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Article *in* Journal of Sport Rehabilitation · May 2017

DOI: 10.1123/jsr.2017-0002

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Journal of Sport Rehabilitation, 2018, 27, 257-262
https://doi.org/10.1123/jsr.2017-0002

Human Kinetics
ORIGINAL RESEARCH REPORT

The Effects of Blood Flow Restricted Electrostimulation on Strength and Hypertrophy

Joshua T. Slysz and Jamie F. Burr

Context: The combined effect of neuromuscular electrical stimulation (NMES) and blood flow restriction (BFR) on muscle mass and strength has not been thoroughly investigated. ***Objective:*** To examine the effects of combined and independent BFR and a low-intensity NMES on skeletal muscle adaptation. ***Design:*** Exploratory study. ***Setting:*** Laboratory. ***Participants:*** Twenty recreationally active subjects. ***Main Outcome Measures:*** Subjects had each leg randomly allocated to 1 of 4 possible intervention groups: (1) cyclic BFR alone, (2) NMES alone, (3) BFR + NMES, or (4) control. Each leg was stimulated in its respective intervention group for 32 minutes, 4 days per week for 6 weeks. Mean differences in size (in grams) and isometric strength (in kilograms), between week 0 and week 6, were calculated for each group. ***Results:*** Leg strength increased 32 (19) kg in the BFR + NMES group, which differed from the 3 (11) kg change in the control group ($P = .03$). The isolated NMES and BFR groups revealed increases of 16 (28) kg and 18 (17) kg, respectively, but these did not statistically differ from the control, or one another. No alterations were statistically significant for leg size. ***Conclusion:*** Compared with a control that received no treatment, the novel combination of BFR and NMES led to increasing muscular strength of the knee extensors, but not muscle mass which had a large interindividual variability in response.

Keywords: muscular adaptations, occlusion, training, electromyostimulation

The preservation and promotion of skeletal muscle mass and strength is essential for athletes and nonathletes alike; whether the goal is improved performance or maintaining one's quality of life. Sufficient skeletal muscle is required for functional movement and also plays a vital role in whole-body glucose metabolism,[1] lipid oxidation,[2] and is one of the greatest modifiable contributors to the resting metabolic rate.[3] The maintenance of skeletal muscle becomes increasingly important with advancing age, as low levels of muscle mass are strongly correlated with a loss of independence, mobility, and an increased risk of disability and functional impairment.[4] Current recommendations for the maintenance of muscle health suggest that relatively high-load resistance exercise must be undertaken. The American College of Sports Medicine[5] recommends using a resistance equivalent to 60% to 70% of an individual's 1-repetition maximum to experience gains in strength and mass.

This high-load exercise required to induce muscular adaptation may not be practical for certain segments of the population, or during select training/recovery phases for athletes. Examples of those who are unable to withstand the high stresses of heavy training may include persons recovering from injury, persons with chronic health conditions, or older persons. There is emerging evidence that low-load resistance exercise (ie, <25% 1-repetition maximum) can lead to significant muscular adaptations in strength and mass, when blood flow to the muscle is restricted or occluded during the exercise.[6] As such, persons for whom traditional high-load training may be too cumbersome, or even contraindicated, the option to adopt a lighter training load in combination with blood flow restriction (BFR) may offer an important alternative.

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Neuromuscular electrical stimulation (NMES; electrical currents applied through the skin to evoke muscle contractions) has long been used to promote muscle hypertrophy during prolonged periods of immobilization, through the promotion of muscle protein synthesis.[7] Despite the potential of NMES to improve muscle strength and mass, there is a general lack of agreement regarding efficacy.[8] A main limitation of NMES for stimulating strength and hypertrophy is that the degree of adaptation is directly correlated with the electrical current intensity (leading to stronger contractions), yet the level of current intensity necessary to cause muscle contractions effective at increasing strength and hypertrophy are highly uncomfortable and prohibitively painful.[9] The discomfort caused by the use of a high-intensity electrical stimulus could conceivably be overcome without sacrificing efficacy by combining a relatively low-intensity electrical stimulus with BFR. The combined, and perhaps synergistic, effect of these 2 stimuli and the relative contribution of electrical stimulation and BFR have not been thoroughly investigated.

