# *Inducing hypertrophic effects of type I skeletal muscle fibers: A hypothetical role of time under load in resistance training aimed at muscular hypertrophy*

# Inducing hypertrophic effects of type I skeletal muscle fibers: A hypothetical role of time under load in resistance training aimed at muscular hypertrophy

Jozo Grgic[1] Jan Homolak[2] Pavle Mikulic[3] Javier Botella[1] Brad J. Schoenfeld[4]

[1]Institute of Sport, Exercise and Active Living (ISEAL), Victoria University, Melbourne, Australia

[2]School of Medicine, University of Zagreb, Zagreb, Croatia

[3]Faculty of Kinesiology, University of Zagreb, Zagreb, Croatia

[4]Department of Health Sciences, CUNY Lehman College, Bronx, NY, USA

**Word count:** 2054 words

**Corresponding Author**

**Jozo Grgic**

Institute of Sport, Exercise and Active Living (ISEAL), Victoria University, Melbourne, Australia

**E-Mail:** jozo.grgic@live.vu.edu.au

## Abstract

An emerging body of evidence is starting to suggest that the hypertrophy of skeletal muscle fibers might be load specific. In other words, it may be that resistance training with high loads (i.e., ≥60% of 1 repetition maximum [RM]) emphasizes a greater growth of type II muscle fibers, while resistance training with low loads (i.e., <60% of 1RM) might primarily augment hypertrophy of type I muscle fibers. Type I and type II muscle fibers possess certain distinct characteristics, with type II muscle fibers having faster calcium kinetics, faster shortening velocities, and ability to generate more power than type I muscle fibers. Alternatively, compared to type II fibers, type I muscle fibers have a higher oxidative capacity and a higher fatigue threshold. Due to the lower fatigability of type I muscle fibers, it may be hypothesized that a greater time under load is necessary to stimulate an accentuated growth of these fibers. An increase in time under load can be achieved when training with lower loads (e.g., 30% of 1RM) and to momentary muscular failure. The present paper discusses the hypothesis that a greater hypertrophy of type I muscle fibers may be induced with low load resistance training.

## Introduction

Resistance training is a popular form of physical exercise in people across all age groups. It is commonly performed with a goal of achieving skeletal muscle hypertrophy. Current guidelines state that, within a structured resistance training session, loads that correspond to 70-85% of 1 repetition maximum (RM) are necessary for achieving skeletal muscle hypertrophy [1]. However, recent evidence suggests that, provided a set is performed to momentary muscular failure, skeletal muscle hypertrophy can be achieved across a broad range of loading zones [2].

The findings mentioned above have been observed in studies that used different methods for assessing muscular hypertrophy, including ultrasound, magnetic resonance imaging, and computed tomography [2]. In contrast to these methods, muscular hypertrophy can also be assessed using muscle biopsy sampling. This approach allows for differentiation of various types of muscle fibers, most commonly identified as type I and type II muscle fibers (in human skeletal muscle further divided to type IIa and IIx muscle fibers); adding more information about the specificity of hypertrophy across the muscle fibers. It is often purported that type II muscle fibers have a greater hypertrophic potential with resistance training [3]. However, an emerging body of evidence suggests that the hypertrophy of muscle fibers may be load specific. In other words, it might be that training with higher loads (i.e., ≥60% of 1RM) results in greater growth of type II muscle fibers, while training with lower loads (i.e., <60% of 1RM) might primarily augment hypertrophy in type I muscle fibers [4, 5]. The present paper discusses the hypothesis that greater hypertrophy of type I muscle fibers may be induced with low load resistance training.

## Physiological differences between type I and type II muscle fibers

It is important to note that type I and type II muscle fibers possess certain distinct features, with type II muscle fibers having faster calcium kinetics, faster shortening velocities, and ability to generate more power than type I muscle fibers [6]. Alternatively, compared to type II fibers, type I muscle fibers have a higher oxidative capacity and a higher fatigue threshold. Because methods for studying muscular hypertrophy primarily focused on heavier loading schemes, the data important for understanding the physiology of hypertrophy in type I muscle fibers are scarce and difficult to interpret.

