

**“Hypertrophy and Hyperplasia: Adaptations of Muscular Tissue  
to Various Resistance Training Protocols”**

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**I. Introduction**

A. Objectives:

This review of related literature aims to bring to light the most current scientific knowledge and trends in study concerning hypertrophy and hyperplasia in response to resistance training protocols.

The researcher will present the histological mechanisms of all the said adaptations. Then the studies relevant to the application and the implications thereof will be made known. Last, the researcher will attempt to link these histological adaptations with the concepts of sports physiology and sports science through the use of current theories, as well as cellular, biochemical, and bioenergetic factors.

B. Significance:

To date, the link between sports science and sports physiology remains unclear. While bioresearch has demonstrated the occurrence of muscular adaptations and physiology has explained the mechanics of such adaptations, it is the realm of sports science that has examined and sought the optimum means of achieving these adaptations for the

sake of improving sports performance. However while sports science has found the methodology for inducing adaptation, what exactly occurs and why it occurs has been left to histology and bioresearch respectively – unexamined, and unconsidered. By applying the sub-cellular and cellular understanding inherent to histology with the field research currently available and the leading sports science knowledge, this review aims to bring depth into the understanding and application of all avenues where muscular adaptation is relevant, such as rehabilitation, sports medicine, and physical culture.

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## **II. Discussion**

### Hypertrophy

Hypertrophy is defined as the increase of the individual cross-section of a muscle fiber. It accounts for most gains in total muscle cross-section, as the presence of other factors such as hyperplasia are still heavily disputed<sup>2</sup>. The cross-sectional size of a muscle fiber consists of a contractile region with contractile protein filaments (myofibrils), and a non-contractile region called the sarcoplasm (muscle cell cytoplasm)<sup>9</sup> – the semi-fluid interfibrillar substance that contains various enzymes, proteins, and organelles that do not contribute directly to maximal voluntary contractile tension.<sup>20</sup> The increase in cross-sectional size can be attributed to an increase of the size of either or both regions, with varying degrees of predominance.

Hypertrophy resulting principally from an increase of the cross-sectional area of the contractile region is called myofibrillar hypertrophy. The muscle fiber shows an increase in number and total volume of myofibrils. The myosin filaments tend to display the greatest amount

of increase.<sup>2,8</sup> Such hypertrophy results in a larger muscle fiber with a greater density of contractile fibers.<sup>20</sup> Because of the increase of actin-myosin cross-bridges, a muscle fiber that displays such hypertrophy exhibits a greater tensile strength and contractile force.

The model for myofibril splitting is as follows. The actin-myosin lattice is arranged in a hexagonal lattice form and the actin filaments are slightly displaced as they run from the Z-disc to the A-band. When the myofibril is placed under sufficient tension shearing forces pull on the Z-lines (composed of  $\alpha$ -actinin). Given enough tension, the  $\alpha$ -actinin filaments snap and the myofibril splits longitudinally into two or more daughter fibrils. With the myofibrillar mass subdivided, the sarcoplasmic reticulum and transverse tubular systems invade the gap between the newly formed daughter myofibrils allowing the daughter myofibrils to increase in volume. This longitudinal splitting has been observed in its various stages by electron microscopy of the muscles of weight trained humans, but the exact training protocols for eliciting the response are undefined.<sup>10</sup> Through this splitting, the number of myofibrils in the muscle cell increase and after the recovery phase, protein anabolism increases the overall volume of the myofibrillar mass.

In theory, training protocols that aim to induce predominantly (though not necessarily exclusively) myofibrillar hypertrophy must subject muscles to tensions greater than that commonly encountered. The loading protocols should progressively increase to continuously stress the tensile strength of the myofibrils. Therefore it is theoretically expected that such hypertrophy is most prevalent in strength athletes such as elite powerlifters and weightlifters whose training protocols may involve lifts that are within 90 to 100% of their maximum voluntary concentric contractile force, and whose loading progressively increases alongside increases in maximum capacity for strength expression.<sup>20</sup> However, such has yet to be scientifically verified.

