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**Section:** Original Investigation

**Article Title:** Dose-Response of Weekly Resistance Training Volume and Frequency on Muscular Adaptations in Trained Males

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**RUNNING HEAD:** Training volume for muscle remodeling

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## ABSTRACT

**Purpose:** A linear dose-response relationship between resistance training (RT) volume and hypertrophy/strength has been proposed when  $\leq 10$ -12 weekly sets are implemented. The present study aimed to understand the impact of low-to-high weekly RT volume on muscular adaptations in trained young males over 6-weeks of RT. **Methods:** RT-experienced males ( $n=49$ ) were randomly allocated to a LOW ( $n=17$ ), moderate (MOD;  $n=15$ ) or HIGH ( $n=17$ ) volume group, performing 9, 18 or 27 weekly sets of biceps RT, respectively, for 6-weeks. RT was performed once (LOW) or twice (MOD and HIGH) weekly. Post-exercise protein intake was controlled with both dietary intake and external training volume recorded. Prior-to and following RT, assessments of biceps muscle thickness (MT) via ultrasound, isometric and one repetition maximum (1RM) strength were performed. Data were analyzed using one-way ANOVA (baseline characteristics) and repeated measures ANOVA (within and between group pre-to-post change) **Results:** MT significantly increased in all groups ( $4.3 \pm 7.9\%$ ,  $9.5 \pm 11.8\%$  and  $5.4 \pm 6.3\%$  for LOW, MOD, HIGH, respectively,  $p < 0.05$ ) as did 1RM strength ( $p \leq 0.001$  for all). Isometric strength increased significantly in HIGH only ( $8.5 \pm 15.1\%$ ,  $p < 0.05$ ). There were no significant differences between groups in MT or indices of strength. However, effect size estimates revealed the magnitude of response was 'moderate-to-large' for MOD and HIGH when compared with LOW. **Conclusion:** Our findings demonstrate that 9 weekly sets of biceps-focused RT, performed in one weekly session, is sufficient to increase MT, whilst 18-27 sets, performed over two weekly sessions, may confer greater strength increases.

## INTRODUCTION

Skeletal muscle is pivotal in the maintenance of a healthy lifestyle <sup>1</sup>, favouring preservation and/or accretion of muscle mass, strength and power. The most potent, non-pharmacological, stimulus inducing skeletal muscle hypertrophy and strength is resistance training (RT). Mechanical tension and metabolic stress induced by RT are thought to activate intramuscular signalling pathways, leading to increased protein translational efficiency and muscle mass accretion over time <sup>2,3</sup>. Although muscle mass accretion may explain some of the increase in strength and power with RT, neural adaptations are thought to play a more prominent role<sup>4</sup>. Manipulation of RT variables such as intensity <sup>5</sup>, volume <sup>6</sup>, frequency <sup>7</sup>, inter-set rest period <sup>8</sup>, contraction type <sup>9</sup> and time-under-tension <sup>10</sup> can alter the intracellular signalling and muscle protein synthesis (MPS) response to RT <sup>11</sup>. Thus, understanding how the manipulation of RT variables can maximize muscle hypertrophy is important for evidence-based practical recommendations.

RT variables thought to be particularly important for maximizing muscle hypertrophy and strength are volume, defined as the product of sets by repetitions by load or the number of weekly sets per muscle group <sup>12</sup> and frequency. Meta-analyses indicate that moderate-to-high weekly RT volumes may elicit marginally greater strength gains than low weekly RT volume, and that increasing RT frequency is one way to achieve this stimulus <sup>13,14</sup>. For muscle hypertrophy, a RT frequency of two times per week has been suggested to be superior to one weekly session (when total volume is matched) <sup>7</sup>. However, the optimal RT volume and frequency to maximize muscle hypertrophy and strength remains unclear. Several potential relationships between RT volume and skeletal muscle hypertrophy/strength have been postulated: i) a dose-response relationship where gradual increases in weekly RT volume lead to a greater increase muscle mass and strength <sup>6</sup>, ii) an inverted-U relationship whereby increasing weekly RT volume beyond a certain threshold negatively impacts skeletal muscle

accretion<sup>12</sup>, iii) no relationship between weekly RT volume and muscle hypertrophy or strength<sup>15-17</sup>. To date, research has failed to identify the optimal RT volume per muscle group to maximize muscle hypertrophy and strength. Furthermore, the existing body of research has focussed on muscular adaptations to relatively low-volume RT ( $\leq 10$ -12 weekly sets), highlighting a clear need to investigate this relationship at much higher weekly RT volumes ( $>10$ -12 weekly sets)<sup>6</sup>.

The failure to identify weekly RT volume dose to maximize muscular adaptations is also likely to be a consequence of experimental design nuances and control measures. For example, many previous studies have been performed in small cohorts of RT novices. Extrapolating meaningful interpretations from untrained to trained individuals is problematic, as untrained individuals may experience neural modifications<sup>18</sup> and an extended MPS response to acute RT<sup>19-21</sup>. Additionally, important control measures such as dietary intake and post-RT protein supplementation have often been overlooked in studies of RT volume and muscle hypertrophy. To tackle these shortcomings, there is a need for rigorously controlled studies examining the relationship between RT volume and muscle hypertrophy.

Therefore, the purpose of the present study was to identify the relationship between low-to- high weekly RT volume and muscular adaptations, whilst addressing some of the shortcomings of existing studies. Biceps brachii muscle thickness (MT), isotonic and isometric strength, were measured before and after six weeks of RT with 9, 18 or 27 weekly sets in RT experienced males. We hypothesized that RT-induced changes in muscle mass and strength would be greater in response to 18 vs. 9 weekly sets (performed over two and one weekly session(s), respectively), but would not increase any further with 27 weekly sets performed over two weekly sessions; indicative of a ceiling or inverted-U effect, as previously proposed

## METHODS

### Participants

Male participants were included in the study if following criteria were met (i) aged 18-35yrs; (ii) completing RT  $\geq 3$  times weekly for  $\geq 1$  yr (iii) healthy as assessed via a general health questionnaire. Participants were excluded if (i) diabetic; (ii) a regular smoker; (iii) lactose intolerant; (iv) found to be drinking alcohol within 24hrs of a RT session; (v) trained their elbow flexors outside the study. Fifty-one males were included in the study with two participants withdrawing due to non-compliance with external training (n=1) and alcohol (n=1) restrictions. Therefore, forty-nine (n=49) participants completed the study and were included in the final data analyses. Ethical approval was granted by the University of Birmingham (#ERN-16\_1084) in accordance with the 7<sup>th</sup> version of the declaration of Helsinki. All participants gave informed written consent to participate.

