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Strength Training: In Search of Optimal Strategies to Maximize Neuromuscular Performance

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DUCHATEAU, J., S. STRAGIER, S. BAUDRY, and A. CARPENTIER. Strength training: in search of optimal strategies to maximize neuromuscular performance. *Exerc. Sport Sci. Rev.*, Vol. 49, No. 1, pp. 2–14, 2021. *Training with low-load exercise performed under blood flow restriction can augment muscle hypertrophy and maximal strength to a similar extent as the classical high-load strength training method. However, the blood flow restriction method elicits only minor neural adaptations. In an attempt to maximize training-related gains, we propose using other protocols that combine high voluntary activation, mechanical tension, and metabolic stress.* **Key Words:** mechanical tension, metabolic stress, blood flow restriction, muscle hypertrophy, neural adaptations

Key Points

- Mechanical tension and metabolic stress contribute to training-related muscle hypertrophy and increase in maximal strength.
- As the magnitude of the neural adaptations after low-load exercise with blood flow restriction is less than that elicited by high-load strength training and this method is difficult for some individuals and insufficient for well-trained athletes, we suggest there is a need for new strength training protocols.
- One training option is to combine different levels of mechanical tension and metabolic stress that are optimized to the training status of the individual.

INTRODUCTION

The increase in muscle strength is classically based on the "overload" principle (1). This principle, which states that a minimal load/contraction intensity must be exceeded during the training sessions to increase muscle strength, is used in sport training and in clinical and rehabilitation settings. Based on this concept, moderate to high mechanical loading of the muscle (≥60%–70% of the one repetition maximum [1RM]) has long been considered as the main stimulus (*i.e.*, mechanical tension) for muscle hypertrophy and thereby an increase in muscle strength (2–4). More recently, however, studies using training loads of less than 50% of 1RM performed until failure (5) or with blood flow restriction (BFR) (ischemic/hypoxic condition) have reported gains in maximal strength and comparable levels of muscle hypertrophy to that observed with conventional heavy-load strength training (for recent reviews, see (6–8)). These studies suggested that the accumulation of fatigue-related metabolites (*i.e.*, metabolic stress) may play a role in the exercise stimulus, leading to an increased accretion of muscle mass and strength (9,10).

The current Perspective for Progress article compares training programs performed with high loads to those involving low loads under BFR and the adaptations elicited by each approach. As one of the objectives was to examine the possible contribution of metabolic stress on muscle hypertrophy, we chose to compare low-load exercise with BFR to high-load strength training, as the former method produces more metabolic stress and needs fewer repetitions to reach failure (*i.e.*, greater efficacy) than low-load training performed under normal blood circulation (5). We also explore the utility of the approach of combining moderate to high loads (mechanical stress) and brief rest intervals between sets (metabolic stress) to maximize muscle hypertrophy and strength gains in untrained and trained individuals. Although the efficacy of low-load training with BFR is particularly relevant for patients and healthy untrained or aged individuals, for whom heavy-load strength training may be problematic and contraindicated (6–8,11,12), such training may be insufficient in well-trained athletes who require high level of strength or power (13).

Although increases in maximal strength are due to both muscle and neural adaptations, the purpose of our article is not to provide an in-depth review of the molecular mechanisms

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Accepted for publication: July 20, 2020.

Associate Editor: Roger M. Enoka, Ph.D.

0091-6331/4901/2–14

Exercise and Sport Sciences Reviews

DOI: 10.1249/JES.0000000000000234

underlying muscle hypertrophy or to discuss the numerous neural adaptations induced by strength training. Such information can be found in the following reviews on muscle (13–17) and neural (18–22) adaptations.

HIGH-LOAD STRENGTH TRAINING VERSUS LOW-LOAD EXERCISE WITH BFR

Muscle Adaptations to High-Load Strength Training

Based on a substantial literature on traditional strength training, the American College of Sport Medicine (2) recommends the use of moderate loads (70%–85% of 1RM, 8–12 repetitions per set for 1–3 sets per exercise) for novice and intermediate individuals and high loads (70%–100% of 1RM, 1–12 repetitions per set for a minimum of 3–6 sets per exercise) for trained athletes to increase both muscle hypertrophy and maximal strength.

High mechanical loading of the muscle (≥70% of 1RM) traditionally is considered to be an essential stimulus for increases in maximal strength (2–5,21,23). At the muscle level, the primary adaptation is an increase in muscle size (*i.e.*, hypertrophy). Strength training increases force capacity by increasing the quantity of contractile proteins in individual muscle fibers and thereby the cross-sectional area (CSA) of the muscle. In pennate muscles (*e.g.*, gastrocnenmii, vastus medialis, and vastus lateralis), however, the angle of pennation of muscle fascicles increases with strength training (24,25), which reduces the force contributed by each fiber to the tendon (longitudinal force vector) due to an increase in the oblique angle of pull. The training-related increase in the force produced by individual muscle fibers in pennate muscles, therefore, is attenuated by increases in the pennation angle (22,24). The magnitude of this adaptation likely explains some of the variability between muscle strength and anatomical CSA seen among individuals.

Although it has been instructed for a long time that muscle hypertrophy is greater when the exercise involves a moderate load (~70% of 1RM) with many repetitions than a higher load (>80% 1RM) with fewer repetitions (2,26,27), more recent publications do not support that claim, at least in untrained or medium-trained individuals (see [5]). The meta-analysis by Schoenfeld *et al.* (5) even indicates that similar gains in muscle hypertrophy can be obtained for a large range of loads (~30%–80% of maximum) provided that sets are performed to failure. A load equal to 20% of 1RM seems, however, insufficient to promote muscle hypertrophy (28). In contrast, greater gains in maximal strength are observed for training with higher load (>60% of 1RM) compared with lower load (≤60% of 1RM). The relative greater increase in maximal strength than in muscle hypertrophy with high-load training is usually explained primarily by a greater contribution of neural changes (2,18,21) and muscle cytoskeletal remodeling associated with force transmission (29).

