Exercise training effects on skeletal muscle plasticity and IGF-1 receptors in frail elders

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Abstract

Age-related sarcopenia inhibits mobility, increasing the risk for developing many diseases, including diabetes, arthritis, osteoporosis, and heart disease. Tissue plasticity, or the ability to regenerate following stress, has been a subject of question in aging humans. We assessed the impact of 10-weeks of resistance training on markers of skeletal muscle plasticity and insulin growth factor-1 (IGF-1) receptor density in a sub sample of subjects who, in an earlier study, demonstrated enhanced immunohistochemical labeling of IGF following resistance training. Muscle biopsies from the vastus lateralis of five elderly men and women were taken prior to and following 10 weeks of resistance training (N = 3) or a control period (N = 2). Immunogold labeling and quantitative electron microscopy techniques were used to analyze markers of IGF-1 receptor density and tissue plasticity. The experimental subjects showed a 161% increase in Z band damage following resistance training. Myofibrillar central nuclei increased 296% (P = 0.029) in the experimental subjects. Changes in the percent of damaged Z bands were associated with alterations in the presence of central nuclei (r = 0.668; P = 0.0347). Post hoc analysis revealed that the relative pre/post percent changes in myofibrillar Z band damage and central nuclei were not statistically different between the control and exercise groups. Exercise training increased myofibrillar IGF-1 receptor densities in the exercise subjects (P = 0.008), with a non-significant increase in the control group. Labeling patterns suggested enhanced receptor density around the Z bands, sarcolemma, and mitochondrial and nuclear membranes. Findings from this study suggest that the age-related downregulation of the skeletal muscle IGF-1 system may be reversed to some extent with progressive resistance training. Furthermore, skeletal muscle tissue plasticity in the frail elderly is maintained at least to some extent as exemplified by the enhancement of IGF-1 receptor density and markers of tissue regeneration.
Introduction

Production of insulin-like growth factor-1 (IGF-1) is stimulated by liver growth hormone receptors and released to the circulation. Localization of the growth hormone receptor in skeletal muscle is predominantly cytoplasmic (Lincoln et al. 1998), however, the exact location of the IGF-1 receptor within muscle is a topic with sparse documentation. Once the IGF-1 hormone binds to the receptor on muscle fiber sarcolemma, it signals a cascade of events in the muscle itself to initiate protein synthesis. Should the IGF-1 receptor become saturated, a typical situation when IGF-1 receptor number decreases, yet circulating IGF-1 hormone remains the same, the events downstream from the receptor will cease. This metabolic chain of events becomes more predominant with age and compromises protein synthesis.

Human (Castaneda et al. 2000; Marcell et al. 2001) and animal (Edwall et al. 1989; Ullman et al. 1990) studies suggest that IGF-1 is an important regulator of skeletal muscle growth. Human investigations report that serum (Rollero et al. 1998) and skeletal muscle (Welle et al. 2002) concentrations of IGF-1 are lower in older adults. The IGF-1 receptor plays a dominant role in age-related downregulation of the endogenous IGF-1 system (Lincoln et al. 1998; Marcell et al. 2001, Welle et al. 2002) that directly affects skeletal muscle strength and mass (Rudman et al. 1990; Oudin et al. 1998; Alexandrides et al. 1989; Adams 1998). In the sedentary older adult the ability to upregulate growth factors in response to overload such as exercise is especially compromised (Underwood and Van Wyk 1985). Many lifestyle factors, including exercise and nutrition influence the IGF-1 system’s regulation of myogenesis and muscle metabolism (Willis and Parkhouse 1994; Frost and Lang 2003; Fiatarone et al. 1999; Poehlman and Copeland 1990; Willis et al. 1997; Nicklas et al. 1995). The consequences of physical inactivity are strength impairment and loss of muscle mass associated with a progressive decline in functional mobility and an elevated risk for metabolic-related diseases, including osteoporosis, arthritis, diabetes, and cardiovascular disease. Willis and Parkhouse (1994) measured protein turnover rates in in-vitro isolated soleus preparations in acutely exercised mice with and without IGF-1 presence. The authors reported that muscle protein synthesis was elevated with and without IGF-1 administration 12 h following an acute exercise bout. Furthermore, the degree of net protein degradation was intensity related.

We recently explored the effects of a 10-week progressive resistance-training program on muscle plasticity in frail elders, aged 72–98 years (Fiatarone et al. 1999). Post muscle biopsy specimens showed an increased appearance of IGF-1 and regeneration potential from baseline atrophy. The 257% increase in strength following resistance training was associated with a 141% increase in ultrastructural damage and a 491% increase in IGF-1 immunofluorescence staining. Since the IGF-1 receptor plays a dominant role in muscle IGF signaling, we speculated that an increase in IGF-1 receptor number in association with markers of muscle damage and regeneration can expand existing knowledge regarding the response of the IGF-1 receptor to exercise stress in older adults. One aim of this study was to identify, localize, and quantify the IGF-1 receptor in elderly human skeletal muscle in relation to regeneration markers (Fiatarone et al. 1999). Muscle biopsies taken from the vastus lateralis of five elderly (85–98 years) men (N = 3) and women (N = 2) prior to and following 10 weeks of resistance training were prepared for electron microscopic examination of immunogold labeling samples.

Materials and methods

Subjects

The tissue samples used in this study were taken from the vastus lateralis muscle from a subset of five subjects (three men and two women) who volunteered in a randomized control trial of progressive resistance training (Fiatarone et al. 1999). Two subjects were placed in a multi-nutrient supplementation (S) group and three experimental subjects underwent progressive resistance training (E, N = 2) or a combination of S plus E (N = 1). All statistical analyses of ultrastructural and IGF-1 staining in the larger scale study (Fiatarone et al. 1999) showed that the nutritional supplement use had no independent or interactive effect on any of these variables, lending support for collapsing subjects into exercise or no exercise groups. This subset of subjects in this study comprised the exercise (N = 3: two men and one woman) and control (N = 2: one man and one