Review article

Resistance training and androgenic anabolic steroids on aged skeletal muscles: a review about methodological approaches

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Abstract

One of the most frequent effects of aging is the involuntary loss of muscle mass, strength and function, termed sarcopenia. Longitudinal data suggest that muscle strength is a robust predictor of functional decline that occur during aging. Since strength capacity appears to also be indicative of disability, resistance training may serve as an effective mode of physical activity to directly improve functional capacity. There is also a growing evidence to indicate that age-related decline in production and activity of hormones plays an important role in aging muscle. Testosterone deficiency has been associated with a marked decrease in measures of whole body protein anabolism and decrease strength. The purpose of the present study was to explore the characteristics of the methodological approaches used in the studies related to the role of resistance training and androgenic anabolic steroids in the aged skeletal muscle that have been published in the last ten years. A literature review was conducted in April 2011 using the following databases: PubMed; Medline; Lilacs; and Scielo. We found sixty two articles analyzing the influence of resistance training on skeletal muscle of aged samples, seven articles which proposed to verify the chronic influence of androgenic anabolic steroids and only one article mixing both interventions. The great variety of analysis methods is notable. Morphological analysis was done in only few articles.

Keywords: androgenic anabolic steroids, aging, skeletal muscle.

1 Introduction

In humans, skeletal muscle is the most abundant tissue in the body comprising 40-50% of body mass and playing vital rules in locomotion, heat production during periods of cold stress, and overall metabolism (KARAGOUNIS and HAWLEY, 2010). Muscular weakness plays a principal role in the pathogenesis of frailty and functional impairment that occurs with aging, and contributes to numerous disease processes (PETERSON, RHEA, SEN et al., 2010). One of the most frequent effects of aging is the involuntary loss of muscle mass, strength and function, termed sarcopenia (PETERSON, RHEA, SEN et al., 2010; SNIJDERS, VERDIJK and VAN LOON et al., 2009). Moreover, increased longevity has led to a higher frequency of sarcopenia, and respective escalating health care expenditures for complications associated with declines in functional health and loss of independence (PETERSON, RHEA, SEN et al., 2010). Sarcopenia and muscle weakness are not considered to be disease states, but rather conditions which translate to acute functional deficit and disability, as well as related comorbidity and mortality (RUIZ, SUI, LOBELO et al., 2008).

Longitudinal data suggest that muscle strength is a robust predictor of functional decline that occur during aging (RANTANEM, GURALNIK, FOLEY et al., 1999). Since strength capacity appears to also be indicative of disability (JANSSEN, HEYMSFIELD and ROSS, 2002), resistance training (RT) may serve as an effective mode of physical activity to directly improve functional capacity (PETERSON, RHEA, SEN et al., 2010). There is also a growing evidence to indicate that age-related decline in production and activity of hormones plays an important role in aging muscle (AHMED, MATSUMURA and CRISTIAN, 2005). Testosterone deficiency has been associated with a marked decrease in measures of whole body protein anabolism and decrease strength (BROWN, 2008). Because sex hormones are markedly reduced with age, and we are living longer, there has been recent interest in restoring hormones to physiologic levels in aging men and women, and significant gains in muscle mass and strength, with and without resistance training, have been realized (LAMBERT, SULLIVAN, FREELING et al., 2002; BHASIN, WOODHOUSE, CASABURI et al., 2005; BROWN, 2008).

Understanding the mechanisms that lead to loss of muscle and physical inability with age is a priority for those who work in health care, including public health intervention programs (BRAGGION, MAIFRINO and MIRANDA et al., 2010). Hence, it is necessary to investigate the impact of the resistance training and supplementation of testosterone, usually cited as androgenic anabolic steroids, upon the morphological aspects of the skeletal muscle in the process of sarcopenia in individuals engaged in physical activities as they age. Morphological studies are important to quantify and analyze the anatomical structures which may assist to verify the possible changes due to many processes such as muscular synthesis or degradation (MANDARIN-DE-LACERDA, 1995). Taking into consideration the importance of identifying the tendencies of the morphological approaches and the type of study outlines used in researching the topics cited above on the morphological aspects of aging, a national and international literature review on this topic was conducted, which may assist the health professionals who work with morphology and endocrinology of aging.

The purpose of the present study was to explore the characteristics of the methodological approaches used in the studies related to the role of resistance training and androgenic anabolic steroids in the aspects of the aged skeletal muscle that have been published in the last ten years.