The theory appears to be valid due to the following rationale. With the increase of total myofibrillar cross-sectional area, the tension on the muscle fiber should be distributed over a greater area, reducing the effective tensile stress (relative to an unhypertrophied muscle fiber) on the Z-disk filaments. Therefore a muscle fiber that has undergone myofibrillar hypertrophy should be less prone to more myofibril splitting, hence requiring the progressively heavier loads that sports theory posits.

The other type of hypertrophy that is characterized primarily by an increase in the volume of the interfibrillar substance is called sarcoplasmic hypertrophy. The sarcoplasmic increase is predominantly composed of interfibrillar fluid, mitochondria, glycogen, adenosine triphosphate (ATP), and phosphocreatine (PC) stores.<sup>3,8</sup> Muscle fibers also show large increases in capillarization.<sup>8</sup> Such hypertrophy results in a larger muscle fiber with a lesser density of contractile fibers.<sup>20</sup> Such a muscle fiber exhibits no increase in maximal contractile tension but instead, a greater increase in fatigue tolerance.

Sports theory posits that sarcoplasmic hypertrophy is the predominant adaptation induced by repetitive bouts of exhaustive exercise occurring through the ATP/CP and glycolytic pathways.<sup>20</sup> Unlike myofibrillar hypertrophy that is supposedly tension induced, sarcoplasmic hypertrophy is supposedly fatigue induced. To validate this theory it is important to note the histochemical bases and manifestations of fatigue.

Fatigue leading to failure of contraction can either be related with the central nervous system (CNS), the neuromuscular junction, or the muscle itself.<sup>8</sup> The last – local muscular fatigue – is what is posed to elicit a predominantly sarcoplasmic hypertrophic response. When a muscle is placed under tension so that it is completely exhausted (unable to contract voluntarily) after a period of 100 to 110 seconds,<sup>9</sup> many things happen. After the first 9 or 10 seconds, the ATP and

PC stores become depleted. After the entire 100-110 second bout the glycogen stores become depleted as well. Due to the anaerobic glycolysis, lactic acid becomes abundant within the muscle.  $H^+$  interferes with the excitation-coupling process by inhibiting  $Ca^{2+}$  release from the sarcoplasmic reticulum and inhibiting the binding of  $Ca^{2+}$  to troponin, thereby reducing the amount of interacting actin-myosin cross-bridges.<sup>6</sup>  $H^+$  also inhibits the activity of phosphofructokinase, a key glycolytic enzyme.<sup>8</sup> Glycolysis quickly becomes unable to produce sufficient energy. Therefore due to aerobic demands in an effort to relieve the anaerobic pathway, oxygen and blood supply becomes inadequate.

The chronic result of this depletion of glycogen stores, ATP-PC stores, blood supply, and  $Ca^{2+}$  activity is an observed supercompensation<sup>2</sup> in favor of greater amounts of the aforementioned. During the recovery phase when stores are restocked and proteins are re-synthesized there is a shift toward greater anabolism and reduced catabolism of sarcoplasmic soluble proteins and increase in storage of the various cellular fuels.<sup>10,19</sup>

In theory, such hypertrophy should be most prevalent in bodybuilders and middle distance sprinters, whose training protocols consist of exhaustive bouts lasting near the duration aforementioned, and who express the fatigue tolerance expected of the adapted muscles.<sup>20</sup> But again, such has strictly theoretical basis and the actual increase in sarcoplasmic area has yet to be empirically verified.

A comparative sampling of the mitochondrial to sarcoplasmic area ratios of the muscles of athletes engaged in various athletic disciplines has yet to be done. Only such a study could validate whether myofibrillar or sarcoplasmic hypertrophy can be preferentially induced through different resistance training protocols.