### Study design

Participants were randomly allocated to a low (LOW; n=17), moderate (MOD; n=15) or high (HIGH; n=17) weekly RT volume group (characteristics are outlined in Table 1). Participants trained their elbow flexors, focusing on the biceps brachii, at a moderate-to-high intensity with the LOW, MOD and HIGH group respectively completing 9, 18 and 27 weekly sets for six weeks. One week prior to training, participants underwent pre-training assessments of anthropometric characteristics, muscle architecture, isometric and isotonic strength. Post-exercise protein supplementation was controlled and participants were asked to record diet and permitted external RT (i.e. no elbow flexion) throughout. One week after training completion, participants repeated pre-training assessments. Training adherence for the completed participants was 99.2% (482 out of 486 sessions attended), and all were included in the final analysis.

## Resistance training programme

Participants completed six weeks of biceps-based RT. LOW trained once per week and both MOD and HIGH trained twice per week. Multiple training sessions were separated by at least 48 h. Each LOW and MOD training session consisted of 9 sets (three sets each of (i) seated supine biceps curl; (ii) supine grip bent over row; (iii) supine grip pulldown). The first weekly HIGH training session consisted of 5 sets of seated supine biceps curls and supine grip bent over rows and 4 sets of supine grip pulldowns. The second weekly HIGH session consisted of 4 sets of the first two exercises and 5 sets of supine grip pulldowns. Participants performed 10-12 repetitions per set, using the repetitions in reserve (RIR) model<sup>22</sup>. Exercise training intensity was monitored after each set using the Borg category ratio scale (CR-10)<sup>23</sup>, with 10 being maximal effort. Participants aimed to end their sets with ~2 RIR, (i.e. target score of ~8 on the CR-10). The load lifted in the first set was ~75% of 1RM, which was altered accordingly in subsequent sets and training sessions, should the RIR score fall outside the desired 8. Participants were instructed on correct lifting technique and were supervised throughout to maintain form and tempo (3-1; eccentric-to-concentric contractions). Rest periods of 3 min were given between sets to facilitate MPS<sup>8</sup> and to maximise increases in strength in our trained participants<sup>24</sup>. Training sessions were performed at a time convenient for the participants, who were encouraged to train at the same time of day throughout the duration of the trial. Verbal encouragement was given and participants were allowed to play music. Participants consumed 40g of whey protein in 250ml of water immediately after every RT session to ensure maximal stimulation of post-exercise MPS<sup>25</sup>. One week following the final RT session participants underwent post-training assessments. Tests were performed identical to and at the same time of day as pre-training assessments. The RT programme for each group is detailed in Table 2.

## **Pre-and post-training assessments**

*Anthropometric characteristics:* Height and weight were recorded using a stadiometer and digital weighing scales. A bioelectrical impedance scanner (Bodystat, Quadscan 4000, Douglas, Isle of Man, UK) was used to measure body fat percentage, with electrodes attached to the back of the hand and either side of the ipsilateral ankle according to the manufacturers' guidelines.

*Muscle thickness:* Biceps brachii MT was measured in the participants' self-reported dominant arm (i.e. the arm used most on a daily basis) via ultrasound (Diasus Application Specific Ultrasound, Dynamic Imaging Ltd, Livingston, UK). Participants were seated in an upright position facing the operator, with their arm relaxed in a supine extended position. The ultrasound probe (7.5MHz transducer) was covered in transmission gel (Henleys Medical Supplies, Hertfordshire, UK) and placed parallel to the muscle fibres at 50% of the distance between the supraglenoid tubercle and radial tuberosity. The site of biceps MT assessment was marked weekly on each arm and photographed to keep track of the precise scan location. Five ultrasound images were taken. The highest quality image (i.e. the image with the clearest, most parallel aponeuroses) was subsequently used to determine MT, defined as the perpendicular distance between the superficial and deep aponeuroses. The same un-blinded operator performed all scans to reduce intra-operator variability (coefficient of variation based on all obtained images was ~0.7%). Images were analyzed using ImageJ (version 1.51i)

*Maximal isometric strength:* Biceps isometric strength was assessed using a KinCom dynamometer (Chattanooga Group Inc, Hixson, Tennessee, USA). The dynamometer was calibrated to measure the peak torque of the elbow flexors during a maximal voluntary isometric contraction. Participants were secured in a seated position with straps across their shoulders, torso and waist. The dominant arm was secured in a flexed position at 55° with the elbow flexion attachment, with arm lever length being recorded. Participants were instructed



to “*push up as hard as possible*” against the lever pad for 3 s to produce a peak torque. Participants were given 120 s rest between a total of 6 attempts, comprising an initial three sub-maximal warm-ups, and three maximal “all-out” efforts. On screen instructions and verbal commands informed the participant when to begin and cease contracting. Of the three maximal attempts, the highest score was recorded.

*Maximal isotonic strength:* The maximum load that could be lifted in a single repetition (1RM) was assessed for each exercise, and sequenced according to the RT protocol. As such, 1RM for each exercise was assessed bilaterally, rather than in the dominant arm. Participants first completed a seated supine biceps curl warm up of three sets of 10 repetitions with an unloaded 9kg bar. Participants then self-selected a load they felt would elicit volitional fatigue after 4-5 repetitions. This was adjusted in each subsequent set to ensure fatigue after 3-4 repetitions, 2-3 repetitions and, finally, 1 repetition. Sets were separated by 2 min of passive rest, and multiple 1RM attempts separated by 3 min. After 3 min of rest, 1RM testing of the following exercise commenced using the same protocol, but without the initial warm up. Verbal encouragement was provided by the researchers throughout. Failure to lift the load or lifting with incorrect technique disqualified the attempt.

### **Dietary and training control**

Participants were instructed to maintain their normal dietary and supplement intake. Participants were forbidden from consuming any caffeine on the day of testing and RT sessions to prevent any positive acute effects on strength<sup>26</sup>. External training was permitted; however, participants were requested to avoid exercises that incorporated the elbow flexors (a verbal list was given) and encouraged to check with a member of the research team on their external upper-body routine. Participants recorded diet and external training in self-report diaries. Diet was recorded over 3 days of every training week (2 weekdays and 1 weekend). external training

diaries were submitted every two weeks. Diet diaries were assessed using DietPlan6 (Forestfield Software Ltd, Horsham, UK). Training diaries were analysed to determine upper- and lower-body weekly RET (expressed as total tonnage).

### **Statistical analysis**

Data was analyzed using SPSS (version 22, IBM Statistics, Chicago, Illinois, USA). A one-way ANOVA was used to compare baseline physical characteristics between groups, and repeated measures ANOVA was used to assess the significance of each measure; pre-to-post, as well as between groups. Bonferroni post hoc tests were used to examine differences where significant effects were found. Significance was set at  $p < 0.05$ . Effect sizes (ES), using Cohen's  $d$ , were calculated to assess magnitude of effect from pre- to post-RT within- and between-groups. Threshold values were set at 0.2, small; 0.5, moderate; and 0.8, large. Individual raw data (i.e. pre and post values) was used for statistical analysis and percent change from pre-to-post RT was calculated for muscle thickness and strength. Tabulated data are expressed as means  $\pm$ SD and figures as means  $\pm$ SEM.