Changes in skeletal muscle growth are the result of changes in the balance between protein synthesis and protein degradation. Muscle fibers with high oxidative metabolism (i.e., type I muscle fibers) also have a substantial capacity for protein synthesis; one of the factors important for muscular hypertrophy [7]. In human skeletal muscle, protein synthesis rates and total ribonucleic acid (RNA) content correlate with the abundance of type I myosin heavy chain (MHC) mRNA and are inversely correlated with the expression of MHC II [7, 8]. Muscle fibers with higher oxidative capacity also show a high rate of amino acid uptake [9]. Moreover, oxidative fibers contain more myonuclei per volume cytoplasm, a greater percentage of myonuclei that belong to satellite cells and a higher rate of addition of new myonuclei through nuclear accretion. These are all important factors in the process of muscular hypertrophy [7, 10].

The above discussed anabolic-related factors point to type I muscle fibers as having significant hypertrophic potential. Despite this modestly increased protein synthesis capacity, protein degradation mechanisms, such as autophagy, are known to be increased in the oxidative fibers [7]. This is supported by findings that cathepsins, important factors in lysosomal proteolysis that are usually abundant in tissues with high protein turnover, are present in higher concentrations in muscle fibers with a high oxidative capacity [11, 12]. Due to a greater oxidative capacity of type I muscle fibers, higher accumulation of reactive oxygen

species and metabolites are expected to occur, lowering the biological potential for hypertrophy due to activation of the pathways responsible for the protein degradation, acting as a quality control system [13, 14]. The high rate of protein turnover present in type I muscle fibers reflects the high adaptive potential of the tissue. In the context of hypertrophy, future research should focus on stimuli that upregulate the protein synthesis machinery without largely increasing protein degradation, which in turn would facilitate a net increase in protein aggregation.

The body of knowledge on molecular pathways mediating skeletal muscle hypertrophy is considerable, and it is now known that the mechanistic target of rapamycin (mTOR) is the master kinase controlling the protein synthesis pathway [15]. Furthermore, protein degradation is known to be promoted by the energy sensor AMP-activated protein kinase (AMPK) [16]. Multiple proteins have been involved in the interaction between these pathways; however, the current knowledge is still insufficient to provide a clear answer to the intriguing question of fiber-type differences in the regulation of hypertrophic adaptability. Nonetheless, it can be hypothesized that a different stimulus might be needed to elicit a maximal hypertrophic response in different types of muscle fibers due to the nature of their machinery. Recent evidence seems to support this hypothesis, pointing towards preferential hypertrophy of type I muscle fibers when resistance training is carried out with low loads. The molecular pathways underlying this adaptation are still poorly understood, although they already captured the attention of some scientists [17]. If this hypothesis is confirmed, further investigation of molecular pathways regulating hypertrophy in type I muscle fibers following low load resistance training will provide a valuable piece of the physiological puzzle.

**Time under load**

There is evidence that aerobic exercise, specifically cycling, leads to type I, but not type II muscle fiber hypertrophy, and that this effect is independent of age [18, 19]. These findings are specific to aerobic exercise; however, they do suggest that longer-duration activities with a prolonged loading time on the activated muscle, may predominantly result in hypertrophy of type I muscle fibers (i.e., muscle fibers with a lower fatigability). Therefore, in resistance training, it can be hypothesized that a greater time under load (TUL) is necessary to stimulate an accentuated growth of these fibers [20, 21]. In this regard, training with low loads will necessarily result in a greater TUL compared to high load training given that repetition duration is controlled between conditions. For example, a low load set of 20 RM performed with a 3-second repetition duration would result in a TUL of 60 seconds; a higher load set of 8 RM performed with the same repetition duration would last just 24 seconds. Conceivably, the longer TUL in the lower load condition would provide a superior growth stimulus to type I fibers by taxing their endurance capacity. Research by Lamas and colleagues [22] provides intriguing findings in this context. They compared two groups, of which one performed high load training (4-10 RM), while the other group performed a power-type training routine consisting of loads in the 30-60% of 1RM range, performed for 6-8 repetitions. Both groups were instructed to perform each repetition at maximum speed through both the concentric and eccentric phases. Following the 8-week training period, the high load group experienced an increase in the cross-sectional area of type I, type IIa and type IIx muscle fibers by 15%, 18%, and 41%, respectively. In contrast, the low load, power training group, increased the cross-sectional area of type IIa and type IIx muscle fibers by 15% and 19%, respectively. However, type I muscle fibers in this group experienced atrophy following the training intervention and decreased in size by 5%. By observing the training protocol, it is evident that TUL in the power group was around 10-15 seconds per set, which may be inadequate to induce sufficient muscular fatigue, and thus hypertrophy of type I

