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ORIGINAL PAPERS

How Important Are the Animal Models Studies in Understanding Obesity, the Relevance of the Physical Exercises or Exercise-Induced Muscle Enlargement?

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Abstract

Generating and studying animal models is a fundamental tool in understanding most of the human specific disorders. However, it is important to mention from the beginning that an animal model will never perfectly replicate the very complex human symptomatology. In the present report, our group will focus on revising the most important animal models studies in understanding obesity, the relevance of the physical exercises or exercise-induced muscle enlargement, by describing the most relevant models used in animals such as rats, dogs, cats, monkeys, birds or even zebrafish.

Keywords: physical exercising, animal models.

Introduction

Animal studies are extremely important for a better understanding and a better management for a variety of disorders. However, it is important to mention from the beginning that an animal model will never perfectly replicate the very complex human symptomatology (Lefter et al., 2014). Despite that, animal modeling is a fundamental tool in understanding most of the human specific

disorders.

In this way, for example our group has some previous experience in understanding and developing new and classical animal models of neuropsychiatric disorders (Ciobica et al., 2010, 2011, 2015, Foyet et al., 2011, Ababei et al., 2015), and also lately animal models related to obesity and physical exercise performances (Ciobica et al., 2015, 2016, Trofin et al., 2014).

In addition, in the literature there are several different animal models that are created for inducing and studying obesity (Lutz et al., 2012) or even muscle hypertrophy, models that aspire to produce similar results to progressive resistance training protocols in humans. Thus, in the case of muscle hypertrophy for example, which can be defined as an adaptive response to overload, it is considered distinct and separate from muscle hyperplasia and during hypertrophy, contractile elements enlarge and the extra cellular matrix expands to support growth (Vierck et al., 2002). This is in contrast to hyperplasia, which results as an increase in the number of fibbers within a muscle.

Progressive resistance exercise is considered to be the best possible way to achieve hypertrophy in humans. It is widely accepted that the 3 primary factors responsible for initiating the hypertrophic response to resistance exercise are the following: mechanical tension, muscle damage, and metabolic stress (Evans et al., 2002).

Mechanical tension is produced by both, the generated force and also by the stretch of the muscle. It is considered to be essential to muscle growth, and the combination of the before mentioned two stimuli has been found in the literature to have the most significant hypertrophic effect (Hornberger et al., 2006). To be more specific, mechanical overload increases muscle mass, while the unloading results in atrophy. Studies have shown that this process appears to be largely controlled by the protein's synthetic rate (Kimball et al., 2002).

Thus, resistance training can result in localized muscle damage tissue. The muscle damage it is considered, under certain conditions, to generate a hypertrophic response. Damage can be specific to just a few macro molecules of tissue or even as a result in large tears in the sarcolemma (the transparent tubular sheath which envelops the fibbers of skeletal muscles), basal lamina, or in the supportive connective tissue (Vierck et al., 2000).

In addition, numerous studies support the anabolic role of metabolic stress induced by resistance exercises in hypertrophy (Smith et al., 2005). To a greater extent, some authors have speculated that metabolite accumulation may be even more important than the high force development in optimizing the hypertrophic response to resistance training (Shinohara et al., 1998). Although, many studies have clearly showed that metabolic stress does not seem to be an essential part of muscular growth (Shinohara et al., 2002), a large body of evidence shows that it can have a significant hypertrophic effect, either in a primary or secondary manner, as we will describe later on.

Therefore, the literature regarding mechanism underlying the idea that strength increases through resistance training is marked largely by references to the role of muscle mass enlargement. It is also important to mention that, there are other strength related changes as well, such as alteration in the contractile characteristics of the muscle, or muscle architectural changes (Widrick et al., 2002). Nevertheless, the idea that muscle mass plays a vital role in muscular strength is considered to be indisputable. There is also little question regarding the notion that neural factors play an important role in muscle strength gains (Aagaard et al., 2003).

In a clinical setting, where the therapist needs to restore the function that has been lost or impaired through illness or injury, rehabilitation can require the restoration of not only strength, but also range of motion, balance and coordination. The specificity of the functional needs of every patient should determine the exercises and activities prescribed, including the exercise selection, the intensity, volume of strength training used.