Muscle Adaptations to Low-Load Exercise Under BFR

In the mid-1990s, it was suggested that the accumulation of fatigue-related metabolites may contribute to an increased accretion of muscle mass and maximal strength (9,10). This idea was supported by subsequent studies showing that training with loads ranging from 20% to 50% of 1RM performed under BFR increased muscle hypertrophy and maximal strength (30,31). In these studies, blood flow was restricted to a muscle group by the application of external pressure via a tourniquet, an inflated cuff, or an elastic band applied over the proximal portion of either the upper or lower extremities. This external pressure varied across muscle groups and studies but typically ranged from 60 to 270 mm Hg (7). In most conditions, the external pressure applied around the limb was sufficient to maintain some arterial flow but blocked venous blood return distal to the occlusion site (32). Such reduction in blood flow induces an ischemic/hypoxic environment that may augment the training effect of the exercised muscle compared with the normal blood flow condition (30,31).

The gains in muscle size and strength achieved with low-load exercise training performed under BFR have been reported to be similar to those elicited by conventional heavy-load strength training. For example, Takarada *et al.* (31) reported that a 16-wk (two sessions per week) low-load (50% of 1RM) exercise training of the elbow flexor muscles performed under BFR (100 mm Hg) increased muscle CSA and strength (~19% and 18%, respectively), which was similar to the increases (~15% and 22.5%) achieved with high-intensity strength training (80% of 1RM) without BFR and much more than an identical low-intensity (50% of 1RM) protocol without ischemia (~5% and 1%). Similar observations have been reported with lower loads combined with BFR (20%–30% of 1RM; [33–35]). Even in athletes, low-load (20% of 1RM) training with the knee extensors performed under hypoxic or vascular-occlusion conditions led to similar increases in maximal strength (14.8% vs 13.3%) and muscle hypertrophy (6.1% vs 6.6%) (36). However, this exercise stimulus may be insufficient to increase the 1RM load in well-trained athletes (37) such as powerlifters for example (38).

Meta-Analyses Comparison

Depending of the inclusion criteria adopted, recent meta-analyses have reached slightly different conclusions (6–8). One analysis on patients with musculoskeletal disease (7) and another analysis on various population of individuals (8) both indicated that the increase in muscle strength was less after low-load exercise training with BFR than with high-load strength training. In the latter meta-analysis (8), between-group comparisons indicated significantly greater gains (~7%) in muscle strength for high-load strength training than for low-load exercise training with BFR. Similar findings were observed when the gain in muscle strength was evaluated with the same exercise modality used during training (1RM with an inertial load, isometric contraction, or isokinetic testing). However, none of the characteristics related to the level of external blood pressure, cuff width, or external pressure prescription (individualized or not) seem to have influenced the gain in muscle strength.

In contrast, the meta-analysis performed by Grønfeldt *et al.* (6), which included results on healthy populations ranging from young to older adults and from untrained to well-trained participants, found no differences between the two training methods. This conclusion is likely a consequence of the more restrictive inclusion criteria. For example, studies that used within-subject measurements (*e.g.*, comparison of muscles from the ipsi- and contralateral limb) or subjects not randomized were not included in the meta-analysis. In addition, only one strength variable was extracted in studies that obtained multiple strength outcomes (1RM load and isometric maximal voluntary contraction (MVC) or isokinetic testing) in the same subjects.

In addition, the inclusion criteria did not distinguish between studies performed on individuals with different training histories (patients, sedentary, or trained) or account for differences in sex or age.

The capacity of training with low loads under BFR to increase muscle mass was reviewed in the meta-analysis by Lixandrão *et al.* (8). The results indicated similar levels of muscle hypertrophy (average gain difference of <1% in favor of high-load strength training) with the two methods. As noted for the increases in maximal strength, blood pressure-related parameters do not seem to influence the level of muscle hypertrophy.

Overall, these meta-analyses suggest that low-load exercise training with BFR is an effective method to increase maximal strength; the effect is greater than that achieved with a similar training load without BFR when the number of repetitions is equated (7). Nonetheless, its relative efficacy compared with conventional high-load strength training seems to depend on the comparison group. As low-load training with BFR is relatively safe (7,11,12), it can be an alternative to high-load strength training as a method to increase neuromuscular capacities in patients (7) and healthy sedentary or active young and older adults (6,8), but is likely an insufficient stimulus for well-trained athletes (37,38). However, the mechanisms by which the metabolic stress elicited by BFR contributes to muscle hypertrophy and strength gains are currently unclear.

MECHANISMS CONTRIBUTING TO MUSCLE HYPERTROPHY

Mechanical Factors

Early animal studies found that mechanical tension acts as a primary mechanism for muscle growth and thereby increases in muscle strength (for a review, see [39]). For example, removal of a synergist muscle (*i.e.*, chronic overload) led to the hypertrophy of the remaining muscles (40), and increases in the mechanical strain on a muscle attenuated the atrophy caused by unloading (41). Subsequently, studies found that imposing high mechanical tension or lengthening of activated muscles is a major mediator of myofibril protein synthesis (42).

Mechanotransduction and Growth Factors

Muscle hypertrophy observed after chronic mechanical overload results from an increase in the net protein synthesis and in the number of myonuclei that mediate the increase in the volume of contractile proteins within a muscle fiber (15). The process by which the mechanical stress is translated into chemical signals that trigger an intracellular signaling cascade leading ultimately to the production of muscle proteins is known as mechanotransduction. Briefly, in the presence of chronic muscle overload, focal adhesion kinases (FAK) bind to mechanoreceptors (*i.e.*, integrin receptors) that connect the extracellular matrix to the sarcolemma. Through its action, FAK converts mechanical tension into a chemical signal that mediates intracellular anabolic (mammalian target of rapamycin complex 1 [mTORC1]) and catabolic (family of transcription factors [FOXO]) pathways (for more details, see [15,16,43]). When associated with sufficient nutritional intake (15,44), this process favors protein synthesis over its degradation, resulting in a net increase in contractile protein and muscle fiber hypertrophy (Fig. 1) (16).