muscle fibers. This would, at least in part, explain the reasons for the lack of growth of type I muscle fibers in the power-type training group.

Vinogradova and colleagues [4] also compared the effects of high and low load resistance training; however, in contrast to Lamas et al. [22], they used a protocol in which the low load group performed sets with loads corresponding to 50% of 1RM without relaxation (i.e., with continuous maintenance of muscle tension), whereby the total duration of sets was 50–60 seconds. The high load group used a load corresponding to 80-85% of 1RM. The researchers reported that a greater growth of type I muscle fibers occurred in the low load group while a greater growth of type II muscle fibers occurred in the high load group. Using a similar protocol, Netreba and colleagues [5] observed the same results in 14 untrained men, which further supports the notion that TUL may be an important variable for inducing a greater growth of type I muscle fibers.

Despite the suggested benefits of using low loads regarding hypertrophy of type I muscle fibers, it is possible that, when the load is too low, it may be difficult to maximize peripheral fatigue with resistance training [23-26]. This effect was shown in a study by Mackey and colleagues [27]. The researchers employed a protocol in which the low load group trained with 15% of 1RM for ten sets of 36 repetitions. Albeit TUL was high, the protocol was insufficient to induce significant hypertrophic effects in type I and type II muscle fibers. If greater TUL is the primary factor in inducing greater hypertrophic effects in type I muscle fibers when using lower loads, the group mentioned above should have experienced robust growth of these fibers following the protocol. One confounding variable to these results is the fact that sets in the training routine were stopped well short of volitional failure. It seems that training to momentary muscular failure is needed for the activation of the entire motor unit pool and thus, for maximizing growth across fiber types [28]. Therefore, it may be hypothesized that an interplay between external load, training to momentary muscular

failure, and greater TUL might determine the extent of the hypertrophic effects of type I muscle fibers. Surprisingly, in the same study [27], a high load protocol that consisted of 10 sets of 8 repetitions at 70% of 1RM was also insufficient to result in any evident hypertrophy of either fiber type. The possible reasons for the absence of hypertrophic effects in both groups remain unclear, especially since the study involved resistance training-naïve individuals. It is well documented that such individuals can experience robust gains in muscle fiber size following similar loading programs [29], which might call into question the robustness of the findings reported by Mackey and colleagues [27].

Metabolic stress has been suggested to play an important role in muscular hypertrophy [30]. Of relevance are also the findings that show that high-intensity training (i.e., 30 seconds maximal isokinetic contractions) induces higher metabolic stress in type II versus type I muscle fibers [31]. Therefore, such training schemes may stimulate anabolic signaling to a greater extent in type II muscle fibers, and thus, result in greater type II muscle fiber hypertrophy. In contrast, according to the size principle, low load resistance exercise performed to momentary muscular failure firstly recruits the lower-threshold motor units, and as these motor units become fatigued, the higher-threshold motor units are sequentially recruited; therefore, at the end of the training set, the metabolic stress across the muscle fiber types may be comparable. This also can be the case in low load exercise with partial blood flow restriction, which has been shown to exert an acute preferential stress of type I fibers [32]. Studies that investigated the effect of isometric contraction (in essence, an exercise with partial blood flow restriction) found a greater concentration of lactate in type I muscle fibers compared to type II muscle fibers [33, 34]. Therefore, it can be hypothesized that when low load resistance training is performed with a high TUL (and to momentary muscular failure) elevated anabolic signaling in type I muscle fibers might be stimulated, and thus, result in the greater growth of these fibers.