2 Methods

To investigate studies published on the role of resistance training and androgenic anabolic steroids in the aspects of aging muscle, a literature review was conducted in April 2011 using the following databases: PubMed; Medline; Lilacs; and Scielo from the last 10 years (2001-2011). These databases were chosen because they include worldwide publications in the field of health sciences and two of them include Latin American and Caribbean literature (Lilacs) and Brazilian literature (Scielo), which in general are not indexed in major databases like Medline. The search was conducted using the "skeletal muscle', "aging", "resistance training" and "androgenic anabolic steroids" as keywords searching for words that appear in all fields. The languages selected in the search were Portuguese, Spanish, and English. The publications found were cataloged regardless of the methodological approach adopted. The articles were then selected based on some inclusion criteria such as those characterized by full-text articles or abstracts published in indexed journals in the last ten years written in Portuguese, Spanish, and English. The publications involving human and/or animal subjects and which related to the key words were considered. Nevertheless, publications such as theses, monographs, books, book chapters, papers presented at conferences, reports, government, reviews, meta-analysis as well as national and international entity material, and studies that do not include the inclusion criteria were disregarded. For the last, a secondary exclusion criteria was done and papers which analyzed the administration of nutritional supplements, metabolic diseases and concurrent training programs which used aerobic exercise were also excluded.

3 Results and discussion

Due to the considerable number of publications found using the words skeletal muscle and aging, the search results were refined, limited, and added to the findings obtained with the word resistance training. Afterwards, the search was redone to the publications containing the word androgenic anabolic steroids, and for last, the search was refined using both the key words resistance training and androgenic anabolic steroids (Table 1).

The search resulted in one hundred and sixteen publications using the Pubmed database showing that the majority of the important publications are made in journal indexed for this database.

Using the Pubmed data, the Table 2 shows other variables of interest as number of publications using humans and/or animals, and the most frequently language used for this kind of study.

The Table 3 shows the methodology used to determine the responses of skeletal muscle. It is notable the amount of resources utilized by the researches. On Table 4, the experimentation type of study is demonstrated from studies which verified the responses from resistance training protocols.

Table 1. Frequency distribution of the publications retrieved second database and queried keywords search.

Database	A	B	C	D
Pubmed	2895	116	18	1
Medline	2807	113	17	1
Lilacs	3	0	0	0
Scielo	1	0	0	0

A) Skeletal muscle and aging; B) Skeletal muscle and aging and resistance training; C) Skeletal muscle and aging and androgenic anabolic steroids; and D) Skeletal muscle and aging and androgenic anabolic steroids and resistance training.

Table 2. Distribution of articles in Pubmed Database according to publication language and subjects of study.

Variable	A	B	C	D
Humans	X	95	11	1
Animals	X	18	7	0
English	X	116	18	1
Spanish	X	0	0	0
Portuguese	X	0	0	0

A) Skeletal muscle and aging; B) Skeletal muscle and aging and resistance training; C) Skeletal muscle and aging and androgenic anabolic steroids; and D) Skeletal muscle and aging and androgenic anabolic steroids and resistance training.

Table 3. Methodology used to determine skeletal muscle responses in studies refined from Pubmed database based on secondary criteria of exclusion.

Variable	A	B	C	D
Electromyography	X	7	0	0
Computed Tomography	X	8	1	1
Magnetic Resonance Imaging	X	3	1	0
Muscle Biopsies	X	35	3	0
Ultrasound	X	4	0	0
Dual-energy X-ray Absorptiometry	X	6	3	0
Strength and/or Power tests	X	10	3	1

A) Skeletal muscle and aging; B) Skeletal muscle and aging and resistance training; C) Skeletal muscle and aging and androgenic anabolic steroids; and D) Skeletal muscle and aging and androgenic anabolic steroids and resistance training.

Table 4. Studies type of experimentation analysis of the studies refined from Pubmed database based on secondary criteria of exclusion.

Variable	A	B	C	D
Acute	X	12	0	0
Chronic	X	50	7	1

A) Skeletal muscle and aging; B) Skeletal muscle and aging and resistance training; C) Skeletal muscle and aging and androgenic anabolic steroids; and D) Skeletal muscle and aging and androgenic anabolic steroids and resistance training.