The mTORC1 is not solely activated by high mechanical loads, but also by other stimuli such as insulin-like growth factor-1 (IGF-1) and one of its variants termed mechanogrowth factor (MGF). MGF is produced locally and contributes to upregulate protein synthesis via the activation of the P13K/Akt/mTORC1 pathway (for reviews, see [15,16,43,45]). Because of its rapid expression after mechanical loading, MGF contributes to enhance the postexercise hypertrophic response and to facilitate local repair of muscle damage (Fig. 1) (46), but its intervention does not seem to be obligatory for muscle growth (15,47).

Satellite Cells

In addition to mechanotransduction and growth factors, new nuclei are differentiated from "satellite cells" that are quiescent mononucleated cells located under the basal lamina (48). Although muscle damage associated with strength training exercises, and in particular with lengthening (eccentric) contractions, elicits satellite cell activation and proliferation (49), the actual stimulus needed to activate satellite cells is not known. Pathways involving intracellular signaling via mechanosensitive receptors or indirectly through growth factor–mediated signals and hormonal release (50,51) are the most likely candidates (Fig. 1) (48,52). When activated, satellite cells begin proliferating, and some of them fuse with muscle fiber to add new nuclei to the existing fibers (48,52,53). These new myonuclei produce mRNA and contribute to the production of contractile proteins in response to both high-load strength training (48,53) and low-load exercise with BFR (54). It seems, however, that some muscle hypertrophy can occur without the addition of myonuclei to existing fibers, but their inclusion is necessary for larger increases (>25%) in muscle size (52).

Although most experimental evidence suggests that the hypertrophy of the individual muscle fibers is the main mechanism for the increase in muscle mass, hyperplasia (*i.e.*, increase in the number of muscle fibers) may contribute to an increase in muscle size. However, the extent to which hyperplasia can occur in humans who participate in long-term strength training (*e.g.*, bodybuilders) seems relatively weak (55) or nonexistent (4). Based on immunohistochemical techniques, Kadi *et al.* (48,56) proposed that in addition to their role in the hypertrophy of the existing muscle fibers, satellite cells may fuse to develop new muscle fibers. For example, Kadi and Thornell (56) showed that elite powerlifters, contrary to untrained subjects, displayed small-diameter fibers that expressed embryonic and neonatal myosin heavy chain (MHC) isoforms, which are considered to be markers for the early stages of muscle fiber development. Despite these observations, the role of hyperplasia seems rather weak in humans, and fiber hypertrophy is the primary mechanism responsible for increases in muscle mass after strength training.

Metabolic Factors

Given the low mechanical stress that occurs during BFR, it has been suggested that muscle hypertrophy under this condition may not be due to mechanotransduction and the IGF-1/P13K/Akt/mTORC1 pathway (13,57,58), and other mechanisms have been proposed (Fig. 1) (for reviews, see [11,13,57]). Among the possible mechanisms, we have chosen to evoke the potential direct effects of an increase in the level of metabolites on systemic hormones and muscle activation (Fig. 1) (13,58). Other secondary

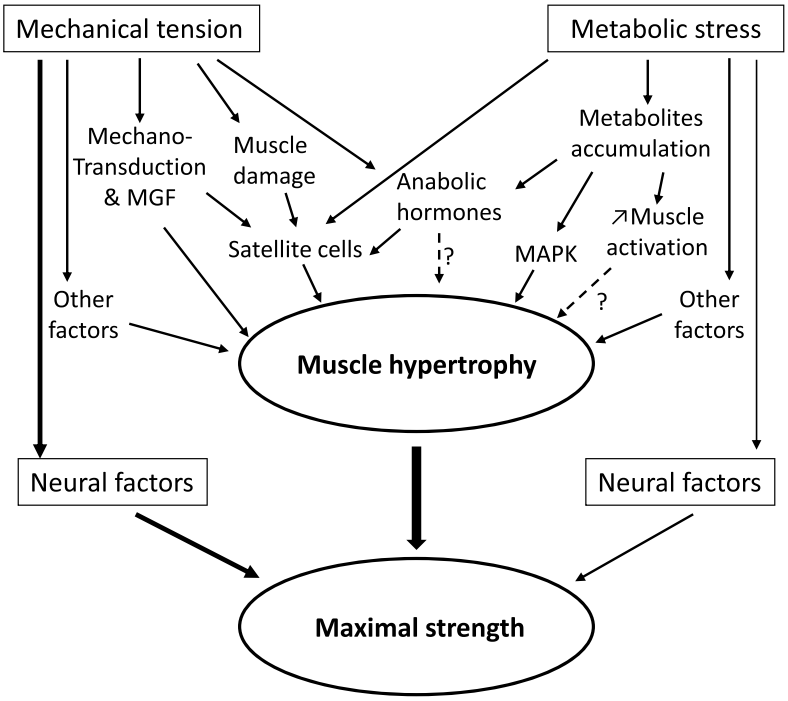

Figure 1. Schematic representation of the main mechanisms involved in muscle hypertrophy and increases in maximal strength. This diagram illustrates the primary action of mechanical tension and metabolic stress on muscle hypertrophy and maximal strength. The arrows with the interrupted line and a question mark (?) indicate that the influence on muscle hypertrophy is indirect and currently equivocal. Both mechanical tension and metabolic stress can modulate the neural factors that contribute to increases in maximal strength. The thickness of the connecting lines indicates the relative contribution of neural factors to the gains in maximal strength. "Other factors" indicates secondary mechanisms that may contribute to the adaptations.

mechanisms, including notably cell swelling, muscle damage, and increased production of reactive oxygen species, have been proposed to play an indirect role in muscle hypertrophy (see [13,57]).