A recently published study investigated the effects of low-intensity NMES combined with BFR to alter muscle size and strength and provided preliminary evidence of potential efficacy. They found a low-intensity NMES training exposure of twice daily, 5 days per week for a duration of 2 weeks induced muscular mass and a concomitant increase in isometric and isokinetic strength, when combined with BFR.[10] Although valuable in many contexts, especially as a proof of concept, this particular protocol may have less direct application in traditional rehabilitative practice or for other training purposes wherein the frequency of training cannot occur multiple times per day. Therefore, the aim of this study was to examine if BFR combined with electrical muscle stimulation was effective for improving muscle strength and mass using a design that closely reflects training practices applicable to "real-world" training and rehabilitation. Second, the individual components of BFR and NMES were tested against the combined stimulus and a control. We hypothesize that the combination of BFR and NMES

will lead to greater muscular strength and mass gain than either of these interventions in isolation.

Methods

Design

Subjects had each leg randomly assigned to 1 of 4 possible interventions, in which dominant/nondominant legs were counterbalanced among these groups. Thus, for each 2-legged individual, his or her leg was randomized into 1 intervention group, while his or her other leg was randomized into another. The intervention groups were (1) BFR + NMES combined (COMB), (2) NMES in isolation, (3) BFR in isolation, and (4) control (CON). Each of the subject's legs were exposed to their respective experimental condition in the laboratory 4 days per week for a total of 6 weeks, with each session lasting approximately 32 minutes. Each participant trained on the same days each week at approximately the same time each day for the duration of the study.

Participants

Twenty participants (10 males and 10 females) were recruited from a population of healthy young adults between the ages of 18 and 45 years. Both participant's legs were randomly assigned to 2 of 4 possible intervention groups, as described below. Many participants had athletic backgrounds, but none were currently in a competitive season and were only recreationally active. The participants were instructed to maintain their habitual physical activity, with no participants being engaged in any specific training for an athletic event ≥6 months prior to the study. The study was approved by the research ethics board of the University of Prince Edward Island, Prince Edward Island, Canada and all participants signed written informed consent prior to participation, in accordance with the Declaration of Helsinki.

Procedures

The BFR intervention group was accomplished using an automated tourniquet system (Zimmer Automated Tourniquet System 1500 model; Soma Technology Inc, Bloomfield, CT) with periodic inflation to 220 mm Hg. An individual intervention session comprised of 3 cycles of 4-minute inflation, 4-minute deflation. The tourniquet system employed 10.2-cm cuffs of varying circumference for individual fit to each participant's leg size, with cotton sleeves worn under the cuffs to prevent soft tissue damage. The cuff was positioned at the proximal end of the leg just distal to the inguinal crease and gluteal fold. A cuff pressure of 220 mm Hg was employed to ensure an effective restriction of blood flow, which was confirmed using near-infrared spectroscopy (MOXY, Hutchinson, MN) with most individuals reaching 0% muscle oxygen saturation within <1 minute of cuff inflation. Full restriction was chosen, as it is believed full restriction of blood flow and the subsequent reperfusion of blood flow are both involved in the BFR effect. Standard NMES stimulation was applied to the quadriceps. Two electrodes (5 cm^2) were placed on the vastus lateralis and vastus medialis at a distal and proximal position that best elicited a muscular contraction. This position was optimized for each NMES session. Stimulation was applied using a pulse train length of 400 μs, delivered at a stimulation frequency of 50 to 100 Hz, and at a maximally tolerable intensity (amplitude) for the individual.[11] The COMB condition employed both modalities simultaneously, while the control condition used neither.

To assess the efficacy of the BFR, NMES, and COMB intervention on the quadriceps, muscular strength, and hypertrophy were measured at week 0 and week 6 (Figure 1). Assessment of post intervention muscular strength and hypertrophy were measured 24 to 72 hours after the last intervention session.

