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Exercise training increases anabolic and attenuates catabolic and apoptotic processes in aged skeletal muscle of male rats

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ABSTRACT

Aging results in significant loss of mass and function of the skeletal muscle, which negatively impacts the quality of life. In this study we investigated whether aerobic exercise training has the potential to alter anabolic and catabolic pathways in the skeletal muscle. Five and twenty eight month old rats were used in the study. Aging resulted in decreased levels of follistatin/mTOR/Akt/Erk activation and increased myostatin/Murf1/2, proteasome subunits, and protein ubiquitination levels. In addition, TNF-α, reactive oxygen species (ROS), p53, and Bax levels were increased while Bcl-2 levels were decreased in the skeletal muscle of aged rats. Six weeks of exercise training at 60% of VO2max reversed the age-associated activation of catabolic and apoptotic pathways and increased anabolic signaling. The results suggest that the age-associated loss of muscle mass and cachexia could be due to the orchestrated down-regulation of anabolic and up-regulation of catabolic and pro-apoptotic processes. These metabolic changes can be attenuated by exercise training.

1. Introduction

The skeletal muscle is crucial for movement and also plays an important role in sugar and fat metabolism, and immune response. Age-associated loss in function and mass of the skeletal muscle is well documented (Bijlsma et al., 2012; Reid and Fielding, 2012). However, the causative mechanism(s) controlling this complex process is not well understood. Enhanced generation of inflammation (Degens, 2010), aging-related increases in the level of reactive oxygen species (ROS) (Hiona and Leeuwenburgh, 2008), altered metabolism (Lawler and Hindle, 2011), and increased rates of protein degradation (Witt et al., 2008) are also on the list of potential causative factors of sarcopenia. Indeed, it has been reported that administration of exogenous tumor necrosis factor alpha (TNF-α) leads to a significant decrease in the mass of the skeletal muscle (Llovera et al., 1993). This cytokine can interfere with the contractile properties of the skeletal muscle causing decreased force generating capacity (Reid et al., 2002). Inflammation can readily increase the concentration of ROS, which above certain levels jeopardizes cellular function (Ji, 2007; Langen et al., 2003; Radak et al., 2005). Recently it has been reported that myostatin, which is a negative regulator of muscle growth and is induced in aged skeletal muscle (Bowser et al., 2013; Brioche et al., 2013), can also add to higher levels of ROS (Sriram et al., 2011). Increased levels of myostatin can readily reduce protein synthesis (Hitachi et al., 2014) and it appears that the rate of protein degradation is enhanced in aged skeletal muscle (Goto et al., 2007). It has also been shown that the ubiquitin–dependent proteasome system can be activated with aging (Radak et al., 2002), and recent information indicates that muscle RING finger 1/2 (Murf1/2), which is a ubiquitin ligase, could have an important role in aging skeletal muscle (Sacheck et al., 2007). Thus, it is obvious that the mechanism(s) affecting muscular atrophy is very complex and extremely complicated.

Physical exercise has been shown to retard age-associated loss of muscle mass (Dickinson et al., 2013) and supplementation of growth hormone (Brioche et al., 2013; Nass, 2013).

Therefore the aim of the present study was to obtain a picture of the signaling anabolic, catabolic and apoptotic pathways of aged skeletal muscle. The role of aerobic exercise training on these pathways was investigated.

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