Thus, an increase in muscle strength should be a desirable outcome of any type of rehabilitation therapy. As before mentioned, an increase in muscle strength is the result of muscle hypertrophy and neural adaptations, and progressive resistance exercise is the primary mode of producing muscle hypertrophy in a rehabilitation setting. There are many reviews that analyzed the specifics of progressive resistance exercise in terms of specificity of training, regarding total volume, frequency, intensity, exercise selection and results (Taaffe et al., 2000)**.** As a confirmation that strength training should be used in most rehabilitation programs, it has been shown that resistance training has an *important beneficial*

role in osteoporosis, stroke, aging, cardiovascular diseases, metabolic disorders and muscular diseases (Parise et al., 2000, Pollock et al., 2000, Sandu et al., 2014).

Although physiological and cellular mechanisms of muscle hypertrophy have been reviewed in many articles, molecular mechanisms that initiate and regulate muscle hypertrophy is still a relatively new topic in the field of exercise science (Carson et al., 2000, Carro et al., 2000). However, while the functional outcomes of progressive resistance exercise have been researched largely using human participants, the majority of the data used in cellular and molecular components of muscle hypertrophy are inferred from studies using laboratory animals as subjects.

Regarding the aforementioned implicated mechanisms, we could discuss also about the oxidative stress status modifications and its relevance in physical exercising (Trofin et al., 2014, 2017), especially considering the importance of the oxidative stress markers methodology (Cojocaru et al., 2055, 2007, 2010) in most of the neuropsychiatric and metabolic manifestations (Rosoiu et al., 2006, 2007, 2009, Achitei et al., 2013, Balmus et al., 2016, Ciobica et al., 2012, Foyet et al., 2015) and the previous discussed and studied (including by our group) relations between exercising performing and a variety of neurological and psychiatric disorders.

In fact, the importance of these animal models is given by the information emerged, which can be used by the clinician to evaluate current strength-related programs and perhaps design new or modified strategies for implementing this type of exercising in patients suffering from various disorders. Thus, the ultimate goal is to optimize the resistance training in humans to acquire better functional results in the clinical environment. Also, the majority of these studies on animals are comparing physically active rodents to those that are more inactive, as we also did in a previous mentioned and cited paper regarding the importance of exercising in Parkinson's disease manifestations (Ciobica et al., 2015).

Also, previous studies in the literature are manipulating the exercise variable by providing or preventing access to a running wheel for 3 to 12 weeks. The results are suggesting that activity-induced increases in neurotransmitters (such as norepinephrine, serotonin), neuromodulators (galanin), and growth factors, including nerve growth factor, vascular endothelial-derived growth factor, insulin-

like growth factor (IGF-1), and brain-derived neurotrophic factor, can result in angiogenesis and neurogenesis as well as contribute to cellular and molecular adaptations that enhance learning and attenuate signs of anxiety and depression (Carro et al., 2000).

What is interesting enough, is that it is unknown whether these effects occur with strength training. Important contributions to the understanding of the mechanisms by which exercise training improves mental health could be made by conducting research that directly examines the brains of animals after strength training.

In the literature we have found the vast majority of the animal models of strength training are conducted on rodents. And there are many ways in which the respective authors have tried to induce strength training to these animals. For example in one study direct electrical stimulation of the muscle was induced while the rodent was anesthetized (Wong et al., 1988), in another one rodents climbed with weights added to the back (Yarasheski et al., 1990) and perhaps the most interesting model was the one in which the rodent performed squats in a squat exercise apparatus (Klitgaard et al., 1988). The problem with these and other rodent models is that they use operant conditioning in order to motivate the animals to perform the resistance movements. These experiments typically involve either tail shock avoidance or food reward in hungry animals (Ishiwari et al., 2004). For example, in one study, food deprived Long-Evans rats were trained to reach for a single piece of pasta and then progressively larger bundles of pasta across 30 days of training (Remple et al., 2001). One may argue that the stress effects of hunger or shock to potentially confound the effects of strength training. This is a crucial research design concern, especially in experiments where brain neurochemistry or mental health inferred from behaviour is studied.