## Conclusions

In conclusion, a greater TUL might play a role in inducing greater hypertrophic effects in type I muscle fibers. Despite emerging research supporting this hypothesis, evidence to date remains equivocal, and thus future studies should seek to provide clarity on the topic. If TUL is indeed an important factor in inducing greater hypertrophic effects in type I muscle fibers, individuals interested in maximizing muscular growth across the muscle fibers should consider including both high load and low load resistance training schemes in their training routines.

**Financial support and conflict of interest disclosure:** None

198 **References**


199 [1] American College of Sports Medicine. American College of Sports Medicine position
200 stand. Progression models in resistance training for healthy adults. Med Sci Sports
201 Exerc 2009;41:687–708.

202 [2] Schoenfeld BJ, Grgic J, Ogborn D, Krieger JW. Strength and hypertrophy adaptations
203 between low- versus high-load resistance training: A systematic review and meta-
204 analysis. J Strength Cond Res 2017;31:3508–23.

205 [3] Fry AC. The role of resistance exercise intensity on muscle fibre adaptations. Sports Med
206 2004;34:663–79.

207 [4] Vinogradova OL, Popov DV, Netreba AI, et al. Optimization of training: development of
208 a new partial load mode of strength training. Fiziol Cheloveka 2013;39:71–85.

209 [5] Netreba A, Popov D, Bravyy Y, et al. Responses of knee extensor muscles to leg press
210 training of various types in human. Ross Fiziol Zh Im I M Sechenova 2013;99:406–
211 16.

212 [6] Schiaffino S, Reggiani C. Fiber types in mammalian skeletal muscles. Physiol Rev
213 2011;91:1447–531.

214 [7] van Wessel T, de Haan A, van der Laarse WJ, et al. The muscle fiber type-fiber size
215 paradox: hypertrophy or oxidative metabolism? Eur J Appl Physiol 2010;110:665–94.

216 [8] Toth MJ, Tchernof A. Effect of age on skeletal muscle myofibrillar mRNA abundance:
217 Relationship to myosin heavy chain protein synthesis rate. Exp Gerontol
218 2006;41:1195–200.

219 [9] Hood DA, Terjung RL. Leucine metabolism in perfused rat skeletal muscle during
220 contractions. Am J Physiol 1987;253:E636–47.

221 [10] Tseng BS, Kasper CE, Edgerton, VR. Cytoplasm-to-myonucleus ratios and succinate
222 dehydrogenase activities in adult rat slow and fast muscle fibers. Cell Tissue Res
223 1994;275:39–49.

224 [11] Parreño M, Pol A, Cadefau J, et al. Changes of skeletal muscle proteases activities during
225 a chronic low-frequency stimulation period. Pflügers Archiv 2001;442:745–51.

226 [12] Soori M, Lu G, Mason RW. Cathepsin inhibition prevents autophagic protein turnover
227 and downregulates insulin growth factor-1 receptor-mediated signaling in
228 neuroblastoma. J Pharmacol Exp Ther 2016;356:375–86.

229 [13] Steinbacher P, Eckl P. Impact of oxidative stress on exercising skeletal muscle.
230 Biomolecules 2015;5:356–77.

231 [14] Powers SK, Kavazis AN, McClung JM. Oxidative stress and disuse muscle atrophy. J
232 Appl Physiol 2007;102:2389–97.

233 [15] Wang X, Proud CG. The mTOR pathway in the control of protein synthesis. Physiology
234 2006;21:362–9.

235 [16] Sanchez AM, Candau RB, Csibi A, Pagano AF, Raibon A, Bernardi H. The role of AMP-
236 activated protein kinase in the coordination of skeletal muscle turnover and energy
237 homeostasis. Am J Physiol Cell Physiol 2012;303:C475–85.