### **RESULTS**

There were no significant differences in any baseline physical characteristics (Table 1). Dietary constituents as well as external RT volume (i.e. RT performed outside the study), are presented in Table 3 (upper and lower sections, respectively). There were no significant within or between-group differences for total energy, fat or carbohydrate intake across the 6-week RT programme. There were no significant between groups differences for protein intake, however protein intake in LOW was significantly lower in weeks 3-4 compared to weeks 1-2 ( $p < 0.05$ ) and weeks 5-6 ( $p < 0.05$ ). There were no significant within or between-group differences in total, upper-body or lower-body external RT volume.

Total study-specific RT volume (i.e. the biceps exercises completed in the study), differed significantly between each group (Figure 1), whereby HIGH>MOD>LOW at every time point (weeks 1-6;  $p<0.05$  for all). Training volume did not significantly change over the 6-week intervention for LOW, but did increase weekly from week 3 onwards for MOD and HIGH only ( $p<0.05$ ), with the exception of week 6 in MOD.

Effect sizes comparing within- and between-group pre-to-post change in indices of muscle mass and strength are presented in Table 4. Biceps MT of the dominant arm is presented as absolute group means and individual % change in Figure 2A and B, respectively. There were no significant between-group differences in MT prior to training. From pre-to-post-training, MT increased in LOW by  $0.1\pm 0.3$ cm ( $p<0.05$ ), in MOD by  $0.3\pm 0.4$ cm (0.59;  $p<0.01$ ) and in HIGH by  $0.2\pm 0.2$ cm ( $p<0.05$ ). There was no between-group difference in the relative or absolute change in MT following RT.

Absolute isometric strength at baseline was similar between groups, and increased significantly from pre-to-post training in HIGH only ( $p<0.05$ ) (Figure 3A). No between-group differences were observed for % change in isometric strength (Figure 3B).

Isotonic strength is presented as absolute group means and individual % change in Figure 4A-H, respectively. Data are expressed as the increase in 1RM for each of the 3 training exercises. There was no significant between-group difference in total 1RM strength or any individual exercise prior to training. From pre-to-post-training, seated supine bicep curl 1RM strength increased in LOW by  $3.4\pm 3.1$  kg, in MOD by  $6.0\pm 3.2$  kg and in HIGH by  $5.4\pm 2.7$  kg ( $p<0.001$  for all groups) with no difference between groups. Supine grip bent-over row 1RM strength increased in LOW by  $6.3\pm 6.6$  kg, in MOD by  $7.8\pm 3.4$  kg and in HIGH by  $11.8\pm 7.1$  kg ( $p<0.001$  for all groups) with no difference between groups. Supine grip pulldown 1RM strength increased in LOW by  $6.4\pm 7.4$  kg, in MOD by  $10.5\pm 7.5$  kg and in HIGH by  $10.7\pm 6.4$  kg ( $p\leq 0.001$  for all groups) with no difference between groups. Total 1RM strength increased

in LOW by  $16.1\pm 9.7$  kg, in MOD by  $24.3\pm 9.3$  kg and in HIGH by  $27.9\pm 10.2$  kg ( $p < 0.001$  for all groups) with no difference between groups.

## DISCUSSION

The existence of a graded dose-response relationship between skeletal muscle hypertrophy, strength and RT volume is largely accepted at lower volumes (i.e.  $< 10$ - $12$  weekly sets) <sup>6</sup>. However, the present study is one of the first to investigate whether differences in muscle adaptations exist between low, moderate and high weekly RT volume, over a short-term training program in trained individuals. We demonstrate that over six-weeks of RT, 9 weekly sets of biceps training (LOW), performed in a single weekly session, elicited muscle thickness (MT) and strength increases that did not statistically differ from 18 and 27 weekly sets, performed over two weekly sessions (MOD and HIGH, respectively). However, effect sizes revealed a ‘*moderate-to-large*’ magnitude of RT-induced strength change for MOD and HIGH over LOW, indicating a possible benefit of moderate-to-high RT volumes on strength adaptation. These findings partly contrast with our initial hypothesis, that both MT and strength increases would be greater with 18 and 27 weekly sets over 9 sets.

There is limited research available to support the idea of a dose-response relationship between skeletal muscle hypertrophy and RT volume holds true beyond relatively low volumes <sup>6</sup>. Congruent with our findings that MOD and HIGH RT volume did not promote superior increases in biceps MT compared with LOW, in trained individuals, Ostrowski, et al. <sup>17</sup> reported no difference in upper and lower-body MT changes between 3-7, 6-14 or 12-28 weekly sets, in trained individuals. From a mechanistic perspective, although a number of acute studies have reported associations between mTORC1-mediated signaling/MPS and RT volume at  $\leq 9$  weekly sets <sup>27,28</sup>, there is evidence of a plateau in this relationship at higher RT volumes. For example, Tibana, et al. <sup>29</sup> reported a down-regulation in the expression of a number of key

proteins implicated in MPS following 24 vs. 12 weekly sets, albeit in rodents. Whether a similar response occurs in humans is unclear as, to the best of our knowledge, no studies have examined the molecular signaling or MPS response to very high RT volumes. Contrary to present findings, Radaelli, et al.<sup>30</sup> reported greater increases in elbow flexor MT with 30 weekly sets per muscle group vs. 6 or 18 sets, albeit in untrained individuals, which may explain the greater response to the higher RT volume. The importance of considering training status when assessing the adaptive response to a given RT programme is underscored by evidence demonstrating that training alters the acute mTORC1/MPS response to RT<sup>31,32</sup>. Thus, whilst evidence has been found to support a graded-dose relationship between RT volume and skeletal muscle hypertrophy in untrained individuals over a prolonged period<sup>30</sup>, our findings indicate no such relationship in trained individuals over a short-term RT programme.

Similar to muscle hypertrophy, a graded dose-response relationship between RT volume and strength has been reported, with relatively low weekly volumes<sup>13,14,33</sup>. In contrast, there is scant evidence of a similar relationship between RT volume and strength at higher weekly RT volumes (i.e. >12 weekly sets)<sup>6</sup>. Furthermore, research supporting a dose-response relationship between strength and RT volume has been conducted in RT-novices<sup>14</sup> who, as previously mentioned, may exhibit greater responsiveness to higher RT volumes than well-trained individuals. Herein, in trained individuals, we demonstrate that isotonic 1RM strength increased significantly from pre-to-post RT, with no significant between-group differences. However, the magnitude of response for 1RM, across all exercises, was ‘moderate-to-large’ in MOD and HIGH when compared with LOW. Furthermore, there was a moderate effect of HIGH over MOD for bent-over row 1RM strength, which aligns with the proposed dose-response effect of RT volume on strength<sup>13</sup>. An increase in isometric strength was only apparent in HIGH, which was likely driven to two very high responders and, in any case, was not statistically different from LOW and MOD and displayed only a small effect size

difference. The absence of a robust increase in isometric strength in our study, likely reflects the absence of any learning effect as RT was performed in an isotonic fashion<sup>34</sup>. Thus, our data point to a possible benefit of MOD and HIGH over LOW weekly RT volume for increasing 1RM strength, that requires further investigation.