General advantages of using animal models in psychical exercising studies

In this way, besides the general aspects we mentioned at the beginig of this report, the exercise variable can be precisely controlled, but more important the environment and nutritional intake are regulated and can be virtually identical for each subject, as of course, it is really hard to achieve that with human subjects. Therefore, animals used in laboratory studies are more homogenous than human

subjects and the studies can be randomized. Therefore the sensitivity and reproducibility of the experimental results is increased.

Another important advantage of using animal models is that after the experiment, animals can be sacrificed and muscles can be removed. Therefore, muscles can be physiological, biochemical, histochemical and molecular analysed for a better understanding of the mechanisms of hypertrophy. Human muscle biopsies can be operated, however there are often irrelevant because of the very small amount of tissue that is obtained. As a consequence these biopsies may be considered limiting regarding the sample size and may not show the adaptations that possibly occur throughout the entire muscle.

As a main disadvantage of using animal models in comparison to human ones, we mention the extent to which the results can be extrapolated to humans. There is a big concern about the potential threat to the external validity of the results obtained in these types of experiments.

Resistance Training in Conscious Animals

Several animal weightlifting models using conscious animals have been created for studying muscle hypertrophy. An important design in the literature is the model in which an apparatus for rats is built and used by several laboratories to mimic the traditional squat exercise performed in human resistance training models (Fluckey et al., 1995). In these studies rats are trained to stand upright and extend their hind limbs, hence lifting a weight added on a belt, vest, or shoulder harness. To obtain a progressive overload similar to the one used in an optimal human resistance training protocol, the intensity during the movement is increased throughout the training period by progressive increasing the weight the rat is lifting.

One of first studies to use this model was by Tamaki et al. The authors designed the first training apparatus that can induce rats to perform human squats. The apparatus was constructed with reference to a power rack or a smith machine, the training machines used by humans to perform squats. All parts were placed on a nylon coated board. A wooded arm was fastened at one end in the axis of vertical gyration. An aluminum holder for the rats was attached to the other end of the arm. The angle of the aluminum holder with respect to the arm was 65

degrees. The magnitude of the angle was determined by the authors during the preliminary experiments. Rats wearing a canvas jacket were able to regulate the twisting and flexion of their torsos and were fixed by the holder in a standing position on their hind limb. An electrical stimulation was given to the tail of the rat through a surface electrode. As a result, the rats extended their legs repeatedly, which lifted the weight on the arm of the training apparatus. The authors set a safety stopper to prevent hyperflexion of the knee and ankle joints during the squat training. A resting stopper was also set to relax the legs during periods of rest. The results showed that at the end of 12 weeks of training the number of fibbers in the plantaris muscles of the squat group was greater by 14% than that in the control and sprint groups (P less than 0.001), suggesting hyperplasia following hypertrophy. These results indicated that the muscle strength-training model presented by the authors may provide a new insight into the muscle hypertrophy associated with hyperplasia induced by heavy resistance training in rodents.

Garner et al., proposed the following rodent strength training model as a method for minimizing some of the before mentioned potential confounding effects of hunger or tail shock. In their study, the rats were motivated to perform 10 weeks of strength training using electrical stimulation of the brain as a reward. After recovery from a brain surgical procedure, animals received electrical stimulation in the brain when they lifted their arms to press a bar. Weight was attached to their backs, and to mimic the progressive overload used in human strength training, the amount of weight attached increased from 30 g to 190 g over a 10-week training period. The authors stated that this intracranial self-stimulation model was not only relatively easy to implement but also did not produce any apparent physical or mental trauma in the animals. However, it remains uncertain whether the effects of strength training alone could be separated from potentially confounding effects of direct tegmental brain stimulation.

