Ageing Research Reviews 12 (2013) 90–102

Contents lists available at SciVerse ScienceDirect

Ageing Research Reviews

journal homepage: www.elsevier.com/locate/arr

Review

Genes, physical fitness and ageing

Nuria Garatachea*, Alejandro Lucia

Faculty of Health and Sport Science, University of Zaragoza, Huesca, Spain (Dr. Garatachea); Universidad Europea de Madrid, Madrid, Spain

ARTICLE INFO

Article history:
Received 21 June 2012
Received in revised form 6 September 2012
Accepted 6 September 2012
Available online 26 September 2012

Keywords:
Ageing
Genes
Physical fitness
Genetic variation

ABSTRACT

Persons aged 80 years and older are the fastest growing segment of the population. As more individuals live longer, we should try to understand the mechanisms involved in healthy ageing and preserving functional independence in later life. In elderly people, functional independence is directly dependent on physical fitness, and ageing is inevitably associated with the declining functions of systems and organs (heart, lungs, blood vessels, skeletal muscles) that determine physical fitness. Thus, age-related diminished physical fitness contributes to the development of sarcopenia, frailty or disability, all of which severely deteriorate independent living and thus quality of life. Ageing is a complex process involving many variables that interact with one another, including – besides lifestyle factors or chronic diseases – genetics. Thus, several studies have examined the contribution of genetic endowment to a decline in physical fitness and subsequent loss of independence in later life. In this review, we compile information, including data from heritability, candidate-gene association, linkage and genome-wide association studies, on genetic factors that could influence physical fitness in the elderly.

1. Introduction

The number of persons aged ≥60 years worldwide is expected to nearly triple—from 760 million in 2010 to 2 billion (~22% of the total population) in 2050 (United-Nations, 2011). The oldest-old group (≥80 years, including centenarians) is the most rapidly expanding group among westerners (Robine and Paccaud, 2005; Waite, 2004). However, longevity comes at a price, including an eventual loss of functional independence (Christensen et al., 2008). In the elderly, functional independence is directly dependent on *physical fitness*, as explained below. Physical fitness has been recently defined as 'the ability to carry out daily tasks with vigour and alertness, without undue fatigue and with ample energy to enjoy [leisure] pursuits and to meet unforeseen emergencies' (Garber et al., 2011). Importantly, physical fitness is operationalized as several measurable health-related phenotypes including mainly cardiorespiratory fitness and muscle performance/function (Garber et al., 2011). With regards to this, old people commonly experience an age-associated decline in the systems and organs that determine the aforementioned physical fitness phenotypes (see below, Section 1.1).

It is important to understand how ageing and its interactions with lifestyle and genetic factors affect physical fitness. This paper reviews the available information on the genetic factors, including data from heritability, candidate-gene association, linkage and genome-wide association studies, that have been so far identified to influence physical fitness and physical fitness related phenotypes in the elderly.

1.1. Main physical fitness related phenotypes: definitions and ageing effects

Among the physiological changes associated with ageing, those affecting the cardiorespiratory and vascular system and skeletal muscles most affect physical fitness (Fig. 1).

1.1.1. Cardiorespiratory fitness

Maximal oxygen uptake (abbreviated $\dot{V}O_2$ max, and sometimes referred to as 'maximal aerobic capacity' or simply 'aerobic capacity' or 'aerobic endurance') is a main indicator of cardiorespiratory fitness. $\dot{V}O_2$ max is the product of multiplying maximal cardiac output by maximal arteriovenous oxygen difference (a-vO_2 diff), and is usually expressed in milliliters of O_2 consumed per kilogram of body weight per minute (ml kg^{-1} min^{-1}). This variable indicates the maximum capacity of the cardiorespiratory and vascular system to transport O_2 from the air to the working muscles, and of the latter to consume O_2 during dynamic exercise involving large muscles, e.g. running, very brisk-walking, bicycling. In a 6-year longitudinal study whose participants were of initial median age 70 years, $\dot{V}O_2$ max losses of 6.9 and 3.9 ml kg^{-1} min^{-1}/decade were estimated in men and women respectively (Hollenberg et al., 2006). In a similar study (participants aged 55–85 years), 10-year losses were 4.3 and 1.9 ml kg^{-1} min^{-1} in men and women (Stathokostas et al., 2004). The 7.9-year longitudinal Baltimore study reported

* Corresponding author.
E-mail address: nugarata@unizar.es (N. Garatachea).