The present study is not without limitations. Firstly, participants were allowed to train outside the study. External training was closely monitored through training logs, and efforts were made to ensure the elbow flexors were not trained. As such, no differences in external training parameters were observed between groups, although we cannot rule out the possibility of misreporting of external training given that men typically focus on upper-body RT<sup>35</sup>. Secondly, the decrease in protein intake during weeks 3 and 4 in LOW could be viewed as a potential confounder. Nevertheless, protein intake over weeks 3-4 was reported as 1.5 g·kg<sup>-1</sup>·day<sup>-1</sup>, almost twice the RDA, which is considered adequate to support muscle mass and strength gains with RT<sup>36</sup>. Thirdly, young trained males were investigated in the present study, and as such, findings cannot categorically be extrapolated to other populations. Furthermore, our training duration of 6 weeks, despite being consistently found to elicit hypertrophy<sup>37-39</sup> and being considered the most active phase of muscle remodeling<sup>40</sup>, may have been too short to detect any potential divergence between groups. For example, 12 vs 4 weekly sets over 6-weeks promoted equivalent changes in MT between groups<sup>16</sup>, whereas 12 weekly sets promoted superior MT increase when extended to a 20-week RT-program<sup>41</sup>. Finally, it is important to acknowledge that the training frequency between LOW and the two other groups differed, which may have confounded the volume comparison of the present study.

## **PRACTICAL APPLICATIONS**

Optimizing RT volume to enhance muscular adaptations to training presents an important line of investigation. The present study explored muscular adaptations to low,

moderate and high RT volumes (9, 18 and 27 weekly sets) in trained individuals and found no significant difference in MT and strength gains between groups. However, effect size estimates point to a potential benefit of moderate-to-high RT volumes for strength gains compared with lower RT volumes. From a practical standpoint, 9 weekly sets of RT, completed in a single session, appears sufficient to maximize MT during a short-term RT programme in trained individuals. In contrast, 18-27 weekly sets, completed over two weekly sessions, may confer greater strength adaptations.

## CONCLUSIONS

In conclusion, the present study demonstrates no significant difference in muscular adaptations between 9, 18 and 27 weekly RT sets over the course of a short-term program in trained individuals. These findings indicate that a relatively low weekly RT volume is sufficient to increase muscle hypertrophy in trained individuals over a short-term RT program, whereas moderate-to-high RT volumes may confer greater strength increases. Future studies should seek to understand whether similar discordance in the relationship between RT volume and muscle hypertrophy/strength is apparent in different muscle groups is evident over a longer duration program (e.g.  $\geq 11$  weeks) and whether the frequency over which weekly training volume is completed exerts a strong influence on these responses.

## **Disclosures**

The authors have no conflicts of interest to declare.

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## **Authorship Statement**

All authors gave their final approval of the version of the article to be published. JB and LB designed the study. SH and JB organized and carried out the training and experiments with the assistance of JM and BS. SH and LB performed all data analyses. SH, JM, BS and LB wrote the manuscript together. SH and LB are the guarantors of this work and take responsibility for the integrity and accuracy of the data analysis.