The ischemic/hypoxic condition produced by low-load occlusion training reduces O_2 supply to the involved muscles and induces a shift from aerobic toward anaerobic metabolism, which has consequences for the rate of adenosine triphosphate rephosphorylation. Low levels of O_2 further accentuates the alterations in ionic concentration gradients (K^+, Na^+, Ca^{2+}, etc.) and the accumulation of metabolic by-products, including lactate, hydrogen ions (H^+), inorganic phosphate (Pi), adenosine diphosphate (ADP), and others (59). Such metabolic stress may act as an anabolic signal (60–62) that engages the mitogen-activated protein kinase (MAPK) pathway (Fig. 1) (57,63). The MAPK pathway does not depend on the exercise load and may be regulated by a metabolic sensor (64).

Although an association between Pi or intramuscular pH and muscle hypertrophy has been observed after low-intensity (20% of 1RM) exercise training with BFR (65), there seems to be a potential role for lactate in muscle hypertrophy (61). For example, blood lactate concentration is significantly greater after training with low-load exercise under BFR (31) and environmental hypoxia (36,66) than for the same exercise protocol performed under normal conditions. Furthermore, greater relative blood lactate concentration, as occurs after low-load exercise with BFR, is accompanied by a greater increase in muscle CSA after the training program compared with high-load or low-load exercise performed in normal conditions (31). These *in vivo* observations are supported by *in vitro* studies showing the anabolic properties of lactate. In cell culture preparations, lactate induces myogenesis (67,68) and increase phosphorylation of p70S6K (a downstream target of mTORC1) (67). Moreover, a rodent model further indicated that high concentrations of lactate seem to modulate muscle differentiation by regulating the associated networks of myogenic protein determination, enhancing MHC expression and myotube hypertrophy (69).

Hormonal Modulation

For a number of years, it has been suggested that muscle hypertrophy in response to a strength training was due, at least in part, to a transient increase (~30 min) in systemic anabolic hormones (testosterone, growth hormone (GH), and IGF-1) after a training session in both untrained individuals and trained athletes (14,70–73).

The proponents of a role for testosterone in muscle hypertrophy suggest either a direct effect by its binding on androgen receptors that mediate gene transcription (71,72,74) or an indirect effect that includes potentiating the release of other anabolic hormones such as GH and IGF-1/MGF (75,76) or mediating satellite cell activation and proliferation (Fig. 1) (50,51). Despite the recognized role of testosterone in developmental processes that regulate muscle growth and hypertrophy after administration of supraphysiological dose of testosterone (77), the augmentation of serum concentrations after strength training may be insufficient to trigger muscle hypertrophy (15,16). As a causal link between acute testosterone production and hypertrophy has not been established and postexercise increases in testosterone are not required for muscle hypertrophy (see [73,78,79]), further studies are needed to determine its functional role, if any, in training-related muscle adaptations (80).

The influence of GH and IGF-1 on the development of muscle mass after strength training also is unclear as its direct involvement in muscle hypertrophy seems negligible (73,81). Nonetheless, others have found that the effects of GH and circulating IGF-1 might be complementary in maximizing muscle anabolism, thereby optimizing the adaptations (45,80). For example, GH might increase the net muscle protein synthesis indirectly by facilitating amino acid transport and availability via both endocrine and locally produced IGF-1/MGF (82) or by inducing muscle growth through satellite cell activation, proliferation, and differentiation (Fig. 1) (see [15,45,50]). As GH can enhance collagen protein synthesis (83), it has been suggested that such adaptations could, through improved force transmission (29), enable the use of higher loads during training, which in turn might stimulate muscle protein synthesis (16). However, several studies have reported that a single session of low-intensity exercise performed under BFR increases the level of GH in the blood drastically (84–86) and to a greater extent than when the same exercise is performed to failure with normal blood circulation or blood flow occlusion without exercise (84). In addition, serum GH increases to a much greater extent in response to low-load exercise under BFR than for higher-load (70% of 1RM) exercise performed under normal conditions (85). Despite the enhanced blood GH concentration in both traditional strength training program and ischemic/hypoxic conditions, it is currently not clear how such increases can contribute to the adaptations that underlie muscle hypertrophy.

Muscle Activation

Another often suggested explanation for the efficacy of low-load exercise training performed under BFR is via the indirect action of metabolites on augmenting muscle activation (58,79,87). When exercises are performed with submaximal loads in unrestricted blood flow conditions, an increase in synaptic input to the motor neuron pool is needed to recruit progressively higher-threshold motor units to compensate for fatigue-related decrease in force of the activated motor units when the task progresses toward failure (88). Although fatigue-related declines in force capacity are multifactorial and cannot solely be attributed to the accumulation of metabolites (see [89]), Pi, H^+, and others are known to impair intramuscular mechanisms associated with force production (90,91). When blood flow is occluded, this effect is further amplified by the lack of O_2 (92).

In normal blood flow conditions, complete recruitment of motor units in limb muscles is reached when the muscle is contracting at high force levels. However, as low-threshold motor units are sensitive to an O_2 deficit (93), as it occurs during contractions with BFR, recruitment range is likely compressed and higher-threshold motor units are recruited at lower forces. Because of this effect, it is often assumed that most motor units are recruited at task failure during low-load ischemic exercises (13,15,31,58). This assumption is indirectly supported by studies showing that BFR conditions augment surface EMG amplitude to a greater extent than in unrestricted blood flow condition during load- and volume-matched protocols (94,95), but to a similar EMG amplitude when both protocols are performed to failure (96).

However, it is noteworthy that low-load (15%–20%) exercise that is either sustained (97,98) or intermittent (99) until task failure in a no-cuff condition does not reach the maximal EMG amplitude recorded before the fatigue protocol. In contrast, repeated movements with a load equal or superior to 40% of 1RM reached near-maximal or maximal EMG at task failure (99). Despite the limitations (signal cancellation) of surface EMG recording to infer the level of neural drive sent to the muscle during fatiguing contractions (100), it is unlikely that the entire pool of motor units is maximally activated (total recruitment and maximal discharge rate) at the completion of each set of exercises even in BFR conditions.

