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SHORT COMMUNICATION

Mechanisms mediating increased endurance following high- and low-load training with and without blood flow restriction

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Objectives: To determine if different mechanisms, i.e., changes in one-repetition maximum (1RM) strength (Δ1RM) or vascular conductance (ΔVC), mediate changes in endurance (ΔEND) following training with 70% 1RM (70/0), 15% 1RM (15/0), and 15% 1RM with blood flow restriction using 40% (15/40) or 80% (15/80) arterial occlusion pressure.

Design: Secondary analysis of data from a previous training intervention study.

Method: Previously, 39 participants trained 2x/week for 8 weeks (4 sets of knee extensions to momentary failure) with 2 of the 4 aforementioned conditions (randomized, 1 per leg). VC, 1RM, and END were tested pre/post-training. A two-wave multiple-mediator model (adjusted for baseline values of 1RM, VC, and END) was constructed to evaluate direct and indirect effects of training on ΔEND (relative to other conditions) with Δ1RM and ΔVC as mediators. Results presented as coefficients (95%CI).

Results: The model accounted for 35.3% ($p < .001$) of the variance in ΔEND. Relative direct effects on ΔEND did not differ across conditions (all $p > .231$). There was an effect of Δ1RM on ΔEND [0.5 (0.0,0.9) repetitions] and evidence that Δ1RM mediated the effect on ΔEND for 70/0 compared to other conditions [vs. 15/0 = 1.4 (0.1,2.9); 15/40 = 1.4 (0.1,2.7); 15/80 = 1.1 (0.1,2.3) repetitions]. There was no evidence of a relationship between ΔVC and ΔEND [0.02 (-0.10,0.13) repetitions] nor of relative indirect effects through ΔVC when comparing conditions.

Conclusions: Differences in Δ1RM translate to increased endurance in the 70/0 condition compared to other conditions, however, differences in ΔVC did not appear to mediate increased endurance across the conditions.

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Key words: vascular conductance ■ capillarity ■ venous occlusion

INTRODUCTION

Low-load resistance exercise combined with blood flow restriction (BFR) is effective for inducing muscle growth, increasing strength, and improving outcomes for physical function.[1] Muscular endurance has also been shown to increase after resistance training with and without BFR,[2] but it is not known if the underlying mechanisms leading to increased endurance differ between modalities.

Recently, Jessee et al.[2] reported increased endurance, measured by one set of unilateral knee extensions to momentary failure at 42.5% of one repetition maximum (1RM), following 8-weeks of training across four different loading and BFR conditions. Although endurance improved after training with all conditions, differences in relative loads (15% versus 70% 1RM) and restriction pressures (0%, 40%, and 80% arterial occlusion pressure (AOP)) likely varied the stimulus across conditions.[3] This could mean that different adaptive mechanisms played a role in improved endurance between conditions. If this is the case, identifying the adaptive mechanisms from each training modality would be valuable for exercise prescription.

One adaptation that could improve endurance performance is increased muscle capillarity. Capillaries are crucial for oxygen transport and are related to the level of metabolic stability achievable.[4] In untrained individuals, muscle capillary density is strongly correlated with the number of repetitions one can complete (i.e., endurance) at 70% 1RM.[5] Furthermore, muscle capillarity has been shown to increase following resistance training with[6] and without[7] BFR. In the same group of participants from the study by Jessee et al.,[2] significant increases in

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vascular conductance (VC), a non-invasive estimate of capillarity, occurred in 70% 1RM and 15% 1RM with 80% AOP training conditions only,[8] suggesting that improved endurance via vascular changes could require high loads, or low loads combined with high BFR pressures.

Additionally, high-load training leads to increased dynamic maximal strength, which may reduce the muscle mass required to lift an absolute submaximal load,[9] subsequently improving endurance. Assuming that the active muscle mass reflects the size principle of motor units, the same absolute submaximal load may be lifted by motor units that are lower in the recruitment hierarchy after a period of high-load training.[10] Reliance on less total muscle mass, comprised of smaller motor units and possibly more efficient muscle fibers,[11] may be related to improvements in muscular work efficiency that have been shown after a period of high-load training.[10, 12] These changes in motor unit activity could also reserve more muscle mass to be progressively recruited for sustaining force as fatigue develops,[13] resulting in improved endurance. In the study by Jessee et al.,[2] increased 1RM compared to baseline was observed after high load training but not after low-load training with and without BFR.

