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The Influence of Pre-Training Muscle Size on Strength Gain: An Exploratory Analysis

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ABSTRACT

Purpose: To investigate whether changes in maximal strength following resistance training were influenced by pre-training muscle thickness.
Methods: We retrospectively analyzed data from a between-subject study that measured elbow flexor muscle thickness and maximum strength before and after a 6-week study. A total of 122 untrained individuals, who were randomly assigned to 1 of 3 groups, were included in the analyses: (a) time-matched, non-exercise control; (b) dominant arm training; or (c) nondominant arm training. The two training groups performed thrice weekly unilateral elbow flexion exercise, starting with up to 5 heavy singles, followed by 4 sets of 8–12 repetitions to task failure.
Results: Increases in strength were observed for both dominant arm [b = 2.29 kg, 95% CI = (1.72, 2.87)] and the non-dominant [b = 2.86 kg, 95% CI = (2.33, 3.39) training groups compared to the time-matched non-exercise control group. However, this increase in strength did not depend upon baseline muscle size for either group. Follow-up mediation analyses suggested that muscle growth mediated changes in strength for the dominant arm but not the nondominant arm training group.
Conclusion: We hypothesized that individuals with larger muscles at baseline would have a greater propensity to increase strength compared to those with smaller muscles. However, the magnitude of strength change was not influenced by pre-training muscle thickness. Follow-up mediation analysis on muscle growth was equivocal.

Keywords: Hypertrophy, Strength, Resistance Training, Muscle Growth, One-Repetition Maximum

INTRODUCTION

A large body of scientific evidence has demonstrated that resistance training leads to increases in skeletal muscle size and strength (Currier et al., 2023), and it has long been believed that such adaptations are causally related (Ikai & Fukunaga, 1970; Moritani & deVries, 1979; Sale, 1988). To date, however, experimental data have been unable to demonstrate that increases in muscle size are necessary (Dankel et al., 2020; Hammert, Moreno, Martin, et al., 2023; Wong et al., 2024) or sufficient (Hammert, Moreno, Vasenina, et al., 2023; Jessee et al., 2018; Kacin & Strazar, 2011) to increase strength, nor do they seem to play a contributory role (Buckner et al., 2021; Dankel et al., 2017, 2020; Hammert, Moreno, Martin, et al., 2023; Mattocks et al., 2017). Indeed, the available evidence for a causal relationship between increases in skeletal muscle size and strength remains largely indirect (Buckner et al., 2016; Loenneke, 2021; Loenneke et al., 2019; Rasch, 1955). The classical papers of Ikai and Fukunaga (1970) and Moritani and deVries (1979) are often used to support the position that hypertrophy is a mechanism for strength gain. Neither actually examined the relationship between changes in skeletal muscle size and strength (Loenneke, 2021; Loenneke et al., 2019), and in fact, Moritani and deVries (1979) did not directly measure muscle growth. Instead, the authors interpreted changes in the relationship between surface electromyography amplitude and muscle force as evidence to suggest that neural factors played a major role in strength development during the initial weeks of training, followed by larger contributions from hypertrophy after the first three to five weeks (Moritani & deVries, 1979). Others have used the shared variance between muscle size and strength at baseline and cross-sectional data to argue that changes in skeletal muscle size must play a role in strength gain (Folland & Balshaw, 2021). However, baseline correlations, even among resistance trained individuals, do not reveal any such mechanisms that may (or may not) be responsible for exercise-induced changes in strength. They simply provide an indication as to whether individuals who have huger muscles tend to be stronger (i.e., in a task that involves that specific muscle) than those with smaller muscles (Dankel et al., 2018).

Although differing viewpoints exist regarding the relationship between exercise-induced increases in skeletal muscle size and strength (Folland & Balshaw, 2021; Loenneke, 2021; Loenneke et al., 2019; Taber et al., 2019), there is a broad agreement that changes within the nervous system play an important role in enhancing strength development (Buckner et al., 2016; Folland & Balshaw, 2021; Folland & Williams, 2007; Gabriel et al., 2006; Hammert, Kataoka, Yamada, et al., 2023; Loenneke, 2021; Loenneke et al., 2019; Taber et al., 2019). Resistance training has been shown to improve the ability to recruit and activate muscles during trained movements (Del Vecchio et al., 2019; Folland & Williams, 2007; Gabriel et al., 2006; Sale, 1988), likely through reductions in intracortical inhibition (Weier et al., 2012), increases in corticospinal (Weier et al., 2012) and motoneuronal (Aagaard et al., 2002) excitability, as well as greater motor unit firing rates and lower recruitment thresholds (Del Vecchio et al., 2019). Hence, if such adaptations improve the capacity to utilize available contractile tissue, it would make conceptual sense that non-resistance trained individuals who have bigger muscles at baseline (i.e., pre-training) may possess a greater potential for task-specific strength improvement due to a larger available contractile reserve (Blazevich et al., 2007). Accordingly, the purpose of this study was to determine, via exploratory analyses, whether pre-training muscle size moderates changes in one-repetition maximum strength following 6 weeks of heavy resistance training. We hypothesized that individuals with greater baseline muscle thickness would demonstrate larger increases in one-repetition maximum strength.

METHODS

Participants

The present study represents a secondary analysis of data derived from a recently completed randomized controlled trial conducted in our laboratory (Song, Hammert, et al., 2024; Song, Yamada, et al., 2024). Analyses were performed on 122 non-resistance trained individuals (67 females, 55 males), who were between the ages of 18 and 35 years, did not regularly use tobacco products, had muscle thickness and one-repetition maximum strength of the elbow flexors measured before and after enrolling in the 6-week experiment. “Non-resistance trained” was operationally designed as not having engaged in any structured resistance exercise (including calisthenics) in the 6 months prior to study enrollment. We did not specifically investigate whether individuals had engaged in resistance exercise before the 6-month period. However, randomization of participants into group should have ensured that any potential impact of previous training history was equally distributed across groups (Senn, 2013). All participants provided written informed consent to participate in the study, which was approved by the University’s Institutional Review Board (Protocol # 23-018).