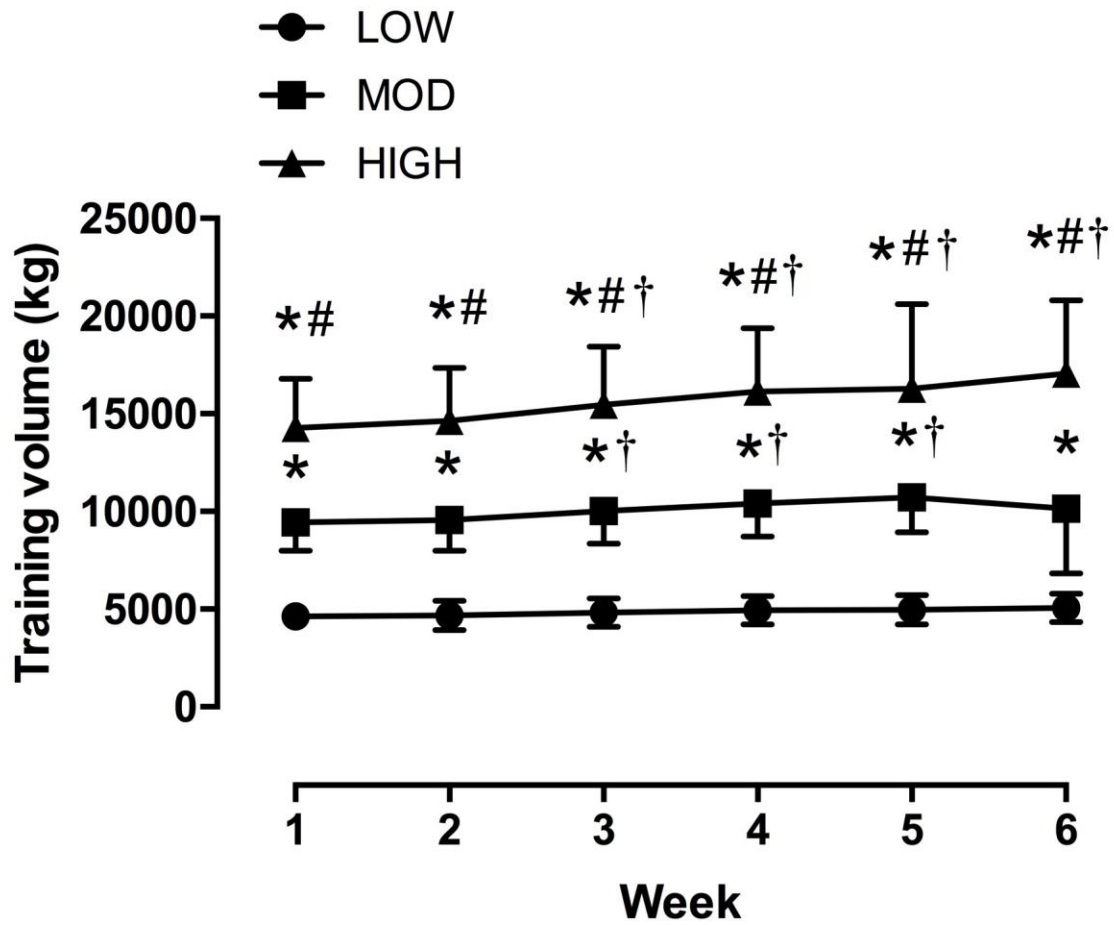
## REFERENCES

1. Wolfe RR. The underappreciated role of muscle in health and disease. *Am J Clin Nutr.* 2006;84(3):475-482.
2. Terzis G, Georgiadis G, Stratakos G, et al. Resistance exercise-induced increase in muscle mass correlates with p70S6 kinase phosphorylation in human subjects. *Eur J Appl Physiol.* 2008;102(2):145-152.
3. Schoenfeld BJ. The mechanisms of muscle hypertrophy and their application to resistance training. *J Strength Cond Res.* 2010;24(10):2857-2872.
4. Dankel SJ, Counts BR, Barnett BE, Buckner SL, Abe T, Loenneke JP. Muscle adaptations following 21 consecutive days of strength test familiarization compared with traditional training. *Muscle Nerve.* 2017;56(2):307-314.
5. Wernbom M, Augustsson J, Thomee R. The influence of frequency, intensity, volume and mode of strength training on whole muscle cross-sectional area in humans. *Sports Med.* 2007;37(3):225-264.
6. Schoenfeld BJ, Ogborn D, Krieger JW. Dose-response relationship between weekly resistance training volume and increases in muscle mass: A systematic review and meta-analysis. *J Sports Sci.* 2017;35(11):1073-1082.
7. Schoenfeld BJ, Ogborn D, Krieger JW. Effects of Resistance Training Frequency on Measures of Muscle Hypertrophy: A Systematic Review and Meta-Analysis. *Sports Med.* 2016;46(11):1689-1697.
8. McKendry J, Perez-Lopez A, McLeod M, et al. Short inter-set rest blunts resistance exercise-induced increases in myofibrillar protein synthesis and intracellular signalling in young males. *Exp Physiol.* 2016;101(7):866-882.
9. Ato S, Makanae Y, Kido K, Fujita S. Contraction mode itself does not determine the level of mTORC1 activity in rat skeletal muscle. *Physiol Rep.* 2016;4(19).
10. Burd NA, Andrews RJ, West DWD, et al. Muscle time under tension during resistance exercise stimulates differential muscle protein sub-fractional synthetic responses in men. *J Physiol-London.* 2012;590(2):351-362.
11. Bird SP, Tarpenning KM, Marino FE. Designing resistance training programmes to enhance muscular fitness: a review of the acute programme variables. *Sports Med.* 2005;35(10):841-851.
12. Figueiredo VC, de Salles BF, Trajano GS. Volume for Muscle Hypertrophy and Health Outcomes: The Most Effective Variable in Resistance Training. *Sports Medicine.* 2018;48(3):499-505.
13. Ralston GW, Kilgore L, Wyatt FB, Baker JS. The Effect of Weekly Set Volume on Strength Gain: A Meta-Analysis. *Sports Med.* 2017;47(12):2585-2601.

14. Grgic J, Schoenfeld BJ, Davies TB, Lazinica B, Krieger JW, Pedisic Z. Effect of Resistance Training Frequency on Gains in Muscular Strength: A Systematic Review and Meta-Analysis. *Sports Med.* 2018;48(5):1207-1220.
15. Mitchell CJ, Churchward-Venne TA, West DW, et al. Resistance exercise load does not determine training-mediated hypertrophic gains in young men. *J Appl Physiol (1985).* 2012;113(1):71-77.
16. Radaelli R, Botton CE, Wilhelm EN, et al. Time course of low- and high-volume strength training on neuromuscular adaptations and muscle quality in older women. *Age (Dordr).* 2014;36(2):881-892.
17. Ostrowski KJ, Wilson GJ, Weatherby R, Murphy PW, Lyttle AD. The effect of weight training volume on hormonal output and muscular size and function. *Journal of Strength and Conditioning Research.* 1997;11(3):148-154.
18. Carroll TJ, Riek S, Carson RG. Neural adaptations to resistance training - Implications for movement control. *Sports Medicine.* 2001;31(12):829-840.
19. Damas F, Phillips S, Vechin FC, Ugrinowitsch C. A Review of Resistance Training-Induced Changes in Skeletal Muscle Protein Synthesis and Their Contribution to Hypertrophy. *Sports Medicine.* 2015;45(6):801-807.
20. Tang JE, Perco JG, Moore DR, Wilkinson SB, Phillips SM. Resistance training alters the response of fed state mixed muscle protein synthesis in young men. *Am J Physiol Regul Integr Comp Physiol.* 2008;294(1):R172-178.
21. Wilkinson SB, Phillips SM, Atherton PJ, et al. Differential effects of resistance and endurance exercise in the fed state on signalling molecule phosphorylation and protein synthesis in human muscle. *J Physiol.* 2008;586(15):3701-3717.
22. Zourdos MC, Klemp A, Dolan C, et al. Novel Resistance Training-Specific Rating of Perceived Exertion Scale Measuring Repetitions in Reserve. *J Strength Cond Res.* 2016;30(1):267-275.
23. Buckley JP, Borg GA. Borg's scales in strength training; from theory to practice in young and older adults. *Appl Physiol Nutr Metab.* 2011;36(5):682-692.
24. Grgic J, Schoenfeld BJ, Skrepnik M, Davies TB, Mikulic P. Effects of Rest Interval Duration in Resistance Training on Measures of Muscular Strength: A Systematic Review. *Sports Med.* 2018;48(1):137-151.
25. Macnaughton LS, Wardle SL, Witard OC, et al. The response of muscle protein synthesis following whole-body resistance exercise is greater following 40 g than 20 g of ingested whey protein. *Physiol Rep.* 2016;4(15).
26. Grgic J, Trexler ET, Lazinica B, Pedisic Z. Effects of caffeine intake on muscle strength and power: a systematic review and meta-analysis. *J Int Soc Sports Nutr.* 2018;15:11.