The purpose in conducting this secondary analysis was to investigate whether changes in VC and 1RM mediate improved endurance in a condition-specific manner. We constructed a multiple-mediator model to evaluate the direct and indirect effects of training on changes in endurance (ΔEND) with changes in vascular conductance (ΔVC) and 1RM (Δ1RM) as mediators.

METHODS

Training Protocol

A detailed description of the training protocol is available elsewhere.[2] Briefly, 39 previously untrained participants trained their knee extensors two times per week for eight weeks with two of four training conditions (one condition randomized to each leg): 70% 1RM alone (70/0), 15% 1RM alone (15/0), and 15% 1RM combined with BFR using 40% (15/40) or 80% AOP (15/80). Although there was no control condition, the 70/0 condition was used as a reference due to being the traditionally recommended mode of resistance training. Participants performed 4 sets of knee extension exercise separated by 90 s (70/0) and 30 s (15/0, 15/40, 15/80) rest to volitional failure or a maximum of 90 repetitions.

Pre/Post Measures of Vascular Conductance, Strength, and Endurance

Within one lab visit at both pre- and post-training time points, measures of VC were taken followed by 1RM, and END, respectively. Calf vascular conductance was measured for each leg using strain gauge plethysmography. A detailed description of measurement procedures is available elsewhere.[8] The original study design did not include measurement reliability, however, previous work suggests that venous strain gauge plethysmography was reliable (CV = 4.0%).[14] Unilateral knee extension 1RM was measured by finding the highest load that each participant could lift from 90° knee flexion to full extension.[2] Endurance was measured by asking participants to perform one set of unilateral knee extensions to volitional failure at 42.5% of pre-training 1RM for each leg at a 2 second cadence. The set was terminated if participants could no longer complete full range of motion or keep pace with the metronome. 42.5% 1RM, the midpoint between 15% 1RM and 70% 1RM, was chosen to avoid biasing the test toward either relative training load.[2]

Statistical Analysis

To evaluate the direct and indirect effects of training on ΔEND (relative to other conditions), with ΔVC and Δ1RM as mediators, a two-wave (i.e., mediator variables and dependent variable were measured pre- and post-training) multiple-mediator model was constructed using the PROCESS 3.5 macro for SPSS.[15,16] To account for their possible influence on an individual's potential for change, pre-training values for 1RM, VC, and END were used as covariates in the model when comparing direct and indirect effects of training conditions on Δ1RM, ΔVC, and ΔEND, respectively. All coefficients for between group comparisons are provided relative to 70/0 (traditional resistance training) unless otherwise noted. The model was recoded and run multiple times with each condition as the reference to ensure all potential comparisons were made. Interpretations of the coefficients from each model path are listed in Table 1. Because each participant contributed observations in two of the four possible training conditions, a supportive analysis was conducted to examine the impact of the non-independence of observations created by the study design. For this analysis, cluster robust standard errors were computed using the TYPE = COMPLEX option, MLR estimator, and the CLUSTER option in Mplus. For the relative indirect effects, parameter estimates and these cluster robust standard errors were used to create Monte Carlo confidence intervals[17] using the MCMED macro.[15] All values are reported as regression coefficients (95% CI) unless otherwise noted (Table 1). Statistical significance was determined if $p \leq .05$.

RESULTS

Relative Effect of Condition on Change in Strength

As demonstrated by Jessee et al.,[2] a significant increase in 1RM from baseline was only observed in 70/0. For the current analysis, comparison of the adjusted mean differences revealed that relative to 70/0, the Δ1RM for 15/0, 15/40, and 15/80 were significantly lower (all $p < .001$; Table 1), but Δ1RM's for 15/0, 15/40, and 15/80 were not statistically different from each other (all $p \geq .404$).