The metabolic and ionic changes in the muscle during fatiguing contractions activate small-diameter afferents of group III and IV fibers (101) that induce progressive inhibitory effects at both spinal and supraspinal levels, further limiting muscle activation (102) and interrupting the activity of some motor units (88). As blood flow occlusion augments the production of metabolic by-products, the inhibitory effect of group III and IV fibers is likely intensified (103,104). Although glycogen depletion has been reported in Type II fibers after low-load exercise (30% of 1RM) performed in unrestricted blood flow condition until task failure (105), this observation does not mean that the corresponding motor units discharged at rates high enough to develop their maximal force capacity. Therefore, the hypothesis that low-load exercise performed under BFR activates all motor units as in high-load exercise and elicits sufficient mechanical tension to trigger protein synthesis (13,31,58) is not convincing and needs to be more carefully examined.

Collectively, these findings indicate that even though increases in muscle strength after a traditional strength training program is due to an increase in muscle mass (24,106), the mechanisms that produce muscle hypertrophy either through the mechanotransduction pathway or indirectly via growth factor-mediated signals still remain a matter of debate (15,16,52, 57,58). Furthermore, despite the experimental evidence that low-load exercise performed under BFR can produce similar gains in muscle performance as high-load strength training, potential alternative mechanisms to the mechanotransduction pathway remain to be defined.

CONTRIBUTION OF NEURAL ADAPTATIONS TO MAXIMAL STRENGTH

It has been known for many years that strength gains elicited by high-load strength training involve both neural and muscular adaptations (107). Indirect evidence of neural adaptations includes the dissociation between the magnitude of structural (muscle size) and functional changes (108). Several methods have been used to measure changes in muscle activation during MVC after completing a strength training program: surface EMG activity (107,109), superimposed electrical stimulation method (110,111), ratio of evoked tetanic force to MVC force (112), and maximal discharge rates of motor units (113). Despite some technical limitations with these approaches (see (20)), these studies reported an increase in the level of voluntary activation (*i.e.*, degree of motor unit recruitment and discharge rate) after strength training that may account for ~1/3 of the increase in maximal strength (114). More insightful electrophysiological approaches (see [18]) have further indicated that neural adaptations are located at both supraspinal and spinal levels (see [19,114]).

Among the few studies that have investigated the neural adaptations in response to low-load exercise training under BFR,

the conclusions seem contrasting. One study reported an increase in surface EMG amplitude of the two vastii during an MVC with the knee extensors after a 5-wk training program with a load of 20% of 1RM (115). In contrast, other studies have not found any changes in surface EMG amplitude after 8–12 wk of training with a load of 20% or 50% of 1RM under BFR for the knee extensors (35) or elbow flexors (116), respectively. In addition, studies using electrophysiological approaches have not observed any changes in the level of voluntary activation as tested with the superimposed twitch technique (35,116) or by assessing the descending drive (V-wave response) and responsiveness of a spinal reflex pathway (H-reflex) (117). These studies indicate that low-load exercise training under BFR induces no more than minor neural adaptations compared with those classically found after high-load strength training (18,20–22).

Together, these findings suggest that although low-load exercise training under BFR can be effective in increasing muscle mass and maximal strength, it does not seem to modulate all strength- and power-related parameters, particularly those associated with voluntary muscle activation.

HOW TO MAXIMIZE NEUROMUSCULAR ADAPTATIONS?

As suggested by Pearson and Hussain (13), one strategy to maximize strength gains is to use training protocols that combine high levels of both mechanical tension and metabolic stress. This can be achieved by alternating high-load and low-load exercise under BFR either in the same or separate training sessions. Alternatively, this goal could be accomplished by using moderate to high loads (high mechanical tension) with brief interset rest intervals to generate high metabolic stress in a brief period.

Influence of Interset Interval

In addition to major training variables, such as load intensity and training volume (2,17,118), the rest interval between sets influences the outcomes produced by a strength training program. The classical recommendations for interset intervals are based on the training goal (maximal strength, muscle hypertrophy, muscle power, and muscular endurance) and the ability to maintain the number of repetitions within a prescribed zone over consecutive sets (2,118). For example, specific training protocols differ between bodybuilders and powerlifters/weightlifters. Although both types of athletes train with high to very high loads, powerlifters typically use few (1–8) repetitions in each set and long interset intervals (>2–3 min), whereas bodybuilders use more repetitions (8–10) in each set performed until failure and shorter rest periods (≤1 min) (26,27,119). Practical wisdom suggests that the bodybuilding protocol favors muscle hypertrophy, whereas the powerlifting protocol leads to greater muscle strength (27). Nonetheless, there is no consensus on the specificity of these adaptations (see review articles by [17,118,120]).

One well-accepted notion is that reducing the recovery period between sets (from 5 to 3 to 1 min) decreases the total number of repetitions with a constant load that can be completed in a multiple-set training, which impacts the total training volume (2,118,121). In addition, more than 3 min of rest may be needed to maintain maximal strength and power during successive sets and to accumulate a high training volume, depending on the training status of the individual, the muscle group being targeted, and the type of exercise (single vs multijoint exercise) performed (17,118). A 3-min interval allows enough time for the resynthesis of phosphocreatine (PCr) through the aerobic system (59) and the elimination of some intracellular metabolic by-products into the bloodstream. When associated with limited O_2 availability (*i.e.*, hypoxia), these alterations slow down the rate of PCr resynthesis and ADP rephosphorylation, which reduce both the maximal strength and speed of contraction (59).