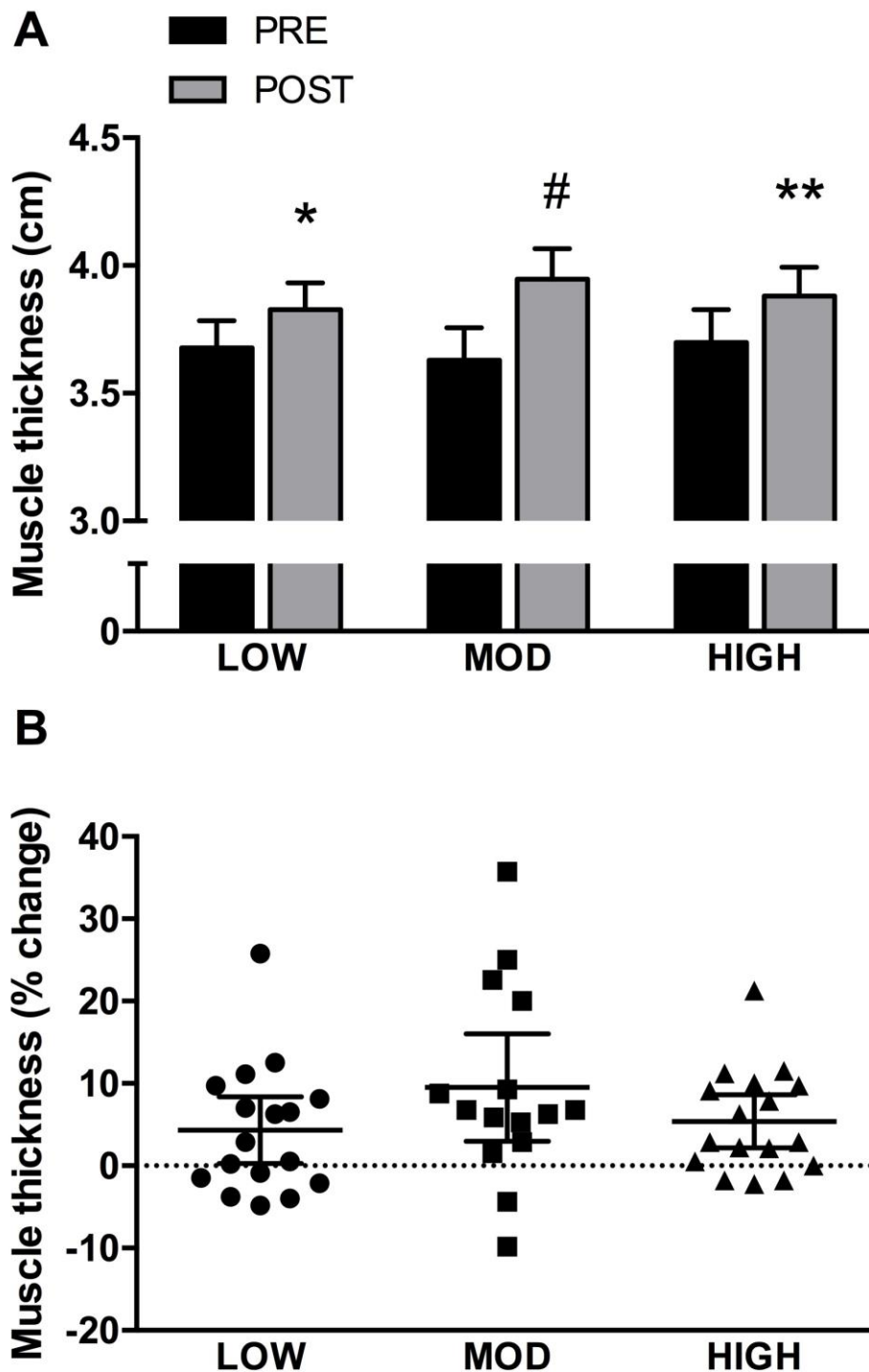
27. Terzis G, Spengos K, Mascher H, Georgiadis G, Manta P, Blomstrand E. The degree of p70 S6k and S6 phosphorylation in human skeletal muscle in response to resistance exercise depends on the training volume. *Eur J Appl Physiol.* 2010;110(4):835-843.
28. Burd NA, Holwerda AM, Selby KC, et al. Resistance exercise volume affects myofibrillar protein synthesis and anabolic signalling molecule phosphorylation in young men. *J Physiol.* 2010;588(Pt 16):3119-3130.
29. Tibana RA, Franco OL, Cunha GV, et al. The Effects of Resistance Training Volume on Skeletal Muscle Proteome. *Int J Exerc Sci.* 2017;10(7):1051-1066.
30. Radaelli R, Fleck SJ, Leite T, et al. Dose-response of 1, 3, and 5 sets of resistance exercise on strength, local muscular endurance, and hypertrophy. *J Strength Cond Res.* 2015;29(5):1349-1358.
31. Kim PL, Staron RS, Phillips SM. Fasted-state skeletal muscle protein synthesis after resistance exercise is altered with training. *J Physiol.* 2005;568(Pt 1):283-290.
32. Gonzalez AM, Hoffman JR, Townsend JR, et al. Association between myosin heavy chain protein isoforms and intramuscular anabolic signaling following resistance exercise in trained men. *Physiol Rep.* 2015;3(1).
33. Marshall PW, McEwen M, Robbins DW. Strength and neuromuscular adaptation following one, four, and eight sets of high intensity resistance exercise in trained males. *Eur J Appl Physiol.* 2011;111(12):3007-3016.
34. Mattocks KT, Buckner SL, Jessee MB, Dankel SJ, Mouser JG, Loenneke JP. Practicing the Test Produces Strength Equivalent to Higher Volume Training. *Med Sci Sports Exerc.* 2017;49(9):1945-1954.
35. La Scala Teixeira CV, Pereira EFM, Evangelista AL, et al. Is the weekly sets volume training performed by trained subjects in accordance with training recommendations guidelines for muscle hypertrophy? *Motriz Revista de Educação Física.* 2018;24(2).
36. Morton RW, Murphy KT, McKellar SR, et al. A systematic review, meta-analysis and meta-regression of the effect of protein supplementation on resistance training-induced gains in muscle mass and strength in healthy adults. *Br J Sports Med.* 2018;52(6):376-384.
37. DeFreitas JM, Beck TW, Stock MS, Dillon MA, Kasishke PR, 2nd. An examination of the time course of training-induced skeletal muscle hypertrophy. *Eur J Appl Physiol.* 2011;111(11):2785-2790.
38. Baroni BM, Geremia JM, Rodrigues R, De Azevedo Franke R, Karamanidis K, Vaz MA. Muscle architecture adaptations to knee extensor eccentric training: rectus femoris vs. vastus lateralis. *Muscle Nerve.* 2013;48(4):498-506.
39. Seynnes OR, de Boer M, Narici MV. Early skeletal muscle hypertrophy and architectural changes in response to high-intensity resistance training. *J Appl Physiol (1985).* 2007;102(1):368-373.

40. Brook MS, Wilkinson DJ, Mitchell WK, et al. Skeletal muscle hypertrophy adaptations predominate in the early stages of resistance exercise training, matching deuterium oxide-derived measures of muscle protein synthesis and mechanistic target of rapamycin complex 1 signaling. *FASEB J.* 2015;29(11):4485-4496.
41. Radaelli R, Botton CE, Wilhelm EN, et al. Low- and high-volume strength training induces similar neuromuscular improvements in muscle quality in elderly women. *Exp Gerontol.* 2013;48(8):710-716.