Due to the number of articles found using the words skeletal muscle and aging, we limited the discussion of the present study analyzing the methodologies of the papers found on the search using only Pubmed database and the limited and refined findings obtained with the key words resistance training and androgenic anabolic steroids. After refining the search, we found sixty two articles analyzing the influence of resistance training on skeletal muscle of aged samples, seven articles which proposed to verify the chronic influence of androgenic anabolic steroids and only one article mixing both interventions. The great variety of analysis methods is notable. The number of methods to measure skeletal muscle responses to resistance training or use of androgenic anabolic steroids may be viewed in Table 3. The method used in most of the works was muscle biopsies which was presented at thirty eight articles. Most of them used the molecular biology analysis (POOLE, ROBERTS, DALBO et al., 2011; DALBO, ROBERTS, HASSELL et al., 2011; AHTIAINEN, HULMI, KRAEMER et al., 2011; MANINI, VINCENT, LEEUWENBURGH et al., 2011; ROBERTS, KERKSICK, DALBO et al., 2010; FRY, GLYNN, DRUMMOND et al., 2010; WILLIAMSON, RAUE, SLIVKA et al., 2010; THALACKER-MERCER, DEL´ITALIA, CUI et al., 2010; BUFORD, COOKE and WILLOUGHBY, 2009; MAYHEW, KIM, CROSS et al., 2009; DENNIS, ZHU, KORTEBEIN et al., 2009; MELOV, TARNOPOLSKY, BECKMAN, 2007; THOMPSON, McCLUNG, BALTGALVIS et al., 2006; CARSON, LEE, McCLUNG et al., 2002). All of the publications had the experimental design as rule of frame. But if we take a look in Table 4, it´s also notable that human samples are majority (POOLE, ROBERTS, DALBO et al., 2011; SATTLER, BHASIN, HE et al., 2011; DALBO, ROBERTS, HASSELL et al., 2011; AHTIAINEN, HULMI, KRAEMER et al., 2011; MANINI, VINCENT, LEEUWENBURGH et al., 2011; ROBERTS, KERKSICK, DALBO et al., 2010; CANDOW, CHILIBECK, ABEYSEKARA et al., 2011; FRY, GLYNN, DRUMMOND et al., 2010; WILLIAMSON, RAUE, SLIVKA et al., 2010; THALACKER-MERCER, DEL´ITALIA, CUI et al., 2010; LOWNDES, CARPENTER, ZOELLER et al., 2009; BUFORD, COOKE and WILLOUGHBY, 2009; MAYHEW, KIM, CROSS et al., 2009; DENNIS, ZHU, KORTEBEIN et al., 2009; RAUE, SILVKA, MINCHEV et al., 2009; NOGUEIRA, GENTIL, MELLO et al., 2009; VERDIJK, GLEESON, JONKERS et al., 2009; MELNYK, ROGERS and HURLEY, 2009; TAAFFE, HENWOOD, NALLS et al., 2009; KUMAR, SELBY, RANKIN et al., 2009; REID, CALLAHAN, CARABELLO et al., 2008; SILVKA, RAUE, HOLLON et al., 2008; KOSEK and BAMMAN, 2008; HENWOOD, RIEK and TAAFFE, 2008; DELMONICO, KOSTEK, JOHNS et al., 2008; SCHROEDER, CASTANEDA-SCEPPA, WANG et al., 2007; MELOV, TARNOPOLSKY, BECKMAN, 2007; CANNON, KAY, TARPENNING et al., 2007; MACKEY, ESMARCK, KADI et al., 2007; CAREY, FARNFIELD, TARQUINIO et al., 2007; BOTTARO, MACHADO, NOGUEIRA et al., 2007; NOGUEIRA, GENTIL, MELLO et al., 2009; PETRELLA, KIM, CROSS et al., 2006; HOLVIALA, SALLINEN, KRAEMER et al., 2006; OCHALA, LAMBERTZ, VAN HOECKE et al., 2007; GRANACHER, GOLLHOFER and STRASS, 2006; KALAPOTHARAKOS, TOKMAKIDIS, SMILIOS, 2005; MORSE, THOM, MIAN et al., 2005; PARISI, PHILLIPS, KACZOR et al., 2005; CANEPARI, ROSSI, PELLEGRINO et al., 2005; BARRY, WARMAN and CARSON, 2005; BHASIN, WOODHOUSE, CASABURI et al., 2005; HARRIS, DEBELISO, SPITZER-GIBSON et al., 2004; REEVES, NARICI and MAGANARIS, 2004a; BARRY and CARSON, 2004; BAMMAN, RAGAN, KIM et al., 2004; REEVES, NARICI and MAGANARIS, 2004b; KUBO, KANEHISA, MIYATANI et al., 2003; WILLIAMSON, GALLAGHER, HARBER et al., 2003; FERRI, SCAGLIONI, POUSSON et al., 2003; LAMBERT, SULLIVAN, FREELING et al., 2002; NEWTON, HAKKINEN, HAKKINEN et al., 2002; GODARD, GALLAGHER, RAUE et al., 2002; FIELDING, LEBRASSEUR, CUOCO et al., 2002; JOZSI, DUPONT-VERSTEEGDEN, TAYLOR-JONES et al., 2001; and YARASHESKI, 2001; VINCENT, BRAITH, FELDMAN et al., 2002; TRAPPE, WILLIAMSON and GODARD et al., 2002; PLOUTZ-SNYDER and GIAMIS, 2001; PANTON, FRANKE, BLEIL et al., 2001; BEMBEN and MURPHY, 2001; TRAPPE, GODARD, GALLAGHER et al., 2001). Actually, it was expected that in this kind of research the animal samples should appeared of most. Braggion, Maifrino and Miranda et al. (2010) cited that a possible explanation to the fact that morphology cellular studies are mostly experimental is that they are designed to test the manipulation of variables that interfere with micro and macroscopic aspects of the structures and tissues in humans and animals used in experimentations. Normally, animal models are easily to control