Relative Effect of Condition on Change in Vascular Conductance

As previously reported,[8] significant increases in VC from baseline were observed in 70/0 and 15/80, but not 15/0 or 15/40. Examination of adjusted mean differences revealed that relative to 70/0, ΔVC was lower for 15/0 and 15/40 (both $p < .023$), but not 15/80 ($p = .802$; Table 1). The adjusted mean ΔVC for 15/80 was greater than 15/0 and 15/40 (both $p < .012$;

Table 1 Estimated regression coefficients for the multiple-mediator model

Dependent Variable	R^2	Sub-Path	Antecedent	Coefficient	Units	95% CI	p value
Δ1RM	0.235						< .001
		a_{11}	15/0 vs. 70/0	-3.087	kg	-4.578, -1.597	< .001
		a_{12}	15/40 vs. 70/0	-3.010	kg	-4.541, -1.479	< .001
		a_{13}	15/80 vs. 70/0	-2.460	kg	-3.951, -0.969	< .001
		constant		3.256	kg	1.013, 5.500	< .001
ΔVC	0.238						< .001
		a_{21}	15/0 vs. 70/0	-7.571	mL/mmHg	-13.403, -1.738	.012
		a_{22}	15/40 vs. 70/0	-7.000	mL/mmHg	-13.014, -0.986	.023
		a_{23}	15/80 vs. 70/0	0.731	mL/mmHg	-5.060, 6.521	.802
		constant		13.287	mL/mmHg	6.791, 19.783	< .001
ΔEND	0.353						< .001
		c'_1	15/0 vs. 70/0	0.306	repetitions	-2.958, 3.571	.852
		c'_2	15/40 vs. 70/0	1.828	repetitions	-1.495, 5.152	.276
		c'_3	15/80 vs. 70/0	1.860	repetitions	-1.210, 4.930	.231
		b_1	Δ1RM	0.453	repetitions	0.002, 0.904	.049
		b_2	ΔVC	0.015	repetitions	-0.097, 0.126	.792
		constant		13.351	repetitions	9.293, 17.410	< .001
Indirect Effects							
Mediator: Δ1RM DV: ΔEND		$a_{11}*b_1$	15/0 vs. 70/0 → Δ1RM	-1.399	repetitions	-2.863, -0.099#	
		$a_{12}*b_1$	15/40 vs. 70/0 → Δ1RM	-1.364	repetitions	-2.668, -0.107#	
		$a_{13}*b_1$	15/80 vs. 70/0 → Δ1RM	-1.115	repetitions	-2.312, -0.081#	
Mediator: ΔVC DV: ΔEND		$a_{21}*b_2$	15/0 vs. 70/0 → ΔVC	-0.112	repetitions	-1.013, 0.840#	
		$a_{22}*b_2$	15/40 vs. 70/0 → ΔVC	-0.104	repetitions	-0.932, 0.768#	
		$a_{23}*b_2$	15/80 vs. 70/0 → ΔVC	0.011	repetitions	-0.254, 0.630#	

a_{11}, a_{12}, a_{13} = adjusted mean difference in Δ1RM between each condition and 70/0, a_{21}, a_{22}, a_{23} = adjusted mean difference in ΔVC between each condition and 70/0, c'_1, c'_2, c'_3 = adjusted relative direct effect of each condition on ΔEND compared to 70/0, b_1 = adjusted effect of Δ1RM on ΔEND, b_2 = adjusted effect of ΔVC on ΔEND, $a_{11}*b_1$, $a_{12}*b_1$, $a1_3*b_1$ = adjusted relative indirect effect of each condition on ΔEND through Δ1RM compared to 70/0, $a_{21}*b_2$, $a_{22}*b_2$, $a_{23}*b_2$ = adjusted relative indirect effect of each condition on ΔEND through ΔVC compared to 70/0. #Indicates percentile bootstrap 95% CI (5,000 draws).

Table 1), which were not significantly different from each other (p = .849).

Relative Effect of Condition on Change in Endurance

Overall, the model accounted for 35.3% (p < .001, Table 1) of the variance in ΔEND. Significant increases in END from baseline were observed in all conditions,[2] but in the current analysis there was no evidence of any adjusted mean differences on ΔEND among the conditions (i.e., none of the relative direct effects on ΔEND, c'_1, c'_2, c'_3, were statistically significant (omnibus test p = .475).

Endurance Mediation by Δ1RM and ΔVC

There was an effect of Δ1RM on ΔEND (p = .049), however, there was no effect of ΔVC on ΔEND (p = .792; Table 1). The relative indirect effects of training condition on ΔEND through Δ1RM provided evidence that training condition's effect on ΔEND was mediated by Δ1RM (i.e., the 95% CIs do not contain 0). Relative to 70/0, the indirect effects of training condition on ΔEND through Δ1RM were lower for 15/0, 15/40, and 15/80 (Table 1). The relative indirect effects of training condition on ΔEND through Δ1RM were not different among the 15/0, 15/40, and 15/80 conditions.