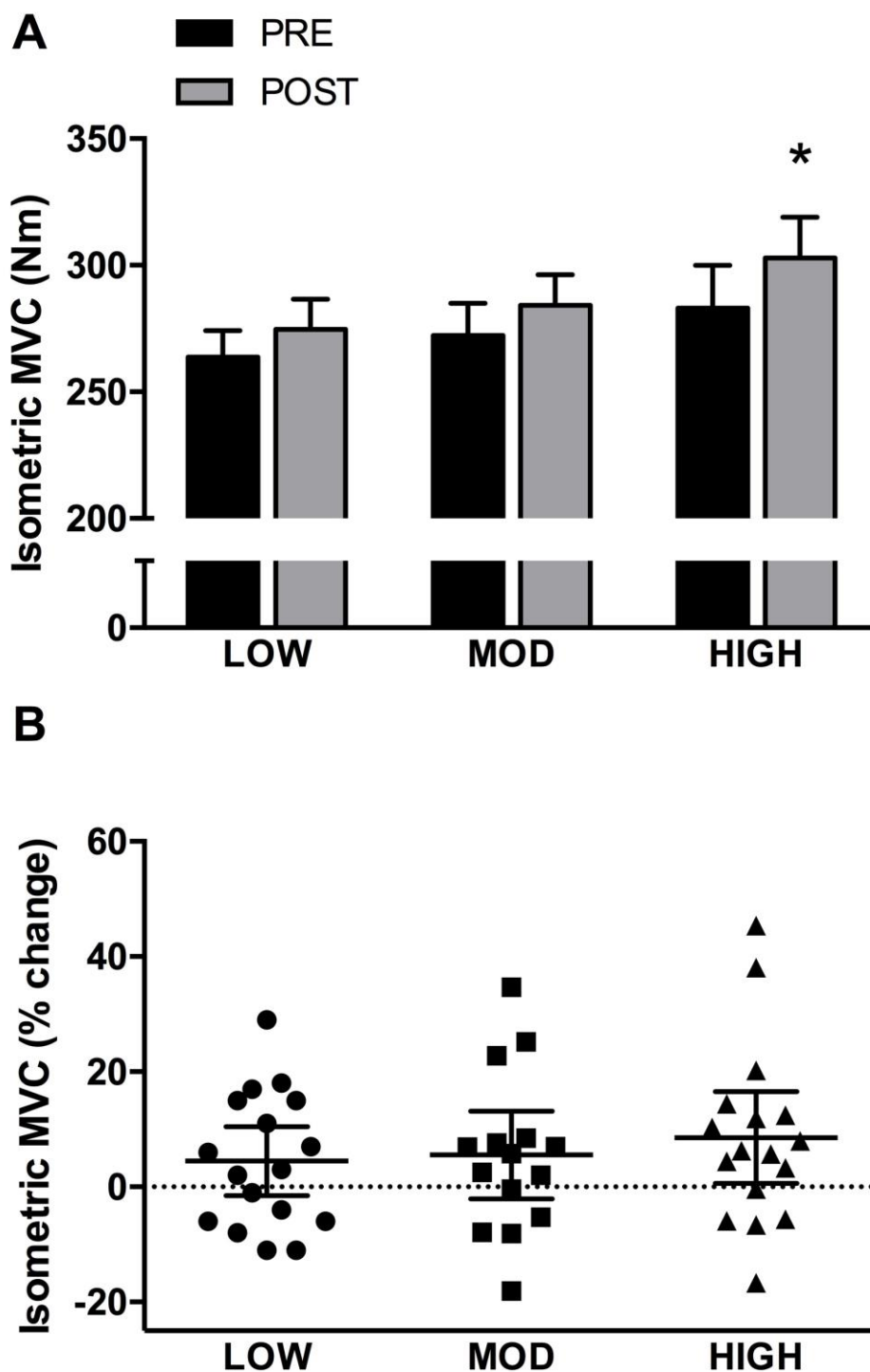
**Figure 1:** Total weekly RT volume per group during each week of RT. Significance was set at  $p < 0.05$ . \* Significantly greater than LOW at the same time point ( $p < 0.05$ ), # indicates greater than MOD at the same time point ( $p < 0.05$ ), † indicates different to previous weeks ( $p < 0.05$ ). Data are expressed as means  $\pm$  SEM.

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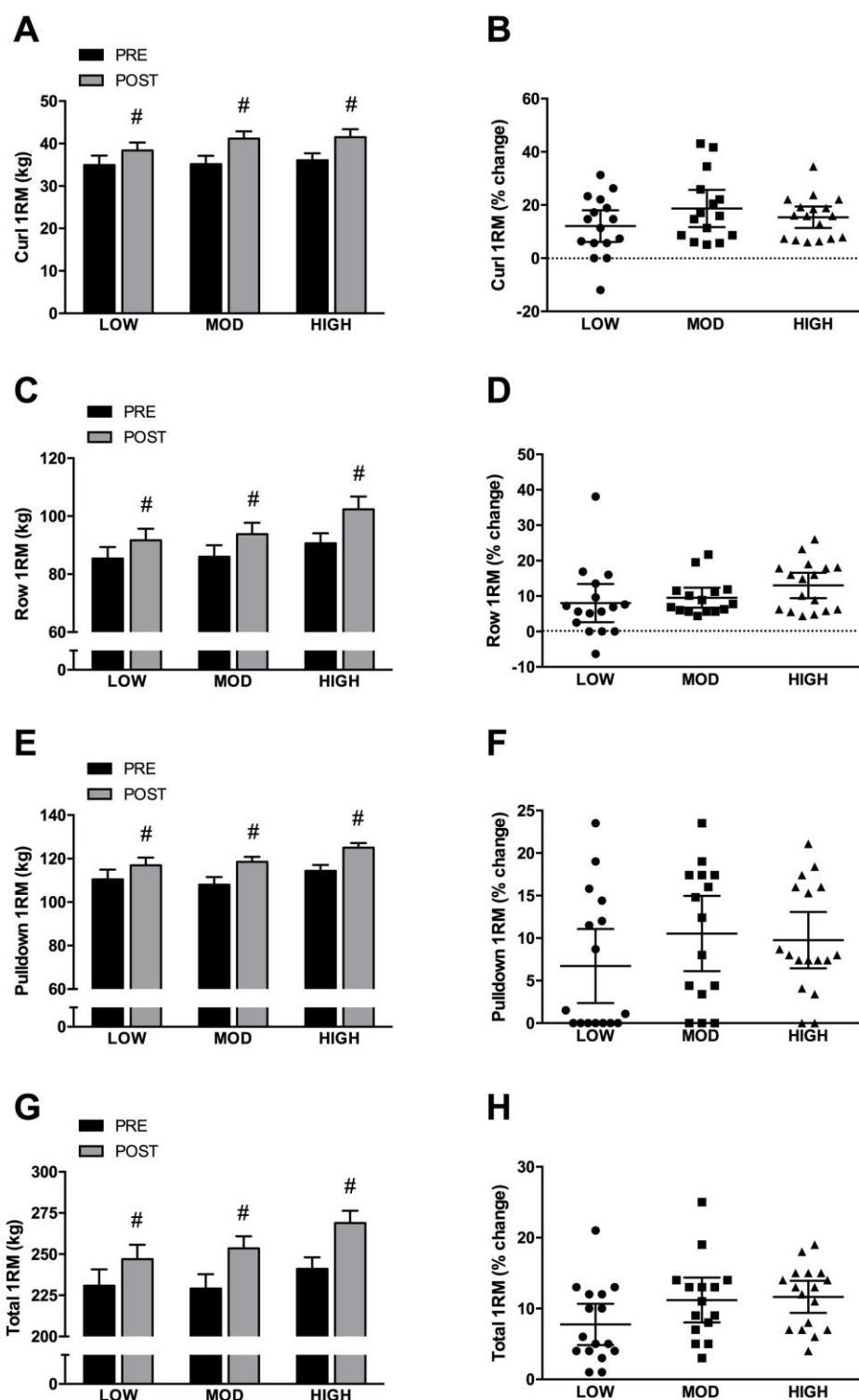


**Figure 2:** Biceps muscle thickness of the dominant arm (MT). Data presented as means  $\pm$ SEM and (A) and individual % change from pre-to-post RT (B). Central line in 2B represents the group mean and bars represent 95% confidence intervals. Significance was set at  $p < 0.05$ . \* Indicates greater than pre-training ( $p < 0.05$ ), \*\* indicates greater than pre-training ( $p < 0.01$ ) and # indicates greater than pre-training ( $p < 0.001$ ).