Muscular strength was assessed using a custom-designed leg strain measurement device with a high-sensitivity strength gauge. The leg strain measurement device was developed by biomedical engineers (University of New Brunswick, Fredericton, Canada) to test isometric strength of the quadriceps muscles. Participants performed 3 isometric contractions, with a 90° hip angle and their knee at 45° knee flexion while force (in kilograms) was recorded. The force sensor was standardized to the midpoint of the tibia for each measurement. Participants preformed 3 consecutive leg extensions during testing, with each extension lasting 3 seconds followed by 3 seconds of relaxation. Each consecutive extension was approximately 2 times stronger than the previous with the third extension encouraged to be at maximum. Visual feedback was provided to the participants of the force they produced during contractions. This test was repeated twice for each leg with a 1-minute rest between tests. The greater of the 2 trials was considered as the maximal voluntary contraction. Simultaneous measures of electromyography were recorded for verification of maximum with repeated tests to ensure similar or greater recruitment with consecutive trials.

Muscle mass was quantified in grams of tissue using dual-energy X-ray absorptiometry using the fan-beam technology (model QDR 4500A; Hologic, Waltham, MA) at the local medical imaging department (QEH, Charlottetown, Canada). Muscle mass of the thigh was assessed, and the upper and lower margins were defined as the ischial tuberosity and knee joint, respectively. All scans were performed according to hospital protocol by the licensed technician, and a calibration phantom was run each day a scan was acquired.

Statistical Analyses

Alterations in muscle strength and size were calculated as difference scores (delta) between week 0 and week 6 for each leg. Deltas were tested using 1-way analysis of variance to determine if groups differed substantially in their adaptive response compared with control and compared with one another. The precise between-group differences were compared using post hoc Tukey–Kramer tests. Response rates were calculated per group by summing the number of individual positive responders using predefined lowest measurable changes of >1 kg increase in strength and >1 g lean mass. All calculations were made with SPSS statistical software package v.21.0 (SPSS Inc, Chicago, IL). Significance for all tests was set, a priori, at an alpha of $P < .05$.

Results

The physical characteristics of 19 study participants (n = 38 total legs tested) who completed the entirety of the 6-week intervention are displayed in Table 1. One participant did not complete the entire 6 weeks and subsequently withdrew for reasons unrelated to the study.

Mean differences in quadriceps muscle strength, separated by intervention group, are presented in Figure 2 with maximal strength values in Table 2. There were no differences between groups at baseline (week 0) for muscle strength. A difference in intervention response was observed between groups ($P = .03$), with post hoc