Another model, described also by Tamaki is for mimicking the squat exercise in humans used a 35cm-high Plexiglas tube which was fastened to an l-cm-high plateau in a 35cm-long, 25cm-wide and 60-cm-high cage. At the bottom of the tube was a 6-cm-wide and 14-cm-high opening within which one-half of the lower diameter of the tube was filled by a vertical upward gradient made of a Plexiglas plate. This plate and the l-cm-high plateau ensured a fairly identical work position

for the rats, since the height of the pill tube (a tube that contains a vertical pile of food pills) was adjustable in such a way that the rat can only reach the pill by placing its paws as close as possible to the plate. Above and opposite the opening were two parallel grooves. The groove above the opening had an adjustable support system, whereas the opposite groove had an adjustable hinge.

Therefore a suspended lever could be adjusted to the desired height. Likewise the lever could be raised with its pivot in the hinge joint, when the upward movement stopped. This ensured that the rat only carried out the concentric part of the movement. It is important to be mentioned that this study was conducted on old male Wistar rats subject to muscle lose in normal conditions in this period of their lives. Regarding the force applied by the rats, the weights on the lever was increased by 85% ($P < 0.05$) from 67 g in week 1 to 70 g in week 36. Thus, the models used by the authors of this study has proven to produce a significant difference in the mass and the strength of a predominately slow-twitch (soleus) and a predominately fast-twitch (plantaris) muscle between a trained group of rats compared with a control group with the same age and eating rhythm.

In humans, progressive resistance exercise is recognized for its ability to induce skeletal muscle hypertrophy. In an attempt to develop an animal model which mimics human progressive resistance exercise Hornberger et al., in 2004 used Sprague-Dawley rats trained to climb a 1.1-m vertical (80 degree incline) ladder with weights secured to their tail. The rats were trained once every 3 days for 8 weeks. Each training session consisted of 4-9 climbs requiring 8-12 dynamic movements per climb. Based on performance, the weight carried during each session was progressively increased. Over the course of 8 weeks, the maximal amount of weight the rats could carry increased 287%.

In another study on conscious animals Cassilhas et al. used an adaptation of the, before mentioned, vertical ladder climbing model for progressive resistance training in rats, different by adding a unique feature to ensure the homogeneity of the study groups: a period of adaptation to the apparatus without any negative reinforcement followed by a subsequent pairing of animals based on their ability to learn. Despite the lack of difference in body weight between the two groups, the author found that the experimental group showed a morphological change in the muscles, which are responsible for the kinetic motion of the animals

on the apparatus. After the histological assay and the quantification of the increase in gastrocnemius and plantaris fibers, the authors observed that the experimental group suffered 60%, 35% and 38% of hypertrophy, respectively compared to the control group. This hypertrophy in the analyzed muscles is a clear indicator that the apparatus used by the authors and the training were able to mimic the major adaptive responses to resistance training.

Perhaps the most advantageous strength-training animal model would be a nonhuman primate model because the brains and weight-lifting behaviors of monkeys are considered to be more similar to humans than other animals, including cats and rats. We found one observational study that has been conducted with capuchin monkeys. The authors made the monkeys to lift stones weighing from 33% to 77% of their body weight and throw them to break open nuts for food (Liu et al., 2009). The weight of the stones could be manipulated experimentally to achieve progressive overload of the lifted weight, similar to programs used by humans to increase muscle strength. The authors considered that the biomechanics of the capuchins' modality of rock lifting resembles human power pulls and dead lifts (Liu et al., 2009). Another nonhuman primate model of strength training we found was a model on rhesus monkeys.

In addition, we found 4 researches that have used acute weight-lifting exercise performed by these monkeys to better understand central nervous system control over cardiovascular responses to weight lifting (Chefer et al., 1997, Engel et al., 1991, Talan et al., 1986). For example, in 1 experiment, 4 monkeys learned to use 1 arm to raise and lower a weight of 12 kg a distance of 4.5 cm at least once every 6 seconds for 1.5 to 2.5 minutes to avoid a tail shock (Chefer et al., 1997). Simultaneous electrical stimulation of various brain regions was performed during the exercise to better understand brain mechanisms that underlie cardiovascular responses to exercise.