because of the time of experimentation. Practically, the studies involved in this review used studies of short time durations, facilitating the control of the variables of interest. Some studies used acute (DALBO, ROBERTS, HASSELL et al., 2011; POOLE, ROBERTS, DALBO et al., 2011; MANINI, VINCENT, LEEUWENBURGH et al., 2011; ROBERTS, KERKSICK, DALBO et al., 2010; FRY, GLYNN, DRUMMOND et al., 2010; THALACKER-MERCER, DEL´ITALIA, CUI et al., 2010; BUFORD, COOKE and WILLOUGHBY, 2009; BAMMAN, RAGAN, KIM et al., 2004) evaluations and mostly analyzing gene expression after a single bout of resistance exercise (POOLE, ROBERTS, DALBO et al., 2011; DALBO, ROBERTS, HASSELL et al., 2011; MANINI, VINCENT, LEEUWENBURGH et al., 2011; ROBERTS, KERKSICK, DALBO et al., 2010; FRY, GLYNN, DRUMMOND et al., 2010; THALACKER-MERCER, DEL´ITALIA, CUI et al., 2010; BUFORD, COOKE and WILLOUGHBY, 2009; MAYHEW, KIM, CROSS et al., 2009; MATHENY, MERRITT, ZANNIKOS et al., 2009). Matheny, Merritt, Zannikos et al. (2009) studied mice with insulin like growth factor-I (IGF-I) gene disrupted and showed that even when there is severe deficiency of circulating IGF-I the response from resistance training is normal and these data presents evidence for a compensatory growth of muscle. But, in the other hand, the anabolic responses to a single bout of contraction is attenuated with aging and also help to explain the reduced capacity for hypertrophy in aged animals (PARKINGTON, LEBRASSEUR, SIEBERT et al., 2004). For the articles which chronic analysis were done image analysis was presented in seventeen papers. But, even like that some articles verified cellular adaptations. Murlasits, Cutlip, Geronilla et al. (2006) demonstrated that old muscle might suffer more than young muscle of heat shock proteins produced as a response of high intensity training. Ducomps, Mauriège, Darche et al. (2003) presented evidence that different muscle types may respond different to the same exercise protocol. Extensor Digitorum Longus and Rectus Femoris muscles increased collagen concentrations and passive mechanical parameters after a jump period of training when Semimenbranosus Proprius and Psoas Major muscles did not respond as well. Furthermore, Melnyk, Rogers and Hurley (2009) examined the effects of training and detraining on quadriceps muscle area by measurements via magnetic resonance image and showed significant strength changes accompanied by significant alterations in muscle density. Allouh and Rosser (2010) suggested that satellite cells may be key cellular vectors for anabolic steroid induced muscle fiber hypertrophy. On the other hand, computed tomography also has been used in other articles (SILVKA, RAUE, HOLLON et al., 2008; DELMONICO, KOSTEK, JOHNS et al., 2008; LAMBERT, SULLIVAN, FREELING et al., 2002). Delmonico, Kostek, Johns et al. (2008) proposed to determine how dual-energy X-ray absorptiometry (DEXA) compares to computed tomography (CT) for measuring changes in total thigh skeletal muscle mass with strength training. The authors demonstrated that DEXA overestimates baseline and may cause a higher error when compared do CT. DEXA is often used in several papers because of certain advantages that warrant is used in epidemiologic and intervention studies (DELMONICO, KOSTEK, JOHNS et al., 2008). Electromyography, a method used to measure the electrical stimulations in skeletal muscle, was used to verify or compare the effect of a training program between young and old people (CANNON, KAY, TARPENNING et al., 2007). Other article used this method to examine the impact of heavy resistance training on dependent measures (GRANACHER, GOLLHOFER and STRASS, 2006).

Morphological analysis was done in only few articles. Mayhew, Kim, Cross et al. (2009) verified myofiber size and distribuition using immunofluorescence microscope techniques. Using this technique was possible to quantify and classify myosin heavy chain (MHC). Pehme, Alev, Kaasik et al. (2004) verified a change on MHC associated to a different effect of different types of training protocols. Ahtiainen, Hulmi, Kraemer et al. (2011) also verified muscle fiber sizes and type, using the histochemical analysis.

4 Conclusion

From the results obtained in this study, it´s clear that the amount of methods used to study the independent variables influence on this population is many and in the last few years the major concern has been the gene expression analysis.

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