Study Design

Participants were randomly assigned (following the pre-testing visit) into one of four groups: (a) time matched, non-exercise control; (b) dominant arm training; (c) non-dominant arm training; (d) dominant and non-dominant arm training. Because of any potential influence that higher load training in one limb can have on the magnitude of strength gain in the opposite limb (Bell et al., 2023), we elected to exclude the “dominant and non-dominant arm training” group’s data from the current analyses. The post-testing visit, which occurred 2-5 days after the final training visit, at a similar time of day as the initial pre-testing visit (± 1 hour), included reassessments of muscle thickness and one-repetition maximum strength.

The training groups were required to come to our laboratory three times per week, for 6-weeks (i.e., 18 total supervised sessions). Exercise involved the unilateral dumbbell elbow flexion exercise completed on either the dominant arm (i.e., dominant arm training group) or non-dominant arm (i.e., non-dominant arm training group), with heels and back against a wall (i.e., to ensure strict form). Each session began with heavy single training consisting of up to five single concentric repetition attempts (i.e., not five sets, but a maximum of five progressively heavier single lifts). The initial load for the first attempt was set between 70–85% of the participant's most recent one-repetition maximum, selected conservatively to ensure successful completion of the first lift. Load selection within this range was determined by the supervising investigator(s) based on the participant's most recent performance. Following each successful lift, the load was increased in small increments (typically 0.5–2.0 kg) for the subsequent attempt. Each attempt was separated by 90 s of rest. If a participant failed any attempt, no further heavy single attempts were performed during that session. If all five attempts were successfully completed and a new personal best was achieved, that load served as the target to exceed during the subsequent training session. Following the heavy singles, participants rested for 90 s before completing four sets of high-load elbow flexion to task failure using a load corresponding to an 8–12 repetition maximum, with 90 s of rest between sets. Loads were adjusted as needed to ensure failure occurred within the 8–12 repetition range. If a participant exceeded 12 repetitions, they were permitted to continue to failure, and the load was increased for the subsequent set or session to maintain the target range. Repetitions were paced using a metronome set at 60 beats per minute (1 s concentric, 1 s eccentric) to standardize cadence (Song, Hammert, et al., 2024; Song, Yamada, et al., 2024). The control group did not exercise train, but completed the pre- and post-intervention testing visits, which spanned the same 6-weeks as the training groups (i.e., time matched, non-exercise control group) (Hammert et al., 2024, 2025). All participants were instructed to continue their normal diets and activity patterns and refrain from beginning any resistance exercise training outside of the intervention.

Muscle Thickness

Muscle thickness images were taken using B-mode ultrasound (Logiq e, General Electric, Fairfield, CT), as has been detailed elsewhere (Song, Yamada, et al., 2024). Three images were taken and saved for each site on the anterior portion of both arms at 60% and 70% of the distance from the acromion process to the lateral epicondyle (identified by palpation). Muscle thickness was determined as the average distance between the muscle-bone and muscle-adipose interfaces from the stored images, assessed to the nearest 0.01 cm. To limit any bias, all measurements and analyses were taken by the same research investigator throughout the study, who was blinded to each group during all image analyses which were performed only after all testing was completed.

Maximal Strength

Maximal strength of the elbow flexors was determined as the greatest amount of weight the participant could perform for a single repetition in the unilateral biceps curl exercise (i.e., one-repetition maximum) (Song, Hammert, et al., 2024; Song, Yamada, et al., 2024). Testing began on the non-dominant arm, with the participant standing with feet shoulder width apart, heels and back against a wall and arm fully extended and supinated by their side. Participants were handed a loaded dumbbell and verbally encouraged to complete a full concentric range of elbow flexion. Initial attempts began with a submaximal load and were progressively increased until failure. If successful such that the dumbbell was moved through the full range of motion (i.e., from full elbow extension to full elbow flexion) with proper form (i.e., standing with their heels and back against the wall in an upright position), the load was increased prior to the next repetition. If unsuccessful (e.g., too heavy, improper form), the load was decreased until the participant was no longer able to lift a load greater than their previous heaviest, successful attempt. Each attempt was separated by 90 seconds of rest, which was selected given the unilateral nature of the exercise and relatively small muscle mass involved, consistent with previous studies from our laboratory (Bell et al., 2023; Dankel et al., 2020). Participants achieved their one-repetition maximum typically within 5-9 total attempts, with load measured to nearest 0.22 kg. Testing procedures and rest intervals were standardized across all participants.

Statistical Analyses

To investigate whether baseline muscle thickness (average of the 60% and 70% elbow flexor sites from the limb corresponding to the trained arm in each model) moderated the relationship between group (independent variable) and changes in one-repetition maximum strength (dependent variable) from pre- to post-intervention, we conducted retrospective, exploratory moderation analyses using the "PROCESS" macro in SPSS 30.0. More specifically, two separate models were run: one comparing the dominant-arm training group's trained arm to the dominant arm of the time-matched non-exercise control group, and another comparing the non-dominant-arm training group's trained arm to the non-dominant arm of the control group. Irrespective of the model, sex (male or female) and pre-training one-repetition maximum strength were included as covariates, and regression coefficients (b) were reported along with the 95% confidence interval (CI), standard error (SE), and p-value. To visualize a regression model with an interaction, we used Jamovi to produce simple slot plots of the relationships between groups and changes in one-repetition maximum strength across individual pre-training muscle thickness values. If there was statistical evidence of moderation, the Johnson-Neyman approach was employed to test the point in which the pre-training muscle thickness value moderated the relationship between the group and changes in one-repetition maximum strength. Statistical significance was set at $p < 0.05$, and all data are presented as mean (SD).