1568-1637/$ – see front matter © 2012 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.arr.2012.09.003

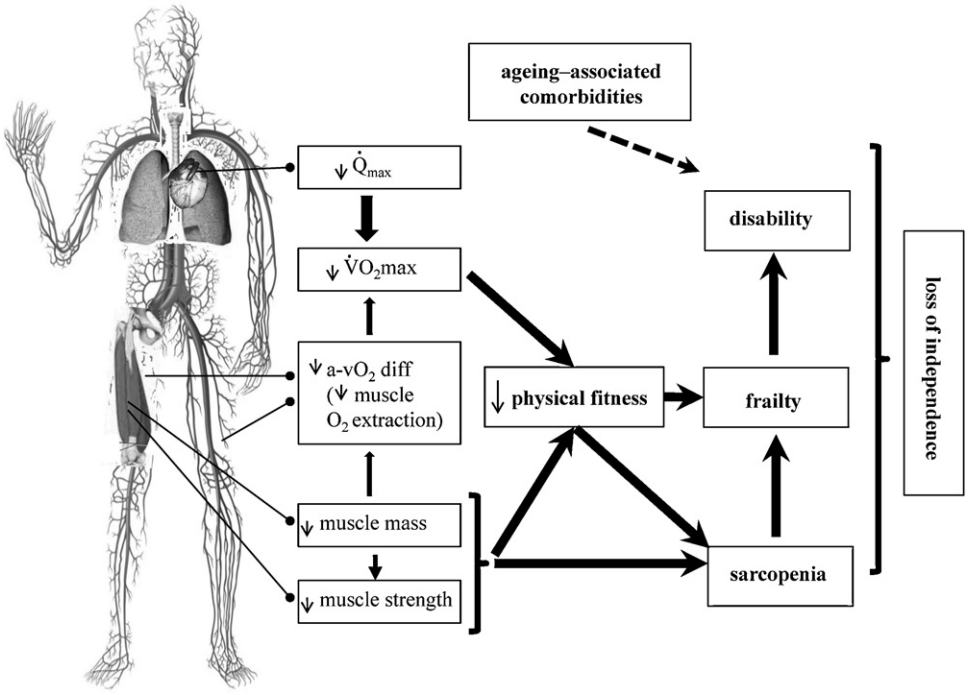

Fig. 1. Summary of the main factors that contribute to age-related declines in physical fitness and physical fitness related phenotypes, resulting in loss of independence. *Abbreviations*: a-vO_2 diff, arteriovenous oxygen difference; *Q*, cardiac output; $\dot{V}O_2$ max, maximal oxygen uptake (or maximal aerobic capacity). See text for recent definitions of sarcopenia, frailty and disability.

$\dot{V}O_2$ max losses of 5%/decade in young adults, and 20%/decade in middle-old (60–69 years) and old-old (≥70 years) individuals (Fleg et al., 2005). Thus, although there are differences between studies, it seems that a $\dot{V}O_2$ max decline ≥4–5 ml kg^{-1} min^{-1}/decade continues into later life (Shephard, 2009).