Several studies have shown that rest intervals of 2–3 min result in significantly greater increases in maximal strength and power compared with shorter rest intervals (30–90 s) (17,120,122–124). Although necessary to maximize the level of voluntary activation and thereby maximal strength, the maintenance of training intensity during successive sets is not usually chosen when attempting to induce muscle hypertrophy (27). The experimental evidence on the influence of short (≤1 min) and long (≥3 min) interset intervals during strength training is mixed. Some studies showed an advantage of long interset intervals for muscle hypertrophy (74,125), whereas others found either better result with short interset intervals (126) or no significant difference (127,128). However, the workout volume in the two training programs was not matched in all of these studies (74,128), which likely influenced the conclusion. In contrast, Goto *et al.* (60) compared the outcomes achieved with a 12-wk strength training program for two groups of subjects who performed protocols that were matched for volume and load intensity (3–5 sets of 10 reps at 70%–75% of 1RM with an interset rest period of 1 min). One group performed the repetitions in each set without any interruption, whereas the other group had a 30-s rest period after the first five repetitions of each set. As expected, blood lactate concentration was significantly greater for the protocol that did not include the 30-s rest. The main finding was that muscle CSA only increased significantly in the group that did not include a rest period during each set, indicating that a strength training protocol leading to high accumulation of metabolic by-product may favor muscle hypertrophy.

In Search of New Training Strategies

Recent work from our laboratory has examined the effectiveness of a new training design (called the 3/7 method) to promote strength gains in the bench press exercise performed by physically active individuals (129). This method, based on a strength training protocol introduced by a French coach named Emmanuel Légeard, is characterized by five sets of an incremental number of repetitions per set (from three repetitions in the first set to seven repetitions in the last set) with a constant load of ~70% of 1RM. Each set was separated by a brief rest interval of 15 s. When compared with the more "classical" method of a constant number of repetitions in each set and matching the load and number of repetitions (*i.e.*, training volume; 4 × 6 method: four sets of six repetitions with 150-s rest interval between sets), the 3/7 method produced a significantly ($P < 0.05$) greater increase in 1 RM load (29.8% vs 21.8%) and maximal strength (22.4% vs 9.9%) as tested with an isokinetic device (Ariel Computerized Exercise System, Ariel Dynamic Inc) after 12 wk (two sessions per week) of training (129). Doubling the number of sets performed with the classical method (*i.e.*, eight sets of six repetitions) increased ($P < 0.05$) the gain in 1RM load (35.9%)

compared with the 3/7 method, but the increase in maximal strength did not differ ($P > 0.05$) between the two protocols (25.5% vs 22.4%). In addition, the increase in peak power was greater ($P < 0.05$) for the 8 × 6 (21.6%) compared with the 3/7 (16.3%) method, but the difference was not significant ($P > 0.05$) when volume was matched for the two protocols (*i.e.*, 3/7 vs 4 × 6) (129).

Subsequently, we examined the relative contributions of neural and muscular adaptations to the gains achieved by the elbow flexors after a 12-wk (two sessions per week) training program with a load of 70% of 1RM performed by moderately trained individuals (130). Training involved a total of ~50 repetitions in each session in an attempt to optimize the dose/response (see (17)). The 3/7 protocol was repeated twice with a 150-s rest between the two bouts and compared with the 8 × 6 method, 150 s of rest between sets. Our results indicated that both protocols (3/7 and 8 × 6) increased the 1RM load (22.2% vs 12.1%; $P < 0.05$) and MVC force during an isometric contraction (15.7% vs 9.5%; $P < 0.05$), with a greater increase in 1RM load ($P < 0.05$) and marginally greater MVC force ($P = 0.07$) for the 3/7 method.

The EMG activity of two elbow flexors (long head of biceps brachii and brachioradialis), normalized to their respective maximal M wave (M_{max}) elicited by supramaximal electrical stimulation of the motor nerve, increased ($P < 0.05$) with no difference between training methods (14.5% vs 8.1%; $P > 0.05$). Despite the limitations of this normalization procedure (131,132), it reduces the confounding influence of differences in recording conditions (electrodes placement) and peripheral changes (subcutaneous tissues, muscle mass, and architecture) between experimental sessions. In contrast, biceps brachii thickness, as measured by ultrasonography, increased to a greater extent (9.6% vs 5.5%; $P < 0.05$) for the 3/7 method. To verify that the brief interset interval and the incremental number of repetitions in the successive sets in the 3/7 method compromised O_2 delivery to the active muscles, we compared the changes in tissue oxygenation with near-infrared spectroscopy in biceps brachii and brachioradialis (133). Our data indicated a greater average deficit in oxygenation for the 3/7 method and, in contrast to the 8 × 6 method, an absence of recovery on O_2 content between sets.

More recently, we compared the 3/7 method to a protocol that reversed the order of the sets (*i.e.*, 7/3 method), similar to a drop-set protocol. Our findings indicated that the gains in 1RM load, MVC force, and muscle thickness were significantly less ($P < 0.05$) for the 7/3 method compared with the 3/7 method (Fig. 2). Although the normalized EMG amplitude of the elbow flexors increased ($P < 0.05$) after both methods, the training gains did not differ significantly.

Together, these observations demonstrate that brief interset intervals and incremental increases in the number of repetitions performed in successive sets result in superior outcomes for the 3/7 method compared with the 8 × 6 and 7/3 methods.

The greater stimulus for muscle hypertrophy associated with the 3/7 method raises questions about the underlying mechanisms. As observed for low-load exercise training under BFR, shortening the interset intervals during high-volume strength training with moderate loads increases the metabolic stress and the acute hormonal response (82,134). Although a short interset rest interval (1 min) blunts the rate of myofibrillar protein synthesis in the early postexercise recovery period, but not ~24 h later, compared with longer rest period (5 min) (81), there is no clear evidence of an association between an acute increase in myofibrillar protein synthesis after a training session and muscle hypertrophy after a strength training program (135,136). The suggestion of Schoenfeld *et al.* (17) that intersets of 1 min or less are likely too brief to promote maximal hypertrophic gains may depend on differences in training variables, such as the total workout relative to the training status of the individual (60,70) and, in particular for trained athletes, the number of sets performed to failure (137,138). With the 3/7 method, the failure stage is reached during the last two sets. The greater gains in 1RM load, MVC force, and muscle thickness for the 3/7 protocol compared with the 7/3 protocol (same training volume and interset rest interval) are consistent with this hypothesis as the 7/3 protocol does not produce task failure.