Following our moderation analysis (primary aim of paper), we decided to investigate if muscle growth mediated the change in strength. This was a secondary aim as previous work (Jessee et al., 2021; Kataoka et al., 2025; Spitz et al., 2023; Wong et al., 2025) has found no evidence to support that changes in maximal strength are mediated by changes in muscle thickness. Two separate simple mediation models were used to investigate the effects of training (*X*) on changes in: 1) non-dominant limb strength and 2) dominant limb strength (*Y* = change in one-repetition maximum strength; post-training minus pre-training), with muscle growth (M = changes in muscle thickness; post-training minus pre-training average of 60% and 70% muscle sites) serving as the mediator. The training groups were compared to the time-matched non-exercise control (i.e., reference group) (Hayes & Preacher, 2014). Based on Roth and MacKinnon (Roth & MacKinnon, 2013), a two-wave, where the mediator and dependent variable were measured both pre- and post-training, was constructed using the PROCESS macro (v.4.3) for SPSS. In this model (Figure 1), pre-training one-repetition maximum strength and sex were included as covariates for changes in muscle strength, while pre-training muscle thickness and sex were included as covariates for changes in muscle thickness (i.e., an autoregressive model). These covariates were chosen to account for their potential influence on an individual's capacity for change. All coefficients for between-group comparisons are reported relative to the time-matched non-exercise control group, unless otherwise indicated. Cross-lagged path analyses, as described by Valente and MacKinnon (2017) were also performed to see if that impacted the results.

RESULTS

The demographics for each group's age, height, and body mass, respectively, are as follows: non-dominant arm training (n = 40; 20 females): 21.7 (3.4) years, 170.9 (9.2) cm, 72.6 (21.1) kg; dominant arm training (n = 39; 23 females): 21.4 (3.2) years, 168.6 (9.7) cm, and 70.9 (18.7) kg; and time-matched non-exercise control (n = 43; 24 females): 21.3 (3.4) years, 169.5 (9.0) cm, and 76.9 (24.9) kg. Baseline one-repetition maximum strength was 12.0 (4.3) kg in the non-dominant arm training group (non-dominant arm), 11.3 (4.3) kg in the dominant arm training group (dominant arm), and 13.2 (4.7) kg and 12.5 (4.4) kg in the time-matched non-exercise control group (dominant and non-dominant arms, respectively). Average baseline muscle thickness (mean of the 60% and 70% elbow flexor sites) was 3.05 (1.19) cm for the non-dominant arm training group (non-dominant arm), 3.03 (1.05) cm for the dominant arm training group (dominant arm), and 3.44 (0.67) cm and 3.30 (0.70) cm for the control group (dominant and non-dominant arms, respectively).

When controlling for sex and pre-training strength, there was evidence that the change in one-repetition maximum strength for the non-dominant arm training group was greater than the time matched non-exercise control group [*b* = 2.86 kg, 95% CI = (2.33, 3.39), SE 0.26, $p < 0.001$]. However, there was no statistically significant group by pre-training muscle thickness interaction [*b* = 0.48, CI = (-0.25, 1.22), SE 0.37, $p = 0.197$]. Likewise, when controlling for sex and pre-training strength, there was evidence that the change in one-repetition maximum strength for the dominant arm training group was greater than the time matched non-exercise control group [*b* = 2.29 kg, 95% CI = (1.72, 2.87), SE 0.29, $p < 0.001$]. However, there was no statistically significant group by pre-training muscle thickness interaction [*b* = -0.076, CI = (-0.91, 0.75), SE 0.41, $p = 0.85$]. The results were robust and remained unchanged across all analyses (i.e., using muscle thicknesses at the 60% and 70% sites individually), when we removed the covariates (i.e., sex, pre-training one-repetition maximum) from each model (data not shown). The relationship between changes in one-repetition maximum strength across different pre-training muscle thickness values for the non-dominant arm training group compared to the time-matched non-exercise control group, as well as the dominant arm training group compared to the time-matched non-exercise control group are illustrated in Figure 2A and 2B, respectively.

For the dominant arm training group compared to the time matched non-exercise control group, the relative direct effect of training on changes in one-repetition maximum strength was positive and statistically significant (Table 1). The 95% bootstrap confidence interval for the relative indirect effect of training on changes in one-repetition maximum strength through changes in muscle thickness suggests that muscle growth mediated the relationship between training and strength gain. For the non-dominant arm training group compared to the time matched non-exercise control group, the relative direct effect of training on changes in one-repetition maximum strength was positive and statistically significant (Table 1). The 95% bootstrap confidence interval for the relative indirect effect of training on changes in one-repetition maximum strength through changes in muscle thickness suggests that muscle growth did not mediate the relationship between training and strength gain. The interpretation for both the non-dominant arm and dominant arm training groups compared to the time-matched non-exercise control group remained unchanged in the cross-lagged path analyses and when the covariates were removed (data not shown). Likewise, the results were consistent when muscle thicknesses at the 60% and 70% sites were analyzed individually using the simple mediation and cross-lagged models (data not shown).