As before mentioned, relatively many animal models of weight lifting have been developed, nevertheless few studies have used them to explore central nervous system adaptations to strength training (Buggy et al., 2005). Many of the mentioned available animal models of strength training could be useful when combined with animal models of psychological processes, for example, canine (Tapp et al., 2003) and rodent (Shannon et al., 2004) models of executive

function, or perhaps in the field of mental health problems, such as anxiety or depression to help in a better understanding of brain benefits of strength training (Ciobica et al., 2016). Other authors recommend that high-resistance physical activities, although not strength training per se, could be incorporated in other model animal systems, such as the zebra fish and the fruit fly, for a better understanding of genetic and molecular mechanisms underlying brain neural adaptations of high-resistance muscular activities (Cahill et al., 2002).

The main problem with these models is the challenge to train the animal to do the desired movement. In some cases, the animal receives a food reward after completing the lift. In the before mentioned model, the rats have been motivated to do squat-like exercises by applying a mild current to the animal's tail. In other cases, failure to lift the weight results in an electric shock. An example of one of these models, Ho et al. trained the rats to respond to a visual stimulus. The animals learned to perform the squat movement within a specified amount of time to avoid a mild electrical shock applied through the floor of the cage. Another model used food as a reward. Klitgaard et al. train the rats to perform the desired movement by requiring them to perform the squat to acquire their daily food.

In these studies, contractile properties were measured on isolated soleus and plantaris muscles from trained and untrained rats. Maximal isometric tetanic tension (the maximal amount of force produced during an isometric contraction) was 37–65% greater in the trained muscles demonstrating that a functional muscle hypertrophy had occurred (Ho et al., 1980).

As opposed to this model, a second type of resistance training that has been used to induce hypertrophy of forelimb muscles in mice (Goldspink et al., 1964), cats (Gonyea et al., 1977) hamsters and rats (Watt et al., 1982) is a weighted lever that is pulled down to obtain food. This model is mimicking the one arm lat pulldown exercise used in humans' resistance training protocols. In the cat model, Gonyea et al. trained the animals to use their right paws to acquire food. When comparing the trained paw (right one) with the untrained one (left), the results showed that after 41 weeks of unilateral training, forelimb muscles of the right paw hypertrophied 7–34% and fiber diameters were 11% greater in the flexor carpi radialis muscle of the right paw compared to the left paw.

As before mentioned rodents do not have the willingness to exercise

without a positive reward such as food or to avoid a negative one such mild electrical shock. However, some large animals such as ponies and horses have an inborn, intrinsic willingness to perform heavy labors. We found an interesting study on ponies by Heck and all. in which the authors designed an unconventional resistance-training model where mature ponies carried a heavy load over their saddle region while walking on a treadmill at a steady pace of 1.9 meters per second. The ponies were trained using a protocol where weights were increased every workout, 3 times per week. At the beginning of the training the ponies started with a 44.5-kg weight, the opening weight carried was then increased by 22.3-kg, so that by the end of the eight-week of the training protocol, the ponies ended up carrying between 146–178 kg. The results showed that after eight weeks of progressive resistance training resulted in increases forelimb girth by 12% with a corresponding 19% increase in muscle diameter.

The main problem with this model is, as before mentioned, the fact that simply many of these animals do not perform resistance exercises voluntarily. In most cases it is necessary to deprive animals of food or use an electrical shock to motivate them to perform the training protocol. These kind of reward-penalty systems may also cause stress, including hormonal fluctuations, which may confound results.

The second problem occurs when studies compare the muscle gains in experimental groups with control groups. Usually in these models the animal in the experimental group will typically do the minimal amount of exercise needed to satisfy their food requirements or to avoid shock, and in doing so they usually consume less food when compared to animals from the control, which eats freely. As a result, these animals grow slowly or lose weight relative to the animals in the non-exercising group.

However, one advantage of these resistance-training models in conscious animals is that they can be similar to human training protocols in terms of experimental design. The intensity, duration, and frequency of the exercise can mimic an optimal training program for humans.