These findings indicate that the effectiveness of the 3/7 method results from a protocol that combines moderate to high mechanical tension and metabolic stress (Fig. 3). In addition to producing muscle hypertrophy, the 3/7 method also seems to elicit neural adaptions that contribute to increases in maximal strength. Additional experiments are needed to optimize the training variables (workout volume, optimal rest interval for mono- vs pluriarticular and upper vs lower body exercises, free weight vs machine) and to determine the relative roles of mechanical tension and metabolic stress in contributing to the outcomes. On a practical point of view, a major advantage of the 3/7 method is its greater efficacy (amount of progress relative to the total number of repetitions) over more classical methods.

PERSPECTIVES FOR PROGRESS

Over the last two decades, our concepts and practice of strength training methods have been strongly shaken. One example is that training with low-load exercise performed until failure or under BFR may augment muscle protein synthesis (139,140), muscle hypertrophy, and maximal strength (25,26,28) to a similar extent as achieved with high-load low volume training in both untrained individuals and trained athletes (for meta-analyses, see [5–8]). Another recent change in dogma is that bodybuilding-type training (moderate load, high volume, and brief interset interval) is likely not the best strategy to augment muscle protein synthesis and thereby the increases in muscle growth (see [138]). Among many others, these two examples have led to numerous questions at both mechanistic and practical levels.

Mechanisms of Action

A major advance in this field is the observation of an acute increase in muscle protein synthesis within a few hours (4–6 h that remains elevated for more than 24 h) after exercise provided nutrition is adequate (see [15,16,135]). Unfortunately, the association between the amount of increase in muscle protein synthesis observed in acute condition and its translation into muscle hypertrophy after long-term training remains to be defined (135,136). It is also not clear how successive sessions within a training program, and thus their frequency (number of sessions per week), modulate the amount of muscle growth.

One of several possible explanations for the lack of association between muscle hypertrophy and protein synthesis is the

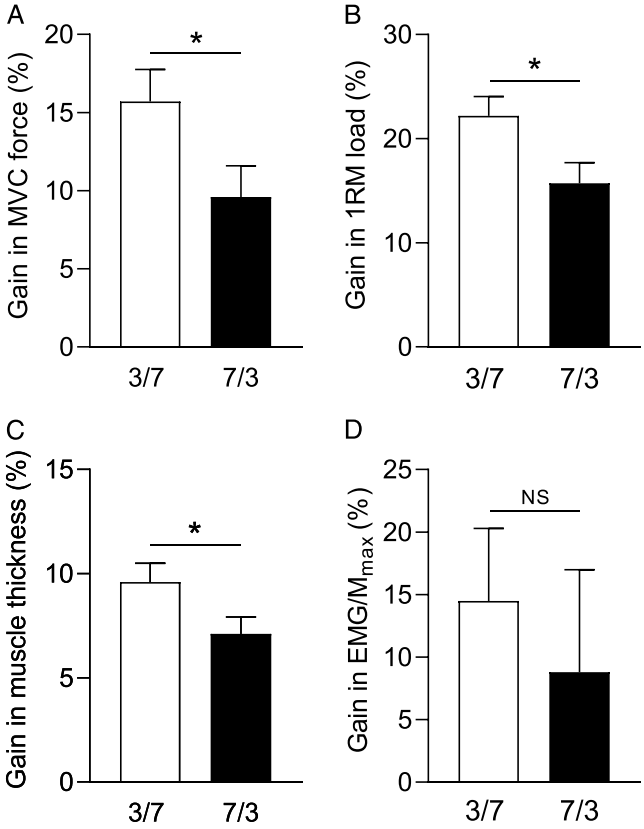

Figure 2. Comparison of the neuromuscular adaptations induced by the 3/7 and 7/3 methods in response to a 12-wk training program. The panels illustrate gains in (A) MVC force and (B) 1RM load for the elbow flexor muscles, (C) thickness of the long head of the biceps brachii, and (D) average EMG normalized to the M_{max} value during the MVC for the long head of the biceps brachii and the brachioradialis. Data are expressed as mean ± SE. *Significant differences ($P < 0.05$) between protocols. NS, nonsignificant.

way in which muscle CSA is measured. Classically, measures of anatomical CSA or muscle thickness are used to assess the amount of muscle hypertrophy. In pennate muscles, however, a more functional measure is the physiological CSA (141), which can be accomplished with ultrasonography when the angle of pennation is taken into consideration. Moreover, muscle CSA can be influenced by changes in other factors, such as muscle fiber swelling in response to training-related damage or modifications in the characteristics of connective tissues (135). Future studies need to assess more carefully the translation of elevated levels of protein synthesis into muscle hypertrophy.

Another issue that needs more attention is the role of anabolic hormones in training-induced adaptations (see [14,50,80,135,136]). Many studies have reported a transient increase in the levels of hormones in the blood (testosterone, GH, and IGF-1), and their relative concentrations seem to depend on several exercise variables, such as type of exercise (mono- vs multiarticular), workout volume, interset interval (72,118), and whether or not the exercise is performed under BFR (13). Although mechanistic studies suggest that these hormones do not play a direct role in muscle protein synthesis (15,16,73), they may have an indirect influence by promoting satellite cell activation and fusion (45,50,80). As exercise-related increases in the levels of these hormones are relatively modest compared with their exogenous administration, it would be useful to determine their dose-dependent effects in both women and men and the influence of various training protocols. The field needs clear experimental designs to establish the functional role, if any, of increases in blood hormone concentrations in short- and long-term adaptations.