The relative indirect effects of training condition on ΔEND through ΔVC suggest no clear indication of mediation by ΔVC (i.e., the 95% CIs contain 0). Relative to 70/0, the indirect effects of training condition on ΔEND through ΔVC were not different for 15/0, 15/40, or 15/80 (Table 1). The relative indirect effects of training condition on ΔEND through ΔVC were not different among the 15/0, 15/40, and 15/80 conditions.

Supportive analysis

The supportive analysis, which accounted for the non-independence of observations created by the study design, indicat-

ed very consistent findings. Inferences for the relative indirect effects did not change when using cluster robust standard errors coupled with Monte Carlo confidence intervals, suggesting that the primary findings were robust to this alternative modeling approach.

DISCUSSION

The main finding of this analysis was that training-induced increases in dynamic strength mediated changes in endurance for the 70/0 condition relative to the 15/0, 15/40, and 15/80 conditions, but not when comparing these other conditions. Increased vascular conductance did not appear to mediate changes in endurance when comparing any of the conditions. This analysis supports the idea that some of the adaptive mechanisms that increase endurance are potentially different depending on the load used in training.

Adaptive mechanisms from high-load training (70/0) that increased dynamic strength appear to have played a role in improving endurance capacity at 42.5% 1RM, but these changes may not have occurred in 15/0, 15/40, and 15/80 conditions given that increased dynamic strength was not observed.[2] The adaptive mechanisms from high-load training could have included neural, structural, and chemical changes,[18] potentially leading to fewer active motor units for the given absolute submaximal force output.[9] This could have delayed the involvement of larger, more fatigable, and less efficient motor units[11] and reserved a greater portion of the muscle mass for recruitment as smaller motor units fatigued, subsequently improving endurance in the 42.5% 1RM test. Future research designed to evaluate shifts in motor unit recruitment during exercise following high-load training may provide more insight into how the adaptive mechanisms from increased strength may lead to improved muscle endurance performance.

Increased vascular conductance in 70/0 and 15/80 did not mediate improved endurance. This was somewhat unexpected, however, there are several possible reasons why the data might not have supported this idea. First, while vascular conductance measures are related to muscle capillarity, they are not a direct measure of muscle capillarity. Conversely, training-induced changes in muscle capillarity may not have played a significant role in improved endurance. Although a relationship between capillarity and endurance at 70% 1RM exists at baseline in untrained individuals,[5] this could be influenced by other factors, and training-induced increases in capillarity may not be important for increased endurance with higher loads. As muscle force production increases with higher loading, blood flow through the muscle is reduced as the vasculature becomes compressed.[19, 20] Consequently, increased capillarity might not be beneficial for endurance when loading is high enough to cause a level of vascular compression that impedes blood flow. In support of this idea, muscle tissue re-oxygenation in the knee extensors has been shown to stop at 25-35% of MVC, suggesting that this relative force could be enough to deprive the muscle of blood flow.[19] Although the 42.5% 1RM test used in the current study consisted of dynamic and not isometric contractions, this load could elicit intramuscular pressures that are high enough to negate the benefits of increased capillarity, despite the greater potential for oxygen delivery. Including low-load endurance testing may be helpful in future research to understand if changes in capillarity may play a role in increased endurance in a load-dependent manner, and it may also be helpful in understanding what changes may have occurred that led to increased endurance in 15/0, 15/40, and 15/80.

Limitations

There are several limitations that affect the application of these findings. There are many other measurement variables that may mediate endurance which were not included in the model as data was not available for secondary analysis. Likewise, it should be considered that these findings can only be applied to endurance for resistance exercise with moderate loads, since a low load test was not used or included for analysis. The exact increase in repetitions for 70/0 through increased strength cannot be determined from this analysis, it can only be said that this relative indirect effect was significantly greater compared to other conditions.

CONCLUSION

Increased strength seems to be one mechanism by which high-load training can translate to improved endurance. Resistance training induced changes in vascular conductance did not appear to mediate increases in endurance, and future research is necessary to determine how resistance training with lower loads leads to better endurance outcomes.

Conflict of Interest

The authors report no relationships that could be construed as a conflict of interest.

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