DISCUSSION

Previous research has indicated that humans are not always able to fully activate their muscles during maximal voluntary isometric contractions (Behm et al., 2002; Dowling et al., 1994; Gandevia et al., 1998; Hucteau et al., 2020; Knight & Kamen, 2001), and that the extent of voluntary muscle

Table 1. Estimated regression coefficients for the simple mediation models (changes in maximal strength). *a* adjusted mean difference in muscle growth (Δ muscle thickness) between each training group compared to the corresponding arm of the time-matched non exercise control group, *b* adjusted effect of changes in muscle thickness changes on changes in one-repetition maximum strength, *c'* adjusted relative direct effect of each training group compared to the corresponding arm of the time-matched non-exercise control group.

	R^2	Path	Coefficient	95% CI	*p*-value
Dominant Arm Training vs. Control					
Δ Muscle Thickness	0.414				
		a	0.221 cm	0.152, 0.291	< 0.001
		constant	0.400 cm	0.101, 0.698	0.009
Δ One-Repetition Maximum Strength	0.559				
		b	2.63 kg	1.00, 4.28	0.002
		c’	1.68 kg	1.02, 2.34	< 0.001
		constant	0.77 kg	-0.89, 2.42	0.358
Indirect Effects (Simple Mediation)					
		a*b	0.584 kg	0.165, 1.140	---
Nondominant Arm Training vs. Control					
Δ Muscle Thickness	0.387				
		a	0.240 cm	0.168, 0.312	< 0.0001
		constant	0.292 cm	0.027, 0.557	0.031
Δ One-Repetition Maximum Strength	0.559				
		b	0.21 kg	-1.40, 1.82	0.796
		c’	2.81 kg	2.15, 3.47	< 0.001
		constant	-1.16 kg	-2.65, 0.34	0.127
Indirect Effects (Simple Mediation)					
		a*b	0.502 kg	-0.320, 0.605	---

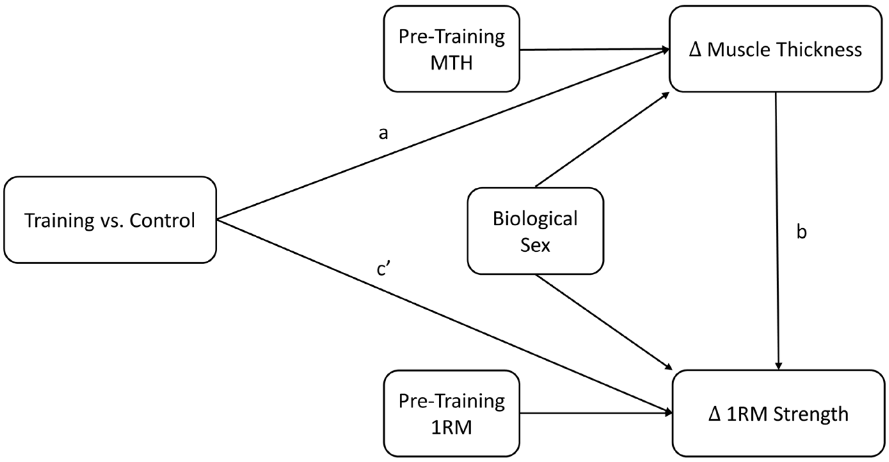

Figure 1. Simple mediation model detailing the conceptual framework for assessing the direct and indirect effects of resistance training (i.e., dominant and non-dominant arm training groups, each compared to the time-matched non-exercise control group) on changes in one-repetition maximum strength controlling for sex and when adjusting changes in muscle size and muscle strength to their respective baseline values. Not shown in the causal diagram, to maintain readability, is the complete role of sex as a covariate (i.e., sex was allowed to correlate with other predictors, including pre-muscle thickness and pre-muscle strength when estimating effects). a adjusted mean difference in muscle growth (Δ muscle thickness) between each training group compared to the corresponding arm of the time-matched non exercise control group, b adjusted effect of changes in muscle thickness changes on changes in one-repetition maximum strength, c' adjusted relative direct effect of each training group compared to the corresponding arm of the time-matched non-exercise control group.

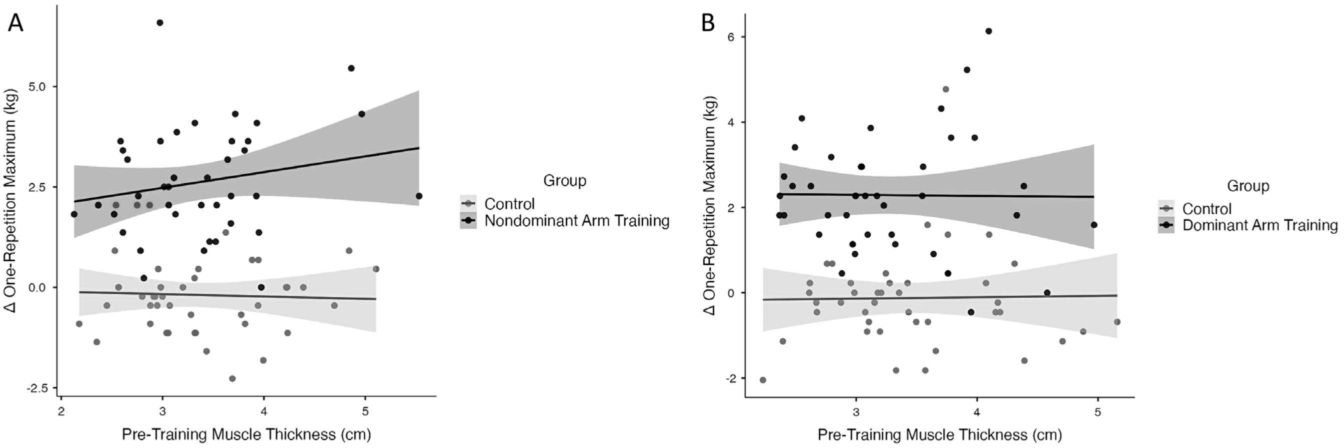

Figure 2. The relationship between changes in one-repetition maximum strength across different pre-training muscle thickness values. (A) The non-dominant arm training group compared to the time-matched non-exercise control group's nondominant arm. (B) The dominant arm training group compared to the time-matched non-exercise control group's dominant arm.

activation can increase following periods of heavy resistance training (Knight & Kamen, 2001). We thus hypothesized that individuals with larger muscles at baseline (i.e., pre-training muscle thickness) would have a greater ability to increase strength compared to those with smaller muscles. In contrast to our hypothesis, however, the results of our moderation analyses showed that the relationship between group and changes in one-repetition maximum strength did not differ according to individuals' pre-training muscle thickness.