Although low-load exercise training with BFR is a valid and safe method to increase muscle hypertrophy and strength in frail and sarcopenic patients (see [6,7,12,55]), the functional consequences for healthy sedentary and older individuals and especially for athletes need to be established. As already mentioned, neural adaptations (*i.e.*, voluntary activation and muscle coordination) play an important role in improving maximal and functional strength (*e.g.*, chair-rise test), but these adaptations are not evident after low-load exercise training with or without BFR. As an example, sedentary and older individuals are typically not able to achieve the maximal level of voluntary activation (142), which reduces their ability to develop maximal strength capacity unless they perform strong contractions on a regular basis (143). Training studies need to distinguish between muscle and neural adaptations to identify the relative training-related responses to low-load and high-load exercises. Approaches are to use electrophysiological methods, such as the superimposed twitch technique, to quantify activation-related adaptations (144) or more insightful methods (see [18]) to obtain information on adaptive mechanisms.

In addition to maximal strength, the development of explosive strength (rate of force development/power) is necessary for many athletes and for older persons so that they produce a reactive response as quickly as possible when balance is compromised (145). Training with rapid contractions increases both the level of voluntary activation (146) and muscle-tendon stiffness (147). Increases in muscle-tendon stiffness, which improve the rate at which force is transmitted to the skeleton (148), can be improved by using high-load concentric or eccentric

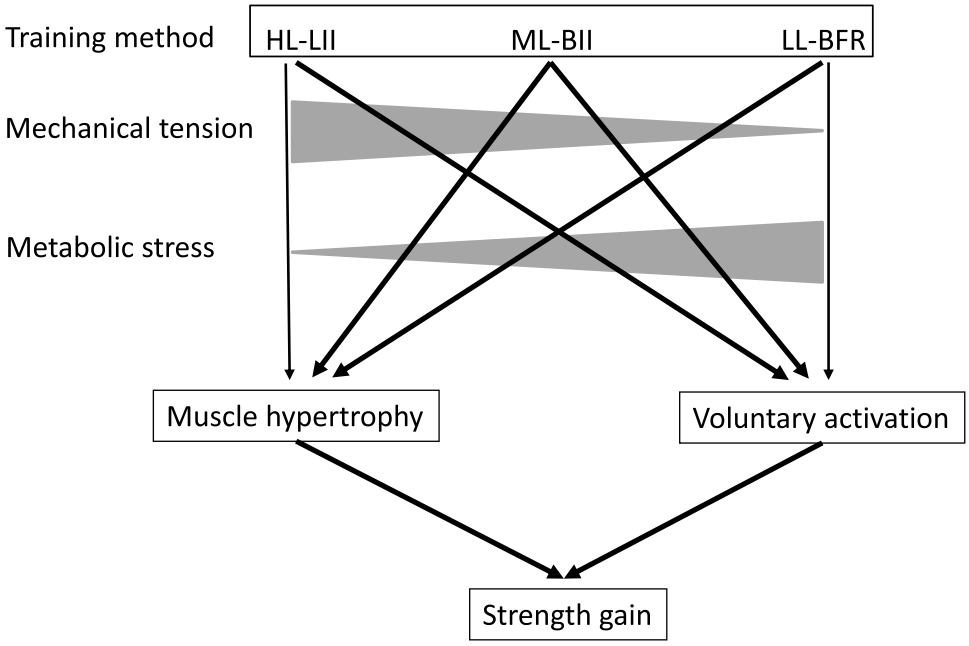

Figure 3. Hypothetical contributions of mechanical tension and metabolic stress (gray triangles) associated with the different training methods to strength gain, which is mediated through muscle hypertrophy and increases in voluntary activation. HL-LII, high load with long interset interval; LL-BFR, low load with BFR; ML-BII, moderate load with brief interset interval. The thickness of the connecting line indicates the relative contributions of each training method.

contractions (149,150) and stretch-shortening-type contractions (151,152). As exercise training under BFR involves low loads and is performed slowly, there are currently no clear evidence that this training modality is effective to increase muscle-tendon stiffness substantially (35,153).

Practical Aspects

In the absence of a clear association between muscle hypertrophy and the levels of metabolic stress as the consequence of the ischemic/hypoxic environment (11,154), Pearson and Hussain (13) suggested that the influence of mechanical tension and metabolic stress may be additive (Fig. 3). However, the relative contributions of these primary factors are not known. In addition, the gains achieved by combining high-load and low-load exercises with BFR in the same session or in separate sessions need to be compared with a program of moderate-load strength training with brief interset intervals (such as the 3/7 method). Well-designed studies are needed to investigate whether it is more effective to optimize the effects of mechanical tension and metabolic stress by combining low-load exercise with BFR and high-load strength training or to use a protocol with moderate loads and brief interset intervals to induce a high level of metabolic stress. An alternative approach, as used by competitive athletes for many years, is to periodize (block training) complementary methods throughout a long-term training program (2). Here also, investigations are needed to determine the most appropriate protocol or the best combination of protocols.

An additional practical criterion that needs to be considered for persons who have time constraints is the benefit-to-cost ratio (amount of progress relative to the time spent during training) of the different protocols. This also is critical for well-trained athletes to improve the efficacy of their training programs and to limit the risk of overtraining. In this context, the 3/7 protocol is appealing as one bout of a given exercise can be completed in ~1.5 min.

In conclusion, recent studies reporting contradictory findings to our well-established knowledge have challenged contemporary concepts about strength training. This uncertainty should be used as an opportunity to advance the field by augmenting our knowledge on the adaptive neuromuscular mechanisms of strength and power training and by offering more consistent guidelines. As the neuromuscular adaptations are modulated by numerous criteria (*e.g.*, age, sex, individual training status and experience, workout volume, number of sessions per week, and muscle group), much remains to be done to determine the optimal training dose that maximizes the performance gains achieved by persons with different characteristics.

Acknowledgment

The authors thank Professor Roger Enoka for editing a draft version of the article.

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