Resistance Training in Unconscious Animals

Another important animal resistance training model used in many studies is the training program that consists in involuntary muscle contractions induced by electrical stimulation which results in muscle hypertrophy. For example, Wong and Booth designed a model in which subcutaneous electrodes are inserted along the plantar flexor muscles of an anesthetized rodent. When these electrodes are stimulated, one hindlimb of the rat contracts against a weighted pulley bar. The results of this study showed that after 16 weeks of training with 4 sets of 6 contractions per set performed every third day, the weight lifted by the trained muscles approximately doubled and gastrocnemius, plantaris, soleus, and tibialis anterior muscles showed a hypertrophy of 13–18%. When the same authors designed two subsequent studies, the importance of the protocol design in resistance studies was highlighted (Wong and Booth, 1990). In the two latter studies, two bouts of exercise were performed each week for ten weeks but during each bout the muscles were stimulated to contract 192 times when compared with 24 contractions in the first study. A different training protocol regarding total training volume presented different results. The 192-contraction protocol resulted in no hypertrophy of gastrocnemius muscles, but a 30% hypertrophy of tibialis anterior muscles was induced compared to the original study, where gastrocnemius, plantaris, soleus, and tibialis anterior muscles showed a hypertrophy of 13–18%.

To ensure that all motor units of all lower leg muscles were maximally activated, Baar and Esser designed a modified weighted pulley bar rat model where an electrode is surgically implanted on the sciatic nerve of one hindlimb, proximal to the muscles. This was considered an important improvement over the subcutaneous electrodes because the studied muscles were not physically damaged by the electrodes. The results reported by the authors showed a hypertrophy in tibialis anterior and extensor digitorum longus muscles of 14% following six weeks of 10 sets of 6 contractions per set, done 2 times per week.

After it was demonstrated that this model is producing muscle hypertrophy, researchers turned their attention the role of S6 protein kinase during the initiation of hypertrophy. S6 protein kinase is a protein that is involved in

regulating protein synthesis in muscle. Baar and Esser designed a suchlike animal model for studying underlying molecular mechanisms of muscle hypertrophy. The authors of this design used a stimulating electrode on the proximal sciatic nerve that produced contractions of all lower leg muscles.

We also found two other studies that have described methods for implanting electrodes on the more distal tibial and peroneal nerves of rodents hindlimbs (Walter et al., 1991, Warren et al., 1998). The authors described these models as advantageous because it is possible to stimulate specific muscle groups instead of the entire lower leg.

One of the main advantages of studying muscle contractions and muscle hypertrophy with this electrical stimulation model is the precise control that the investigator has in terms of the exercise protocol. Training parameters such as stimulation frequency and duration, the percent of maximal muscle strength generated per contraction, the number of contractions, and rest periods between contractions can be carefully controlled in this proposed model. Another advantage may be that this model is beyond animal's voluntary neural drive, therefore should be easier to predict the hypertrophic and functional responses.

The main advantage of stimulating at high frequencies may be the potential activation of all motor units within the studied muscles. If each contraction is maximal also means that each contraction is identical. However, these type of contractions may be considered non physiological because the size principle of motor recruitment is not followed. Nevertheless, these electrical stimulation model may be used for rehabilitative purposes where the order of motor unit recruitment may be less critical than the ability to stimulate the muscle fibers to respond to overload. On the other hand, non-physiological muscle recruitment by electrical stimulation may not be recommended to be used in the rehabilitation of an athlete who main focus should be to perform maximally on the field.

Furthermore, it is demonstrated that strength training is associated with a transition of fibers containing Type IIB myosin to Type IIA myosin (Starron et al., 1994). In contrast, high frequencies of stimulation it was shown to do the opposite. It was demonstrated in one study, in which transformation of fibers containing Type IIA to Type IIB myosin in rat soleus muscle has been reported

following electrical stimulation (Hamalainen et al., 1996). To conclude, depending on the specificity of the desired outcome, the electrical stimulation in unconscious animals may or may not be applicable to clinical progressive training therapies.

Chronic stretch animal models

It has been proven that casting a muscle in a lengthened, rather than in a shortened position results in a significant improvement in maintaining the muscle mass reducing muscle atrophy (Baker et al., 1998). The model of chronic stretch has made similar observations in animals and has taken advantage of the simplicity of this type of experimental design to study hypertrophic responses in muscle mass.