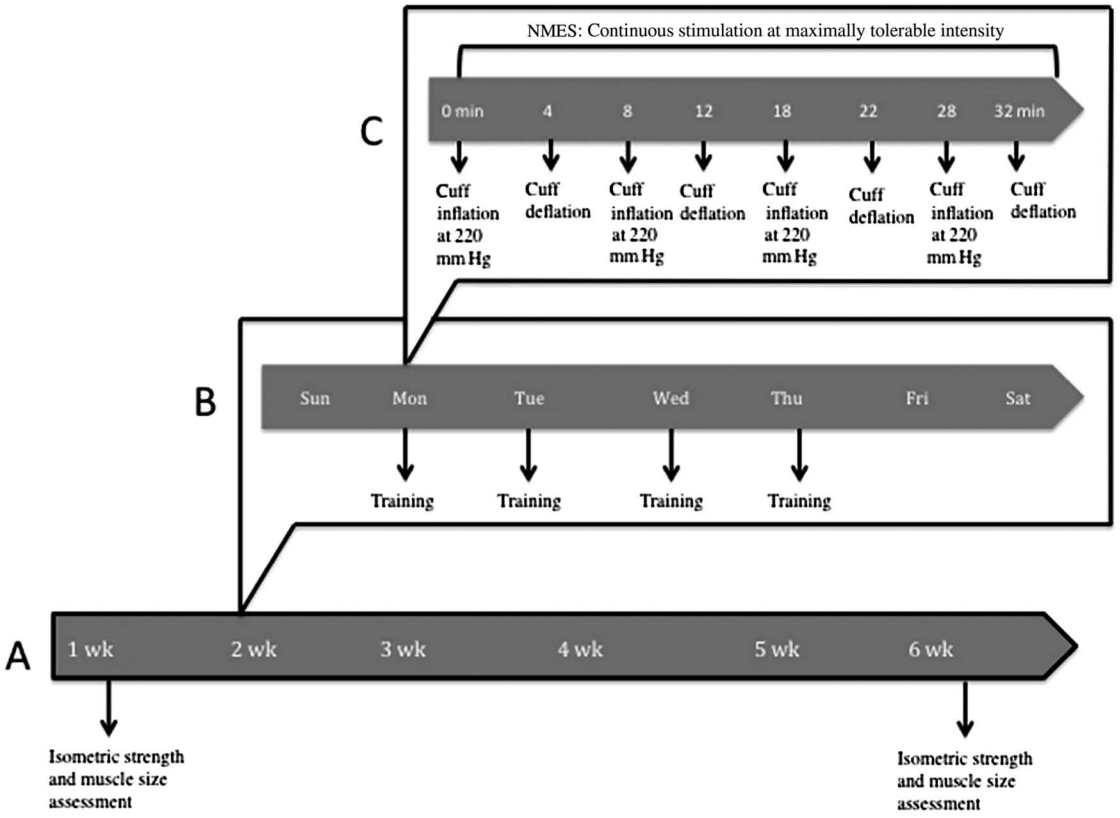

Figure 1 — Timeline demonstrating the experimental protocol during a 6-week study of electrical muscle stimulation and blood flow restriction (BFR) on muscular adaptation. Level A displays how assessments of isometric strength and muscle size were completed at week 0 and week 6. Level B outlines the weekly training schedule of 4 consecutive days per week. Training days were not the same for each subject. Level C illustrates a training session involving 4 minutes of BFR at a cuff inflation of 220 mm Hg followed by 4 minutes of cuff deflation and a restoration of blood flow. This cycle repeated 4 times to complete a 32-minute training session. Neuromuscular electrical stimulation (NMES) was applied continuously for the entire training session.

Table 1 Physical Characteristics of Subjects Who Participated in a 6-Week Study to Examine the Effects of Combining Blood Flow Restriction With Low-Intensity Neuromuscular Electrical Stimulation on Skeletal Muscle Adaptation

	Age, y	Height, cm	Weight, kg	BMI, kg/m^2
Overall	24 (6)	174 (10)	77 (17)	23 (3)
Range	18–45	158–192	50–109	20–30
Males	22 (2)	182 (5)	83 (12)	25 (2)
Females	25 (8)	165 (3)	57 (5)	21 (2)

Abbreviation: BMI, body mass index.

analysis confirming the only difference between the COMB group and CON ($P = .02$). The isolated BFR and isolated NMES groups were not significantly different from each other or any other group. When analyzing the individualized responses in each group, the COMB and NMES group both had 100% responders (>1 kg increase), while the isolated BFR and CON group had 60% and 30% responders, respectively.

Mean differences in quadriceps muscle mass, between week 0 and week 6, for each group are shown in Figure 3, with pre and post muscle mass by intervention group in Table 2. There were no differences between groups at baseline (week 0) for muscle mass. There was no significant difference in leg muscle size by group, although a trend ($P = .07$) was apparent for change scores. Using the cut point of >1 g increase in muscle mass to represent a responder revealed 70% of the COMB group qualified as responders, while 60% of the isolated NMES group responded. The isolated BFR and CON group had 30% and 20% of participants respond, respectively.