As has been discussed, resistance training induces both myofibrillar and sarcoplasmic hypertrophy that manifests during a period of post-workout supercompensatory regeneration. The energetic theory of muscle hypertrophy attempts to theoretically summate the milieu in which sarcoplasmic and myofibrillar hypertrophy occur:

“...the crucial factor for increasing protein catabolism is a shortage in the muscle cell of energy available for protein synthesis during heavy strength exercise. The synthesis of muscle proteins requires a substantial amount of energy... Normally the amount of energy available in a muscle cell satisfies these two requirements [anabolism and muscular work]. During heavy resistive exercise, however, almost all available energy is conveyed to the contractile muscle elements and spent on muscular work.”<sup>20</sup>

In response to this lack of energy for synthesis of muscular proteins, the body increases the amount of resources available to the muscles, in anticipation for continued stress. But the recovery period dictated by resistance training protocols enables the body to shift to an even greater anabolic synthesis of muscular proteins, resulting in supercompensation, both on the level of energy supplies, and of anabolism of muscle proteins. This results in an increase of the volume of various components of the muscle cell.<sup>20</sup>

However, why exactly does the deficit of various components cause a shift toward greater anabolic activity? How does the body signal the muscles to increase anabolic activity post-exercise? A possible mechanism for this anabolic shift is the hormonal response to exercise. Somatotropin (GH), somatomedins (Insulin-like Growth Factor-1 in particular), testosterone, and insulin are acutely and chronically increased by bouts of exercise.<sup>5,12,15</sup> These hormones all have anabolic effects, as will be outlined below. But it is uncertain if the increase of these hormones in response to exercise is enough to account for the muscular and systemic adaptations observed post-training.

Somatotropin, known commonly as growth hormone (GH), is a polypeptide hormone secreted by the anterior pituitary gland<sup>9</sup>. Serum GH levels have been observed to increase in response to bouts of resistance training, however the training protocols of the test subjects were not standardized.<sup>4,12</sup> GH stimulates the liver to produce IGF-1 (insulin-like growth factor), the effects of which shall be examined later. Systemically, GH induces sparing of amino acids, reducing catabolic breakdown of muscle proteins. It also increases retention of nitrogen, a component of amino acids, which leads to improved levels of protein synthesis.<sup>15</sup>

Within the muscle cell, all of GH's effects are mediated by somatomedins, namely IGF-1, a 70 amino acid polypeptide secreted by the liver but produced in muscle cells as well. IGF-1 increases amino acid transport across the sarcolemma, providing more building blocks for protein synthesis<sup>15</sup>. It directly increases levels of protein synthesis,<sup>7,18</sup> leading to a greater level of muscular protein than pre-training. IGF-1 has the most potent effect on muscle growth, and over-expression of IGF-1 has potent muscle-enlarging effects similar to defective myostatin genes. "Overly muscular" untrained mice found to have persistent IGF-1 over-expression demonstrated the potent effects of this hormone.<sup>7</sup>

Testosterone does not have as potent an effect on muscle as IGF-1, and mostly behaves in a stimulatory manner for other more potent anabolic hormones. Increasing in response to bouts of exercise<sup>4,12</sup> testosterone further stimulates the pituitary gland to produce more GH. It also stimulates the hepatic and extra-hepatic production of IGF.<sup>15</sup>

Insulin production by the pancreas is stimulated by the glycogen deficit caused by exercise. Insulin inhibits protein degradation by offsetting the catabolic effect of cortisol. It promotes nitrogen retention and nitrogen sparing leading to a more anabolic milieu in the muscle cells.<sup>15</sup> It

also promotes glycogen uptake into the muscle cells for storage by activating glucose permease, transport proteins located on the sarcolemma that control glucose uptake.<sup>9</sup>

It is possible that it is primarily this hormonal response that triggers the anabolic shift post-exercise. Exercise causes increases in GH, IGF-1, testosterone, and insulin. Hypothetically this increase in serum hormone levels may elicit the increased anabolism and nutrient uptake in muscle fibers shown in vitro by these hormones. If it is as such, it may be the principal cause for supercompensation during the recovery phase, characterized by an overall increase in protein synthesis of various sarcoplasmic and myofibrillar components resulting in hypertrophy.