Reduced maximal cardiac output [=maximal stroke volume × maximum heart rate (HRmax)] is the main contributor to this age-related decline in $\dot{V}O_2$ max. HRmax usually decreases by 3–5%/decade, independently of fitness level or sex (Eskurza et al., 2002; Hawkins et al., 2001), and the relative contribution of this HRmax drop to reduced maximal cardiac output with ageing ranges from 40 to 100% (Hagberg et al., 1985; Ogawa et al., 1992; Stratton et al., 1994). Older adults also show lower stroke volumes during maximal exercise (Hagberg et al., 1985; Ogawa et al., 1992; Stratton et al., 1994). A maximal a-vO_2 diff decrease with ageing (∼−3%/decade) (Hossack and Bruce, 1982; Ogawa et al., 1992) partially contributes to age-reductions in $\dot{V}O_2$ max (Rivera et al., 1989; Wiebe et al., 1999) and reflects less O_2 utilization by skeletal muscles owing to: decreased muscle mass and increased fat (Proctor and Joyner, 1997; Toth et al., 1994), increased peripheral resistance (Lakatta and Levy, 2003), reduced muscle capillary density (Coggan et al., 1992), endothelial dysfunction (Schrage et al., 2007), changes in skeletal muscle microcirculation (Degens, 1998), and reduced muscle oxidative capacity (Conley et al., 2000).

1.1.2. Muscle performance/function

Muscle mass (i.e. the amount of body mass that is made of skeletal muscle tissue) usually peaks at 25–30 years and thereafter begins to decline (Janssen et al., 2000; Lexell et al., 1988). This decline speeds up at the end of the fifth decade, when approximately 10% of total muscle mass is usually lost, such that by 80 years, 40% of muscle mass on average has disappeared (Lexell et al., 1988; Saini et al., 2009). Both a low muscle mass (criterion 1) and low muscle function [i.e. strength (criterion 2) or performance (criterion 3)] are necessary for a diagnosis of *sarcopenia* (Cruz-Jentoft et al., 2010), with the following recently established cut-offs (Fielding et al., 2011): appendicular mass/height^2 ≤7.23 kg m^{-2} (men) and ≤5.67 kg m^{-2} (women) for muscle mass; and gait speed <1 m s^{-1} for muscle function. Factors explaining sarcopenia include: gradual muscle denervation (Deschenes, 2004; Saini et al., 2009); diminished satellite cell numbers/functions (Verdijk et al., 2007); impaired muscle protein turnover, reduced protein synthesis (Kumar et al., 2009); malnutrition (Doherty, 2003); lower anabolic hormone levels (Volpi et al., 2004); increased pro-inflammatory cytokines (Kamel, 2003); greater oxidative stress (Howard et al., 2007); and lower physical activity levels (Cesari and Pahor, 2008). The prevalence of sarcopenia is difficult to determine, mostly because of practical difficulties in assessing muscle mass (von Haehling et al., 2010) and between-study differences in participants' ethnic origin, age or sex (Abellan van Kan, 2009). On average, 5–13% and 11–50% of people aged 60–70 years and ≥80 years respectively suffer sarcopenia (Baumgartner et al., 1998; Frisoli et al., 2011; Janssen, 2006; Janssen et al., 2002; Lauretani et al., 2003; Rolland et al., 2003). Higher prevalences (68%) have been reported in male nursing home residents ≥70 years (Landi et al., 2012).

1.1.3. Frailty and disability

A consequence of the aforementioned effects of ageing on cardiorespiratory fitness and muscle performance/function, alone or in combination with comorbidities, is the *frailty syndrome* (Heuberger, 2011). Although there is no clear consensus, frailty can be defined as 'unintentional weight and muscle loss, exhaustion, and declines in grip strength, gait speed, and activity' (Fried et al., 2001). A main outcome of frailty is *disability* (Sternberg et al., 2011), i.e. 'difficulty or dependency in carrying out activities necessary for independent living, including roles, tasks needed for self-care and household chores, and other activities important for a person's quality of life' (Fried et al., 2004).

Thus, in this review we will report the results of those studies in elderly people which analyzed one or more of the abovementioned phenotypes that determine physical fitness, i.e. mainly $\dot{V}O_2$ max,