238 [17] Popov DV, Lysenko EA, Bachinin AV, et al. Influence of resistance exercise intensity
239 and metabolic stress on anabolic signaling and expression of myogenic genes in
240 skeletal muscle. Muscle Nerve 2015;51:434–42.

241 [18] Harber MP, Konopka AR, Douglass MD, et al. Aerobic exercise training improves whole
242 muscle and single myofiber size and function in older women. Am J Physiol Regul
243 Integr Comp Physiol 2009;297:R1452–9.

[19] Harber MP, Konopka AR, Undem MK, et al. Aerobic exercise training induces skeletal muscle hypertrophy and age-dependent adaptations in myofiber function in young and older men. J Appl Physiol 2012;113:1495–504.

[20] Schoenfeld BJ, Contreras B, Willardson JM, Fontana F, Tiryaki-Sonmez G. Muscle activation during low- versus high-load resistance training in well-trained men. Eur J Appl Physiol 2014;114:2491–7.

[21] Ogborn D, Schoenfeld BJ. The role of fiber types in muscle hypertrophy: Implications for loading strategies. Strength Cond J 2014;36:20–5.

[22] Lamas L, Aoki MS, Ugrinowitsch C, et al. Expression of genes related to muscle plasticity after strength and power training regimens. Scand J Med Sci Sports 2010;20:216–25.

[23] West W, Hicks A, Clements L, Dowling J. The relationship between voluntary electromyogram, endurance time and intensity of effort in isometric handgrip exercise. Eur J Appl Physiol Occup Physiol 1995;71:301–5.

[24] Hunter SK, Enoka RM. Sex differences in the fatigability of arm muscles depends on absolute force during isometric contractions. J Appl Physiol 2001;91:2686–94.

[25] Yoon T, Delap BS, Griffith EE, Hunter SK. Mechanisms of fatigue differ after low- and high-force fatiguing contractions in men and women. Muscle Nerve 2007;36:515–24.

[26] Ozaki H, Loenneke JP, Buckner SL, Abe T. Muscle growth across a variety of exercise modalities and intensities: Contributions of mechanical and metabolic stimuli. Med Hypotheses 2016;88:22–6.

265 [27] Mackey AL, Holm L, Reitelseder S, et al. Myogenic response of human skeletal muscle
266 to 12 weeks of resistance training at light loading intensity. Scand J Med Sci Sports
267 2011;21:773–82.

268 [28] Henneman E. The size-principle: a deterministic output emerges from a set of
269 probabilistic connections. J Exp Biol 1985;115:105–12.

270 [29] Mitchell CJ, Churchward-Venne TA, West DW, et al. Resistance exercise load does not
271 determine training-mediated hypertrophic gains in young men. J Appl Physiol
272 2012;113:71–7.

273 [30] Schoenfeld BJ. Potential mechanisms for a role of metabolic stress in hypertrophic
274 adaptations to resistance training. Sports Med 2013;43:179–94.

275 [31] Tesch P, Sjödin B, Karlsson J. Relationship between lactate accumulation, LDH activity,
276 LDH isozyme and fibre type distribution in human skeletal muscle. Acta Physiol
277 Scand 1978;103:40–6.

278 [32] Cumming KT, Paulsen G, Wernbom M, Ugelstad I, Raastad T. Acute response and
279 subcellular movement of HSP27, αB-crystallin and HSP70 in human skeletal muscle
280 after blood-flow-restricted low-load resistance exercise. Acta Physiol 2014;211:634–
281 46.

282 [33] Tesch P, Karlsson J. Lactate in fast and slow twitch skeletal muscle fibres of man during
283 isometric contraction. Acta Physiol Scand 1977;99:230–6.

284 [34] Humphreys PW, Lind AR. The blood flow through active and inactive muscles of the
285 forearm during sustained hand-grip contractions. J Physiol 1963;166:120–35.