Studies have demonstrated the increases of the aforementioned hormones in response to exercise. Studies have also demonstrated how these hormones affect muscle fibers, to the point that it is textbook matter. However no comparative study exists comparing the histological adaptations in response to 1) standardized exercise protocols, versus 2) hormonal supplementation to mimic the hormonal levels induced by variable 1 (exercise). Through this comparative study one of the following may be established:

- 1) The hormonal increase in exercise is solely responsible for supercompensation in the muscle fiber.
- 2) The hormonal increase is only partly accountable for muscle tissue adaptations
- 3) The hormonal increase is insufficient and therefore unrelated to the adaptation.

### Hyperplasia

Hyperplasia is the increase in the number of muscle fibers as opposed to hypertrophy, which is the increase of the size of present muscle fibers without the creation of new muscle

fibers. Hyperplasia appears to be caused by high tension inherent to intense stretching and heavy exercise<sup>13</sup>, however the method by which they induce hyperplasia is unclear.

There are two mechanisms by which hyperplasia may occur. First is the proliferation and development of satellite cells into mature muscle fibers. Second is the longitudinal splitting of existing muscle fibers into microbuds that mature into muscle fibers.<sup>14,16,17</sup>

Hyperplasia may occur by the maturation of muscle satellite cells. A satellite cell is a derivative of the myoblast population that did not fuse to form myotubes and eventually muscle fibers, during embryonic development.<sup>16</sup> When muscle homeostasis is altered as in the event of injury, the satellite cells undergo rapid mitosis, migrate along the length of the fiber to the site of injury, then fuse to form a multinucleated myotube. This myotube eventually matures into a muscle fiber, as in embryonic development. In this way, a new muscle fiber is formed to replace the necrotic muscle cell. The same mechanism acts in response to exercise induced damage, possibly without simply replacing the cell but instead supplanting it and increasing the amount of mature fibers in the fascicle.<sup>16</sup>

There is another method by which hyperplasia can occur. A muscle fiber, when subjected to high tensile stress may undergo longitudinal splitting. A Yugoslavian study documented the following:

“Biopsies of skeletal muscles obtained from volunteers, young (19-20 years of age) skilled sportsmen have been studied electron microscopically. Sarcolemmic invaginations, deeply intruding into sarcoplasm of the muscle fibres, have been found; they result in muscle microbud formations. Small, round, spindle-like or having irregular form, muscle fibres have been found with longitudinally situated myofibrils in them, as well as narrow long young fibres, their contractile apparatus being incompletely formed, with great number of mitochondria, glycogen granules and polysomes. A suggestion is made that under a systematic physical training the human mature skeletal muscle undergoes hyperplasia of the muscle fibres. New muscle fibres might be formed from myosatellites, from segregating myosatellites and microbuds and also, possibly, by splitting the fibres already existing.”<sup>14</sup>

It therefore appears that muscle splitting may occur in the following manner: first, the sarcolemma invaginates deeply into the sarcoplasm. This invagination splits the muscle unevenly, forming a muscle microbud with immature contractile mechanisms and longitudinally situated myofibrils.<sup>14</sup> With a sufficiently anabolic environment, the immature muscle microbud can mature into a mature muscle fiber, thereby increasing the number of muscle fibers in the fascicle.

Most current sports science, physiology, and histology textbooks dispute the occurrence of any form of hyperplasia in humans.<sup>2</sup> Fox's *Physiological Basis of Exercise and Sport* states that muscle fiber counts are genetically determined and constant.<sup>8</sup> Furthermore, Tudor Bompa resounds the common belief that the even if hyperplasia did occur, contributions of hyperplasia to increases in overall muscle size are likely to be insignificant.<sup>1,2</sup> However with the presence of the following animal studies, Bompa and the others may be wrong on this account.