Discussion

This investigation confirms that external blood flow manipulation has the capacity to improve the efficacy of passive low-intensity muscle contractions and result in a change in training response using ecologically valid and applicable training models. A primary finding of this study is that a combination of BFR and low-intensity

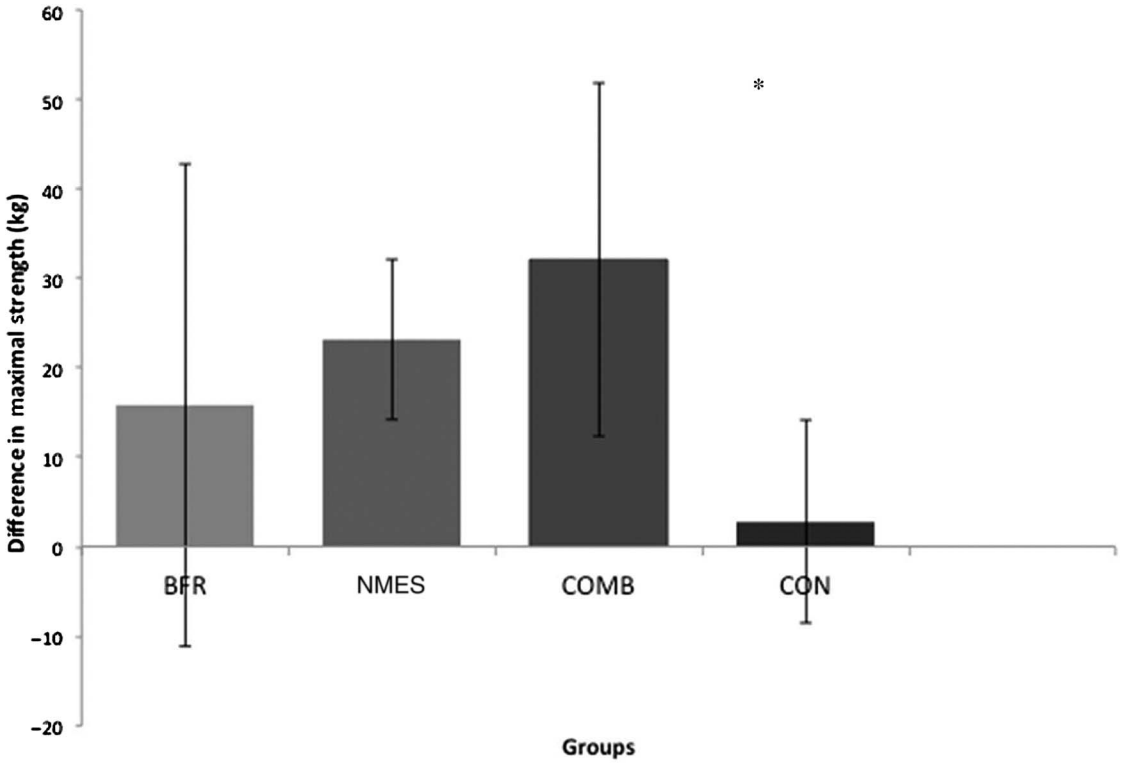

Figure 2 — Differences in maximum strength (in kilograms) of the quadriceps muscle, following 6 weeks of stimulation with either NMES alone, BFR alone, or COMB. Error bars represent SD. CON indicates the control group who did not receive any stimuli; BFR, blood flow restriction; COMB, combination of the 2 stimuli; NMES, neuromuscular electrical stimulation. *Significant difference at $P < .05$.

Table 2 Mean (SD) Maximum Strength (in Kilograms) and Muscle Size (in Grams) of the Quadriceps Muscle, Pre and Post 6 Weeks of Stimulation With Either NMES Alone, BFR Alone, or COMB

	Maximal strength, kg		Muscle hypertrophy, g	
	Pre	Post	Pre	Post
BFR				
Total	167 (46)	183 (50)	9313 (2310)	9418 (2300)
Males	194 (27)	206 (31)	11,045 (1017)	11,169 (855)
Females	126 (37)	142 (49)	6716 (734)	6790 (790)
NMES				
Total	141 (44)	159 (43)	9311 (2551)	9391 (2427)
Males	175 (30)	187 (18)	11,339 (1943)	11,435 (1518)
Females	107 (26)	132 (32)	7283 (1009)	7345 (1054)
COMB				
Total	136 (38)	168 (53)	9139 (2284)	9234 (2256)
Males	159 (28)	201 (41)	10,562 (1584)	10,630 (1468)
Females	103 (20)	117 (22)	7004 (1301)	7139 (1476)
CON				
Total	127 (38)	130 (29)	7385 (1840)	7384 (1738)
Males	153 (34)	142 (34)	10,089 (1036)	9956 (1108)
Females	111 (26)	110 (12)	6304 (467)	6356 (196)