To the best of our knowledge, Blazevich et al. (2007) are the only other researchers who have attempted to investigate the relationship between baseline muscle size and changes in maximal voluntary strength in non-resistance trained individuals. They did not explicitly present the results of their analyses, but stated that there was no correlation between pre-training maximal strength and pre-training quadriceps architecture measures (Blazevich et al., 2007). However, it was stated that the correlation became stronger after training (the exact parameters of the correlation are not clear) (Blazevich et al., 2007). Authors took their findings as evidence that individuals with bigger muscles at pre-training experienced the greatest improvements in maximal strength (Blazevich et al., 2007). Notwithstanding any differences as to how the data were analyzed, it is plausible that the discrepancies between our data and those of Blazevich et al. (2007) may be related to the muscle groups assessed. For example, it has previously been shown that during maximal voluntary isometric contractions, humans can activate a larger proportion of their elbow flexor muscles compared to the quadriceps muscles (Behm et al., 2002; Hucteau et al., 2020). On another hand, the hypothesis that individuals with bigger muscles at pre-training may experience the greatest increases in strength may just be wrong. Instead, the increases in one-repetition maximum strength observed herein may instead have resulted from neurological adaptations related to the principle of training specificity, or even mechanisms intrinsic to the fiber itself (Dankel et al., 2019; Hammert, Kataoka, Yamada, et al., 2023), irrespective pre-training muscle thickness values.

In comparison to previous research (Jessee et al., 2021; Kataoka et al., 2025; Spitz et al., 2023; Wong et al., 2025), which was unable to identify a mediating effect of skeletal muscle growth on changes in strength, the current data provide preliminary evidence suggesting that skeletal muscle growth may play a mechanistic role for increasing one-repetition maximum strength. More specifically, the results of our mediation analyses showed that, for the dominant arm training group, changes in muscle thickness positively mediated changes in one-repetition maximum strength. However, no such mediating effect was observed for the non-dominant arm training group. Any physiological explanation as to why increases in muscle size would be mechanistically implicated in strength gains exclusively for the dominant arm training group remains speculative and is not presently clear. Indeed, all three of the aforementioned analyses (Jessee et al., 2021; Kataoka et al., 2025; Spitz et al., 2023; Wong et al., 2025) were conducted using data from training groups that exercised the dominant arm compared to time matched non-exercise control groups. Among them, the report by Jessee et al. (2021) most closely resembles the current, as they too examined the mediating effects of changes in elbow flexor muscle thickness on changes in elbow flexion one-repetition maximum strength. Notwithstanding the likelihood of a chance finding, it remains possible that these discrepancies may be related to the differences in the employed resistance training protocols. To illustrate, Jessee et al. (2021) ran retrospective analyses on data from an investigation by Dankel et al. (2020), wherein participants performed either 4 sets of high-load exercise to task failure, or up to 5 heavy, single repetitions per session. In comparison, the training protocols employed in the present study had participants perform heavy singles followed by 4 sets of high-load exercise to task failure. Mechanism or not, it should be acknowledged that the dominant arm training group did not appear to lead to greater changes in one-repetition maximum strength compared to the non-dominant arm training group (Song, Yamada, et al., 2024). More research is thus necessary to replicate our data and further demonstrate whether strength changes would differ compared to a training designed to maximize strength and limit the amount of skeletal muscle growth induced (e.g., heavy single training) (Dankel et al., 2018). Indeed, we still know very little about why individuals get stronger following resistance training (Hortobágyi et al., 2021; Loenneke, 2021; Škarabot et al., 2021).

Apart from the retrospective nature of current analyses, there are a handful of limitations of our study that must be acknowledged. Based on previous research (Behm et al., 2002; Knight & Kamen, 2001), which showed that humans cannot fully activate their muscles during maximal voluntary isometric contractions, and that resistance training enhanced voluntary muscle activation, we hypothesized that individuals with larger muscles at pre-training would experience the greatest increases in strength. However, it is not known whether a similar phenomenon would be observed using other measures of strength (e.g., one-repetition maximum strength test), or if individuals who increase voluntary activation the most also gain the most strength. In addition, because we did not include any measurements of voluntary activation, it is not certain whether participants' ability to effectively activate their muscles during the one-repetition maximum strength test was actually influenced by training. Lastly, although our sample size is larger than most exercise science studies, the sample size may still be too small to detect mediation effects that are small to moderate in size (Fritz & MacKinnon, 2007). Why we observed evidence in the dominant arm but not the non-dominant arm training group is not immediately clear, but we have not ruled out "chance" given the number of times we have failed to find a mediating effect of muscle growth on changes in strength.