An interesting fact is that this model has mainly used birds and small mammals in their experiments. For example, hypertrophic responses have been studied from the stretch of chicken and quail wing muscles (Carson et al., 1998). It is worth noting that the results reported by these authors have been the same as those found in rabbit and rat hindlimb muscle stretch models. Although the functional and hypertrophic responses of the stretch model are well documented as before mentioned, the exact mechanism how stretching a muscle is inducing hypertrophy is not yet fully understood.

The design used in these models implies a weight varying from 5% to 10% of the animal's body weight to be attached to one wing. The hypertrophic response is not compared to a control group, but rather with the other wing which is used as an intraanimal control (Carson et al., 1998). The main advantage of his unilateral model is that any systemic alteration, hormonal change, due to the experimental manipulation occur both in the control and stretched muscles, so the exact effects of the mechanical overload can be distinguished. In contrast, a possible disadvantage when using young chickens may be their continuous growth throughout the experimental period. Therefore, the normal process of the muscle may be a confound variable when trying to determine the level of hypertrophy that the stretch induced in the muscle mass.

Therefore, there is an important advantage when using quails, considering that they are fully mature and fully grown by the age of six weeks. However, there is the disadvantage that due to the smaller size, less muscle tissue can be

obtained. Studies have shown that attaching a weight to the wing of a quail results in 100% hypertrophy of the supporting muscles of the wing after only two weeks. The increase in muscle mass continues, and after six weeks of constant stretch it has been reported to be at 150–200% (Antonio et al., 1994). The hypertrophy measured in the before mentioned studies have been obtained in both fast and slow twitching fibers and, as expected, an increase in muscle force production has also been reported (Always et al., 1993).

The chronic stretch model has not been used only in birds but also in rats and rabbits. In one of these models, the rabbit ankle is chronically immobilized in plantar flexion. The results reported have shown a 20% increase in the dorsiflexor muscles after only four days (Goldspink et al., 1995). It is interesting to mention one model which studied the combined effect of the chronic stretch model with electrical stimulation. The results reported shown that the combination of muscle stretch and muscle activity induced by electrical stimulation resulted in a 10% greater increase in muscle mass compared to the stretch model alone.

The main disadvantage of this model is that it cannot be extrapolated to humans. Most studies have used a stretch of 24 hours per day, to induce muscle hypertrophy. This stimulus is clearly not the same as resistance training in humans where the hypertrophy stimulus occurs for only a few minutes each day. For this reason, the hypertrophic response to an intermittent stretch has been studied. This model has also proven to be a potent hypertrophic stimulus in the avian model. In the two studies we found stretch applied to one wing for 24 hours followed by 48–72 hours of rest, for 2 weeks resulted in almost 300% hypertrophy (Antonio et al., 1993).

Therefore, one may conclude that the minimum duration of muscle stretch required to induce a significant hypertrophic change in avian skeletal muscle is likely to be much shorter. Consequently, Bates et al. studied the relationship between the exact duration of the stimulus per day and the extent of hypertrophy this stretch produces. The results reported that a stretch lasting only 30 min per day resulted in nearly 50% when compared to the increase that occurred with eight hours of stretch per day (Bates et al., 1993). This model could be extrapolated to human training protocols, where similar short-duration stretch may be feasible to be combined with resistance training if stretch is capable to amplify

the normal training-induced hypertrophy.

The main advantage of this hypertrophy inducing stretch model is that it produces extremely large and rapid increases in the muscle mass. Furthermore it may be considered superior to other models for the reason that there is no surgical intervention, therefore the collected data is not confounded by surgical trauma or the local edema (Love et al., 1998).

Conclusions

To conclude, even if the adaptations to resistance training in muscles in human models experiments are made in the clinic, it is considered difficult to evaluate hypertrophic responses and the underlying mechanisms behind them. One of the main reasons behind that is the lengthy interval of time the adaptations and results from training require before they become measurable and also there is a large variability in response to resistance exercises among humans. Therefore, an important advantage that various animal models have is that they could induce rapid and extensive muscle hypertrophy and more-so, some models allow a more precise control of the exercise parameters. By studying and improving these animal models of muscle hypertrophy, we could be able to evaluate and use the relevant data from these models to design new programs for optimising the specificity of the progressive resistance training in humans.

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