Abbreviations: BFR, blood flow restriction; COMB, combination of the 2 stimuli; CON, control group who did not receive any stimuli (n = 19, $P > .05$ pre vs post); NMES, neuromuscular electrical stimulation.

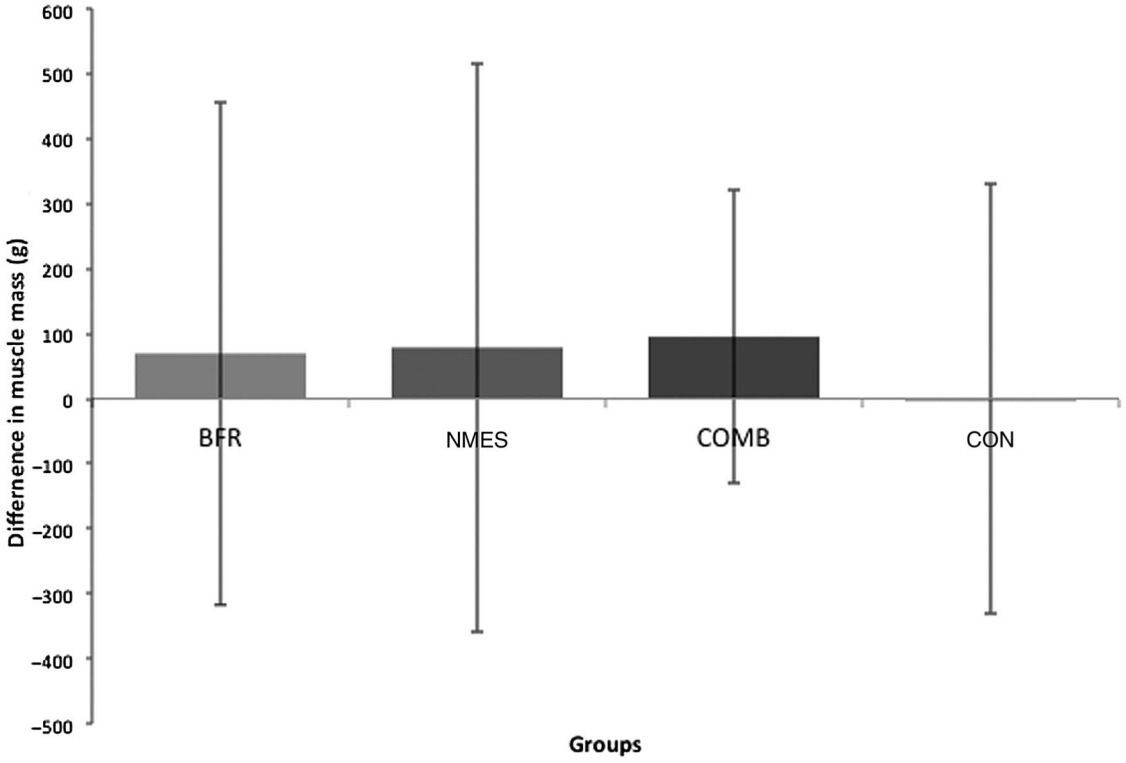

Figure 3 — Differences in quadriceps muscle mass (in grams), following 6 weeks of stimulation with either NMES alone, BFR alone, or COMB. Error bars represent SD. CON indicates the control group who did not receive any stimuli; BFR, blood flow restriction; COMB, combination of the 2 stimuli; NMES, neuromuscular electrical stimulation.

NMES stimuli led to strength gains that were significantly improved from the nontrained control.