CONCLUSION

In previously non-resistance trained individuals, 6-weeks of heavy resistance training led to increases in skeletal muscle size and one-repetition maximum strength. However, the results of our moderation analyses suggest that the magnitude of change in strength was not influenced by pre-training muscle thickness values. Our mediation analyses provide preliminary evidence suggesting that the skeletal muscle growth may be involved in changes in one-repetition maximum strength, albeit only for the dominant arm training group. An explanation as to why we observed an effect in the dominant, but not the non-dominant arm training group, is unclear. Viewed alongside our previous data, which has failed to demonstrate a mediating effect of muscle growth on changes in strength, we believe it may be a “chance” finding.

FUTURE RECOMMENDATIONS

The current data add to the growing body of literature examining the relationship between exercise-induced increases in muscle size and strength. In this respect, more research on the topic appears warranted. Future work could investigate whether using a similar training protocol would lead to differential strength changes compared to a training designed to maximize strength and limit the amount of skeletal muscle growth induced (e.g., heavy single training). Whether heavy resistance training improves the ability to voluntarily activate one’s muscles during a one-repetition maximum strength test, and whether those who increase voluntary activation the most also observe the greatest strength increases might also be of interest.

DATA AVAILABILITY

All data are available upon reasonable request.

CONFLICTS OF INTEREST

Authors are aware of no competing interest.

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ETHICAL APPROVAL

Approved by The University of Mississippi’s Institutional Review Board (Protocol # 23-018).

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REFERENCES

1. Aagaard, P., Simonsen, E. B., Andersen, J. L., Magnusson, P., & Dyhre-Poulsen, P. (2002). Neural adaptation to resistance training: Changes in evoked V-wave and H-reflex responses. Journal of Applied Physiology, 92(6), 2309–2318. https://doi.org/10.1152/japplphysiol.01185.2001
2. Behm, D. G., Whittle, J., Button, D., & Power, K. (2002). Intermuscle differences in activation. Muscle & Nerve, 25(2), 236–243. https://doi.org/10.1002/mus.10008
3. Bell, Z. W., Wong, V., Spitz, R. W., Yamada, Y., Song, J. S., Kataoka, R., Chatakondi, R. N., Abe, T., & Loenneke, J. P. (2023). Unilateral high-load resistance training influences strength changes in the contralateral arm undergoing low-load training. Journal of Science and Medicine in Sport, 26(8), 440–445. https://doi.org/10.1016/j.jsams.2023.06.011
4. Blazevich, A. J., Gill, N. D., Deans, N., & Zhou, S. (2007). Lack of human muscle architectural adaptation after short-term strength training. Muscle & Nerve, 35(1), 78–86. https://doi.org/10.1002/mus.20666
5. Buckner, S. L., Dankel, S. J., Mattocks, K. T., Jessee, M. B., Mouser, J. G., Counts, B. R., & Loenneke, J. P. (2016). The problem of muscle hypertrophy: Revisited. Muscle & Nerve, 54(6), 1012–1014. https://doi.org/10.1002/mus.25420
6. Buckner, S. L., Yitzchaki, N., Kataoka, R., Vasenina, E., Zhu, W. G., Kuehne, T. E., & Loenneke, J. P. (2021). Do exercise-induced increases in muscle size contribute to strength in resistance-trained individuals? Clinical Physiology and Functional Imaging, 41(4), 326–333. https://doi.org/10.1111/cpf.12699
7. Currier, B. S., Mcleod, J. C., Banfield, L., Beyene, J., Welton, N. J., D’Souza, A. C., Keogh, J. A. J., Lin, L., Coletta, G., Yang, A., Colenso-Semple, L., Lau, K. J., Verboom, A., & Phillips, S. M. (2023). Resistance training prescription for muscle strength and hypertrophy in healthy adults: A systematic review and Bayesian network meta-analysis. British Journal of Sports Medicine, 57(18), 1211–1220. https://doi.org/10.1136/bjsports-2023-106807
8. Dankel, S. J., Bell, Z. W., Spitz, R. W., Wong, V., Viana, R. B., Chatakondi, R. N., Buckner, S. L., Jessee, M. B., Mattocks, K. T., Mouser, J. G., Abe, T., & Loenneke, J. P. (2020). Assessing differential responders and mean changes in muscle size, strength, and the crossover effect to 2 distinct resistance training protocols. Applied Physiology, Nutrition, and Metabolism, 45(5), 463–470. https://doi.org/10.1139/apnm-2019-0470
9. Dankel, S. J., Buckner, S. L., Jessee, M. B., Grant Mouser, J., Mattocks, K. T., Abe, T., & Loenneke, J. P. (2018).

Correlations Do Not Show Cause and Effect: Not Even for Changes in Muscle Size and Strength. Sports Medicine, 48(1), 1–6. https://doi.org/10.1007/s40279-017-0774-3