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**Figure 3:** Isometric maximal voluntary contraction of the elbow flexors in the dominant arm (MVC). Data are presented as means  $\pm$ SEM and (A) and individual % change from pre-to-post RT (B). Central line in 3B represents the group mean and bars represent 95% confidence intervals. Significance was set at  $p < 0.05$ . \* Indicates greater than pre-training ( $p < 0.05$ ).



**Figure 4:** 1RM strength for biceps curl, bent-over row, supine grip pulldown and total (the product of the 3 individual exercises) presented as means  $\pm$ SEM and (A, C, E and G, respectively) and individual % change from pre-to-post RT (B, D, F and H, respectively). Central line in 4B, D, F and H represents the group mean and bars represent 95% confidence intervals. Significance was set at  $p < 0.05$ . # Indicates greater than pre-training ( $p < 0.001$ ).



**Table 1:** Participant Characteristics

	LOW (n=17)	MOD (n=15)	HIGH (n=17)
Age (years)	20.1±1.2	19.5±1.4	20.5±1.2
Height (cm)	179.6±4.0	177.0±7.6	181.1±6.7
Weight (kg)	81.3±8.3	76.3±10.2	82.0±10.7
Body fat (%)	22.7±4.2	21.5±6.5	21.7±5.6

Values are expressed as mean ± SD. No significant differences were observed between groups.

**Table 2:** Resistance training protocol for each group throughout the 6 weeks of training.

Group	No. sets per exercise per session	Reps per set	Target CR-10 rating/10	Tempo (eccentric: concentric)	Inter-set rest period	No. weekly sessions	Time between weekly sessions	Total no. weekly sets
LOW	3 Curl 3 Bent-over row 3 Pulldown	10-12	8	3:1	3 mins	1	n/a	9
MOD	Session 1: 3 Curl 3 Bent-over row 3 Pulldown	10-12	8	3:1	3 mins	2	≥48 hours	18
HIGH	Session 2: 3 Curl 3 Bent-over row 3 Pulldown	10-12	8	3:1	3 mins	2	≥48 hours	18
	Session 1: 5 Curl 5 Bent-over row 4 Pulldown	10-12	8	3:1	3 mins	2	≥48 hours	27
	Session 2: 4 Curl 4 Bent-over row 5 Pulldown							

Curl = Seated supine bicep curl; Bent-over row = Supine grip bent over row; Pulldown = Supine grip pull down. Exercises were performed in the above order.

**Table 3:** Dietary constituents and external RT volume throughout the 6 weeks of RT.

	LOW (n=17)			MOD (n=15)			HIGH (n=17)		
	WK 1-2	WK 3-4	WK 5-6	WK 1-2	WK 3-4	WK 5-6	WK 1-2	WK 3-4	WK 5-6
Energy (kcal)	2208±592	1788±399	2278±504	2458±751	2289±826	2320±709	2497±767	2110±840	2576±626
Protein (g)	1.60±0.38	1.50±0.27*	1.67±0.33	1.84±0.34	1.83±0.24	1.74±0.07	1.72±0.42	1.61±0.35	1.65±0.29
Fat (g)	1.22±0.40	0.98 ±0.24	1.11±0.29	1.72±0.22	1.60±0.33	1.65±0.12	1.33±0.20	1.11±0.36	1.29±0.21
Carbohydrate (g)	3.66±1.04	3.74±0.84	3.98±0.63	3.64±0.60	3.8±0.72	3.56±0.75	3.68±0.77	3.55±0.91	3.70±0.66
Total external volume (kg)	35268 ±29549	30083 ±38166	24895 ±31857	31244 ±31147	24550 ±33492	43513 ±36608	37121 ±24368	29942 ±26362	20089 ±29726
Upper-body external volume (kg)	18426 ±15014	16024 ±19755	10905 ±11052	18128 ±16455	15118 ±16355	22622 ±18915	22721 ±11474	14471 ±11573	13979 ±16040
Lower-body external volume (kg)	16945 ±16553	13233 ±21832	17013 ±20760	10426 ±17354	11582 ±16590	20508 ±22658	14400 ±14234	17007 ±16899	11043 ±15752

Energy and macronutrient intake are presented as daily intake, with macronutrients expressed relative to body mass. External RET volume is the work performed outside of the study, expressed as the upper-body, lower-body and total (sum of upper- and lower-body) over weeks 1-2, 3-4 and 5-6. \* Indicates a significant between group difference at the same time point (P<0.05). Data are expressed as mean ±SD.

**Table 4:** Effect sizes for within- and between group changes in biceps thickness and strength.

	LOW PRE-POST	MOD PRE-POST	HIGH PRE-POST	Δ CHANGE LOW VS. MOD	Δ CHANGE LOW VS. HIGH	Δ CHANGE MOD VS. HIGH
Biceps MT	-0.33 <sup>a</sup>	-0.66 <sup>b</sup>	-0.37 <sup>a</sup>	-0.54 <sup>b</sup>	-0.15	0.46 <sup>a</sup>
Isometric MVC	-0.24 <sup>a</sup>	-0.25 <sup>a</sup>	-0.29 <sup>a</sup>	-0.027 <sup>a</sup>	-0.24 <sup>a</sup>	-0.21 <sup>a</sup>
Curl 1RM strength	-0.42 <sup>a</sup>	-0.85 <sup>c</sup>	-0.75 <sup>b</sup>	-0.80 <sup>c</sup>	-0.69 <sup>b</sup>	0.19
Row 1RM strength	-0.40 <sup>a</sup>	-0.51 <sup>b</sup>	-0.71 <sup>b</sup>	-0.30 <sup>a</sup>	-0.80 <sup>c</sup>	-0.75 <sup>b</sup>
Pulldown 1RM strength	-0.40 <sup>a</sup>	-0.92 <sup>c</sup>	-1.1 <sup>c</sup>	-0.55 <sup>b</sup>	-0.62 <sup>b</sup>	-0.03
Total 1RM strength	-0.43 <sup>a</sup>	-0.78 <sup>b</sup>	-0.93 <sup>c</sup>	-0.87 <sup>c</sup>	-1.19 <sup>c</sup>	-0.37 <sup>a</sup>

Left side indicates mean effect of pre-to-post RT values for each group. Right side indicates mean effect of the RT-induced delta change in the first named group minus the second named group (i.e. LOW minus MOD). Subscript *a* indicates a small effect size, *b* indicates a medium effect size, *c* indicates a large effect size.