biomarkers to personalize therapeutic treatment. Pharmacogenomics and nutrigenomics are attractive anti-ageing options for predicting or minimizing drug interactions, increasing drug efficacy and reducing unnecessary costs, however, physical activity remains an important way, which can be used for both maintaining health and youthfulness and extendingthe health-span of longevity.

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