10. Dankel, S. J., Counts, B. R., Barnett, B. E., Buckner, S. L., Abe, T., & Loenneke, J. P. (2017). Muscle adaptations following 21 consecutive days of strength test familiarization compared with traditional training: 1RM Training. Muscle & Nerve, 56(2), 307–314. https://doi.org/10.1002/mus.25488
11. Dankel, S. J., Kang, M., Abe, T., & Loenneke, J. P. (2019). Resistance training induced changes in strength and specific force at the fiber and whole muscle level: A meta-analysis. European Journal of Applied Physiology, 119(1), 265–278. https://doi.org/10.1007/s00421-018-4022-9
12. Del Vecchio, A., Casolo, A., Negro, F., Scorcelletti, M., Bazzucchi, I., Enoka, R., Felici, F., & Farina, D. (2019). The increase in muscle force after 4 weeks of strength training is mediated by adaptations in motor unit recruitment and rate coding. The Journal of Physiology, 597(7), 1873–1887. https://doi.org/10.1113/JP277250
13. Dowling, J. J., Konert, E., Ljucovic, P., & Andrews, D. M. (1994). Are humans able to voluntarily elicit maximum muscle force? Neuroscience Letters, 179(1–2), 25–28. https://doi.org/10.1016/0304-3940(94)90926-1
14. Folland, J. P., & Balshaw, T. G. (2021). Muscle Growth Does Contribute to the Increases in Strength that Occur after Resistance Training. Medicine & Science in Sports & Exercise, 53(9), 2006–2010. https://doi.org/10.1249/MSS.0000000000002732
15. Folland, J. P., & Williams, A. G. (2007). The Adaptations to Strength Training: Morphological and Neurological Contributions to Increased Strength. Sports Medicine, 37(2), 145–168. https://doi.org/10.2165/00007256-200737020-00004
16. Fritz, M. S., & MacKinnon, D. P. (2007). Required Sample Size to Detect the Mediated Effect. Psychological Science, 18(3), 233–239. https://doi.org/10.1111/j.1467-9280.2007.01882.x
17. Gabriel, D. A., Kamen, G., & Frost, G. (2006). Neural Adaptations to Resistive Exercise: Mechanisms and Recommendations for Training Practices. Sports Medicine, 36(2), 133–149. https://doi.org/10.2165/00007256-200636020-00004
18. Gandevia, S. C., Herbert, R. D., & Leeper, J. B. (1998). Voluntary activation of human elbow flexor muscles during maximal concentric contractions. The Journal of Physiology, 512(2), 595–602. https://doi.org/10.1111/j.1469-7793.1998.595be.x
19. Hammert, W. B., Dankel, S. J., Kataoka, R., Yamada, Y., Kassiano, W., Song, J. S., & Loenneke, J. P. (2024). Methodological Considerations When Studying Resistance-Trained Populations: Ideas for Using Control Groups. 38(12), 2164–2171.
20. Hammert, W. B., Kataoka, R., Yamada, Y., Seffrin, A., Kang, A., Seob Song, J., Wong, V., Spitz, R. W., & Loenneke, J. P. (2023). The potential role of the myosin head for strength gain in hypertrophied muscle. Medical Hypotheses, 172, 111023. https://doi.org/10.1016/j.mehy.2023.111023
21. Hammert, W. B., Moreno, E. N., Martin, C. C., Jessee, M. B., & Buckner, S. L. (2023). Skeletal Muscle Adaptations to High-Load Resistance Training With Pre-Exercise Blood Flow Restriction. Journal of Strength and Conditioning Research, 37(12), 2381–2388. https://doi.org/10.1519/JSC.0000000000004553
22. Hammert, W. B., Moreno, E. N., Vasenina, E., & Buckner, S. L. (2023). Muscular Adaptations Between Very Low Load Resistance Training With Pulsed Direct Current Stimulation (Neubie) and Traditional High Load Training. 23(4), 377–385.
23. Hammert, W. B., Yamada, Y., Sallberg, R. W., Metcalf, E., Kataoka, R., Song, J. S., Dankel, S. J., Bell, Z. W., & Loenneke, J. P. (2025). Using historical controls to evaluate resistance training-induced strength adaptations: Does history repeat itself? Journal of Sports Sciences, 43(22), 2809–2819. https://doi.org/10.1080/02640414.2025.2559521
24. Hayes, A. F., & Preacher, K. J. (2014). Statistical mediation analysis with a multicategorical independent variable. British Journal of Mathematical and Statistical Psychology, 67(3), 451–470. https://doi.org/10.1111/bmsp.12028
25. Hortobágyi, T., Granacher, U., Fernandez-del-Olmo, M., Howatson, G., Manca, A., Deriu, F., Taube, W., Gruber, M., Márquez, G., Lundbye-Jensen, J., & Colomer-Poveda, D. (2021). Functional relevance of resistance training-induced neuroplasticity in health and disease. Neuroscience & Biobehavioral Reviews, 122, 79–91. https://doi.org/10.1016/j.neubiorev.2020.12.019
26. Hucteau, E., Jubeau, M., Cornu, C., & Cattagni, T. (2020). Is there an intermuscular relationship in voluntary activation capacities and contractile kinetics? European Journal of Applied Physiology, 120(2), 513–526. https://doi.org/10.1007/s00421-019-04299-z
27. Ikai, M., & Fukunaga, T. (1970). A study on training effect on strength per unit cross-sectional area of muscle by means of ultrasonic measurement. Internationale Zeitschrift For Angewandte Physiologie Einschliesslich Arbeitsphysiologie, 28(3), 173–180. https://doi.org/10.1007/BF00696025
28. Jessee, M. B., Buckner, S. L., Mouser, J. G., Mattocks, K. T., Dankel, S. J., Abe, T., Bell, Z. W., Bentley, J. P., & Loenneke, J. P. (2018). Muscle Adaptations to High-Load Training and Very Low-Load Training With and Without Blood Flow Restriction. Frontiers in Physiology, 9, 1448. https://doi.org/10.3389/fphys.2018.01448
29. Jessee, M. B., Dankel, S. J., Bentley, J. P., & Loenneke, J. P. (2021). A Retrospective Analysis to Determine Whether Training-Induced Changes in Muscle Thickness Mediate Changes in Muscle Strength. Sports Medicine, 51(9), 1999–2010. https://doi.org/10.1007/s40279-021-01470-5
30. Kacin, A., & Strazar, K. (2011). Frequent low-load ischemic resistance exercise to failure enhances muscle oxygen delivery and endurance capacity. Scandinavian Journal of Medicine & Science in Sports, 21(6). https://doi.org/10.1111/j.1600-0838.2010.01260.x
31. Kataoka, R., Hammert, W. B., Yamada, Y., Sallberg, R. W., Kang, A., Song, J. S., Kassiano, W., Metcalf, E. E., & Loenneke, J. P. (2025). Submaximal low-load resistance exercise with blood flow restriction produces similar results to low-load exercise to failure for muscle size and strength, but not endurance. European Journal of Applied Physiology. https://doi.org/10.1007/s00421-025-05949-1
32. Knight, C. A., & Kamen, G. (2001). Adaptations in muscular activation of the knee extensor muscles with strength training in young and older adults. Journal of Electromyography and Kinesiology, 11(6), 405–412. https://doi.org/10.1016/S1050-6411(01)00023-2
33. Loenneke, J. P. (2021). Muscle Growth Does Not Contribute to the Increases in Strength that Occur after Resistance Training. Medicine & Science in Sports & Exercise, 53(9), 2011–2014. https://doi.org/10.1249/MSS.0000000000002662
34. Loenneke, J. P., Buckner, S. L., Dankel, S. J., & Abe, T. (2019). Exercise-Induced Changes in Muscle Size do