One of the earliest accounts of skeletal muscle hyperplasia in animals was done as far back as 1977. "Cats were trained to lift weights with their right forelimb to receive a food reward. After 19-46 weeks of training, the flexor carpi radialis muscle (FCR) was removed and prepared for histochemical examination. The total number of muscle fibers of the right exercised FCR increased significantly (19.3%) when compared with that of the unexercised left FCR ( $p$  less than 0.05). This increase was found to be due to muscle fiber splitting."<sup>11</sup> An increase of 19.3% is definitely not insignificant. Other studies concur. Antonio & Gonyea state the following:

"...recent evidence from several laboratories suggests strongly that fiber hyperplasia contributes to muscle mass increases in adult animals and possibly human athletes. ... [stretch, exercise, and compensatory hypertrophy protocols] provided direct as well as indirect evidence supporting the occurrence of muscle fiber hyperplasia. Direct counts of muscle fibers using nitric acid digestion techniques have shown that both exercise and stretch overload result in significant increases (range = 9-52%) in fiber number. Indirect fiber counts using histological cross-sections have suggested fiber hyperplasia (range = 10-

82%) in all three models [stretch, exercise, and compensatory hypertrophy]. Additionally, the expression of embryonic myosin isoforms have provided indirect evidence for new fiber formation in stretch overloaded muscle.”<sup>11</sup>

Even the minimum 9% increase in muscle cell count is significantly beyond the old view that fiber count is genetically determined and final. However the relevance of these animal studies to humans is still unclear, because in Kelley’s review of related literature it is presented that species vary widely in predisposition toward hyperplasia. Aves displayed an average increase of 20.95% in total fiber count, but mammal studies only displayed an average increase of 7.97%.<sup>13</sup> Therefore it is possible that in agreement more established scientific belief, human skeletal muscle fiber is simply not as predisposed to hyperplasia as the muscle of other species.

But due to the success of Kondalenko’s electron microscopy of athletes,<sup>14</sup> it must be put into question on whether the failing to demonstrate hyperplasia in humans is a result of a lack of predisposition, or a result of inadequate training techniques. It is possible that the training intensities undergone in the setups of the negative studies did not approach that of international caliber athletes and hence was not enough to induce hyperplasia.

It will require much more studies, with greater cooperation between researchers and professional athletic coaches and trainees to verify if indeed hyperplasia occurs, and if so, to what extent. It will also be important to find a non-intrusive means of measuring fiber counts as full muscle biopsies are not plausible in humans – and most definitely impossible in high-caliber athletes.

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### **III. Summary**

The adaptations of muscle tissue in response to resistance training that result in increases in overall muscle size are hypertrophy and hyperplasia.

Hypertrophy is the increase of the size of each muscle fiber. It may be either myofibrillar or sarcoplasmic. Myofibrillar hypertrophy is caused by high levels of tension. Sarcoplasmic hypertrophy is caused by high levels of glycolytic fatigue. Exercise and the damage and depletion it causes triggers an increase of various hormones such as somatotropin, IGF-1, testosterone, and insulin that increase anabolic protein synthesis and nutrient uptake in muscle cells. This hormonal response may be the primary cause for the supercompensation during the recovery phase that results in either form of hypertrophy.

Hyperplasia is the increase in the number of muscle cells caused by the maturation of satellite cells into muscle fibers or the longitudinal splitting of existing muscle fibers. It is caused by very high levels of tension caused by contraction and stretching. The mechanisms through its induction are unknown. The occurrence of hyperplasia is proven in animals, however no comprehensive studies have been done on humans. Only one study has observed signs of hyperplasia in human athletes. The occurrence and significance of hyperplasia in humans remains disputed.

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