A previous study examining the combined effects of NMES and BFR on wrist extensors in individuals with incomplete tetraplegia saw an increase in wrist extensor cross-sectional area after 6 weeks of twice weekly training.[12] The current study observed a lack of statistically significant differences in alterations of muscular mass between and within groups, suggesting no significant effect of any of the interventions for inducing hypertrophy in a period of 6 weeks. Despite this, it is possible that an effect is masked by the relatively large variance in the data. The COMB group experienced an absolute increase in quadriceps mass of 32 g, yet this magnitude of muscle mass change appears to be much lower than typical training modalities. Previous work examining changes in quadriceps mass, using the same measurement method, after 8 weeks of bilateral high-intensity isokinetic knee extensor training, found an absolute change in quadriceps mass of 224 g.[13] Another study that examined changes in quadriceps mass after 6 weeks of isolated NMES only training observed only a 13 g increase in quadriceps muscle mass and was not a significant change from baseline.[14] This is only half of the change in muscle mass observed in the present study that combined NMES with BFR. It is interesting to note, however, that 10% more individuals in the COMB group demonstrated a response in mass compared with isolated NMES, and far fewer positive responses were observed in isolated BFR or the CON groups. This may suggest that it is the combination of both BFR and NMES that affects gains and not just the methods on their own.

Previous work examining strength changes in the quadriceps over a similar duration of 6 weeks of 5 days per week isolated NMES training[15] found only a 10 kg increase in quadriceps strength (on par with the 16 kg increase in the isolated NMES only group) again demonstrating a far greater efficacy in the current trial when combined with BFR. Despite differences in the exposure to this novel stimulus, these results support those of Natsume et al[10] who were the first to show the efficacy of NMES to alter muscular adaptation is augmented by occluding blood flow. This also supports our hypothesis that, similar to what has been observed for low-load dynamic resistance exercise,[6,16] the adaptive response to low-intensity NMES stimulus is amplified when combined with BFR. The percentage of participants in each group that responded to the stimuli offers some insight into the possible phenomena of physiological responders and nonresponders, which may be a consideration for use of this methodology with select training populations, and is useful for interpretation owing to the large response variability about the group mean. Although it is possible, as suggested by Ross et al,[17] that increasing the stimulus intensity, volume, or frequency may result in fewer nonresponders.

Despite intentional differences in training frequency, which we employed to test BFR and NMES in an ecologically valid and readily applicable model, the total training volume was similar when comparing our study with that of Natsume et al.[10] Our group used 24 training sessions (20 min of total BFR), while Natsume employed 20 training sessions (25 min of total BFR). Despite this, the effect size for changes in maximal strength of 0.64 from the Natsume study was smaller than the 0.84 observed in the present study. Analogous to this finding, a meta-analysis by Loenneke et al[16] has shown that muscle strength and hypertrophy were both significantly greater in exercise training groups that performed BFR exercise 2 to 3 days per week compared with those who exercised 4 to 5 days per week. The authors suggest that such a

response occurred as a result of the increased frequency of daily training rather than days trained per week, as 4 out of 7 studies in the 4 to 5 days per week group trained twice per day. A similar dose–response effect could be at play here as well, and such a phenomenon could have important implications for the optimization of BFR electromyostimulation for use in rehabilitation or other training environments. This potential insight into increased efficacy with a lower daily exposure is an important contribution to the literature from the present investigation that warrants confirmation.

This study provides evidence for the efficacy of a combined stimulus of electrical muscle stimulation and BFR, for altering muscle strength, while the ability to induce hypertrophic adaptation remains unclear. Improved muscular strength represents an important finding that is a novel and exciting concept with much potential for application in the areas of rehabilitation. This novel combination of common therapeutic modalities into a single assistive rehabilitative device has the potential to practically assist in the maintenance and rehabilitation of skeletal muscle in postsurgery patients, preventing excess muscle atrophy during long periods of immobilization. In addition to providing a tool in early rehabilitation that requires no load bearing, this method could also serve as a supplementary training tool, providing athletes the opportunity to undergo additional strength training in nonideal training environments with less risk of injury and no cardiovascular fatigue.

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