not Contribute to Exercise-Induced Changes in Muscle Strength. Sports Medicine, 49(7), 987–991. https://doi.org/10.1007/s40279-019-01106-9

35. Mattocks, K. T., Buckner, S. L., Jessee, M. B., Dankel, S. J., Mouser, J. G., & Loenneke, J. P. (2017). Practicing the Test Produces Strength Equivalent to Higher Volume Training. Medicine & Science in Sports & Exercise, 49(9), 1945–1954. https://doi.org/10.1249/MSS.0000000000001300
36. Moritani, T., & deVries, H. A. (1979). Neural factors versus hypertrophy in the time course of muscle strength gain. Moritani, T. (1979). Neural Factors versus Hypertrophy in the Time Course of Muscle Strength Gain. American Journal of Physical Medicine, 58(3), 115-130., 58(3), 115–130.
37. Rasch, P. J. (1955). The problem of muscle hypertrophy: A review. Journal of Physical Education and Sport, 54(9), 525–528.
38. Roth, D. L., & MacKinnon, D. P. (2013). Mediation analysis with longitudinal data. In Longitudinal data analysis (pp. 181–216). Routledge.
39. Sale, D. G. (1988). Neural adaptation to resistance training. 20(5 Suppl), 135–35.
40. Senn, S. (2013). Seven myths of randomisation in clinical trials. Statistics in Medicine, 32(9), 1439–1450. https://doi.org/10.1002/sim.5713
41. Škarabot, J., Brownstein, C. G., Casolo, A., Del Vecchio, A., & Ansdell, P. (2021). The knowns and unknowns of neural adaptations to resistance training. European Journal of Applied Physiology, 121(3), 675–685. https://doi.org/10.1007/s00421-020-04567-3
42. Song, J. S., Hammert, W. B., Kataoka, R., Yamada, Y., Kang, A., Wong, V., Spitz, R. W., Kassiano, W., & Loenneke, J. P. (2024). Unilateral high-load resistance training induced a similar cross-education of strength between the dominant and non-dominant arm. Journal of Sports Sciences, 1–5. https://doi.org/10.1080/02640414.2024.2388997
43. Song, J. S., Yamada, Y., Kataoka, R., Hammert, W. B., Kang, A., Spitz, R. W., Wong, V., Seffrin, A., Kassiano, W., & Loenneke, J. P. (2024). Does Unilateral High-Load Resistance Training Influence Strength Change in the Contralateral Arm Also Undergoing High-Load Training? Scandinavian Journal of Medicine & Science in Sports, 34(12), e14772. https://doi.org/10.1111/sms.14772
44. Spitz, R. W., Dankel, S. J., Jessee, M. B., Wong, V., Bell, Z. W., Abe, T., & Loenneke, J. P. (2023). Does muscle growth mediate changes in a nonspecific strength task? Clinical Physiology and Functional Imaging, 43(4), 223–231. https://doi.org/10.1111/cpf.12810
45. Taber, C. B., Vigotsky, A., Nuckols, G., & Haun, C. T. (2019). Exercise-Induced Myofibrillar Hypertrophy is a Contributory Cause of Gains in Muscle Strength. Sports Medicine, 49(7), 993–997. https://doi.org/10.1007/s40279-019-01107-8
46. Valente, M. J., & MacKinnon, D. P. (2017). Comparing Models of Change to Estimate the Mediated Effect in the Pretest–Posttest Control Group Design. Structural Equation Modeling: A Multidisciplinary Journal, 24(3), 428–450. https://doi.org/10.1080/10705511.2016.1274657
47. Weier, A. T., Pearce, A. J., & Kidgell, D. J. (2012). Strength training reduces intracortical inhibition. Acta Physiologica, 206(2), 109–119. https://doi.org/10.1111/j.1748-1716.2012.02454.x
48. Wong, V., Spitz, R. W., Bentley, J. P., Song, J. S., Yamada, Y., Hammert, W. B., Seffrin, A., Bell, Z. W., & Loenneke, J. P. (2025). Investigating the Influence of Limb Blood Flow on Contraction-Induced Muscle Growth and the Impact of that Growth on Changes in Maximal Strength. 57(4), 867–875. https://doi.org/10.1249/MSS.0000000000003613
49. Wong, V., Spitz, R. W., Song, J. S., Yamada, Y., Kataoka, R., Hammert, W. B., Kang, A., Seffrin, A., Bell, Z. W., & Loenneke, J. P. (2024). Blood flow restriction augments the cross-education effect of isometric handgrip training. European Journal of Applied Physiology. https://doi.org/10.1007/s00421-023-05386-y