



Resistance training induced changes in strength and specific force at the fiber and whole muscle level: a meta-analysis

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Abstract

Purpose Considerable debate exists as to whether increases in strength that occur with resistance exercise are the result of increases in muscle size. Most studies have attempted to answer this question using assessments of whole muscle size and voluntary muscle strength, but examining changes at the individual muscle fiber level may also provide some insight. The purpose of this meta-analysis was to compare adaptations at the whole muscle and individual fiber level.

Methods A meta-analysis was conducted in February, 2018 including all previously published papers and was analyzed using a random effects model.

Results There were no differences ($p = 0.88$) when comparing hypertrophy at the whole muscle (4.6%) and individual fiber level (7.0%), but significantly larger ($p < 0.001$) strength gains were observed at the whole muscle level (43.3%) relative to the individual fiber (19.5%). Additionally, there was an increase in the specific tension of type 1 muscle fibers ($p = 0.013$), but not type 2 muscle fibers ($p = 0.23$) which was driven by similar increases in strength (type 1: 17.5%, type 2A: 17.7%), despite differences in muscle size (type 1: 6.7%, type 2A: 12.1%).

Conclusion These results support the hypothesis that the neural adaptations play a large role in increasing isotonic whole muscle strength, but also demonstrate that an improvement in specific tension of type 1 muscle fibers is present. These results would suggest that some mechanism intrinsic to the muscle fiber, and independent of muscle growth, may also be contributing to strength increases in response to resistance exercise providing an avenue for future research.

Keywords 1RM · Biopsy · Hypertrophy · Muscle fiber · Muscle fibre · Weight lifting

Abbreviations

1RM	One-repetition maximum
CT	Computed tomography
MRI	Magnetic resonance imaging
MVC	Maximal voluntary contraction
NIH	National Institute of Health

Introduction

While it is commonly thought that increases in muscle mass via resistance exercise contribute to increases in muscle strength (Moritani and deVries 1979; Balshaw et al. 2017), this line of thinking has been questioned recently (Buckner et al. 2016, 2017a; Dankel et al. 2018). It is understood that individuals with more muscle mass tend to be stronger (Ikai and Fukunaga 1968), but it can be difficult to tease out whether the increase in muscle size from resistance exercise is causing the increase in strength (Dankel et al. 2018). Our laboratory has recently examined different protocols designed to blunt or eliminate muscle growth in attempt to see if this would blunt or eliminate muscle strength. Interestingly, even in the absence of muscle hypertrophy, strength increases were similar across conditions (Dankel et al. 2017a; Mattocks et al. 2017) which would seemingly question the idea that increases in strength via resistance exercise are the result of increased muscle mass occurring via resistance exercise.

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There are a variety of ways to examine whether increases in muscle size via resistance training cause increases in muscle strength. Thus far, studies have focused on changes at the whole muscle level, but single fiber level changes (tested outside of the body) may provide additional information as these changes cannot possibly be modulated by adaptations to the nervous system. Assessing the importance of changes in whole muscle size while removing any influence of the nervous system can be performed in animals by removing the entire muscle but this cannot be done in humans. Assuming hyperplasia (an increase in fiber number) does not appreciably occur in humans in response to resistance exercise (McCall et al. 1996), the relative increase in whole muscle size should be similar to that observed at the individual fiber level. A direct comparison of relative strength changes at the individual muscle fiber and whole muscle level may, therefore, provide some indication about the role of the nervous system in increasing voluntary strength. That is, if the relative change in muscle size is similar, greater muscle strength at the whole muscle level would likely indicate the degree of involvement of the nervous system in increasing strength. This comparison, however, cannot provide information as to whether the changes in muscle strength that occur at the individual muscle fiber level are occurring due to changes in qualitative (e.g., changes in fiber types, calcium sensitivity, etc.) or quantitative (i.e., increases in muscle size) mechanisms.

The measure of specific tension (i.e., maximal muscle force per unit of cross-sectional area) is often used as a proxy measure to assess whether the increases in individual muscle fiber strength are the result of improved muscle quality (if there is an increase in specific tension) or increased muscle size (if there is no change in specific tension). This differs from the comparison of whole muscle vs. individual muscle fiber strength since the influence of the nervous system is removed. An examination of cross-sectional studies suggests that resistance training increases both muscle size and strength at the individual muscle fiber level; however, conflicting results exist as to whether resistance training may improve specific tension (D'Antona et al. 2006; Shoepe et al. 2003). These conflicting results may be related to the cross-sectional nature of these study designs, which cannot determine whether differences between groups are truly the result of resistance training. Several longitudinal studies have examined changes at both the whole muscle and individual muscle fiber level (Trappe et al. 2000, 2001; Godard et al. 2002; Widrick et al. 2002; Frontera et al. 2003; Cristea et al. 2008; Slivka et al. 2008; Parente et al. 2008; Raue et al. 2009; Pansarasa et al. 2009; Erskine et al. 2011; Claffin et al. 2011; Toth et al. 2012; Paoli et al. 2016; Miller et al. 2017); however, these studies also have detailed conflicting results. Some of these conflicting results may be related to the age of the participants (Welle et al. 1996), the exercise load

prescribed (Campos et al. 2002), and/or the duration of the intervention (Ogasawara et al. 2013b) as these have all been shown to modulate whole muscle adaptations. Therefore, the purpose of this meta-analysis was to quantifiably answer the following questions: (1) how does the relative change in voluntary joint strength differ from that of individual fiber strength? (2) how does the change in whole muscle size differ from that of individual muscle fiber size? and (3) is there a change in the specific tension at the individual muscle fiber level? We also attempted to determine a possible role of age, number of training sessions, and training load in moderating the effects.

Materials and methods

Articles were initially obtained using the following set of search terms in Pubmed, SPORTDiscus, and Scopus: (1) “single muscle fiber” AND “exercise” (2) “single muscle fiber” AND “resistance training” and (3) “single muscle fiber” AND “strength training” up until February, 2018. All previously published papers were eligible for inclusion in the analysis, with the oldest paper meeting the inclusion criteria being published in 2000. These search terms were also repeated using the European spelling of the word fiber “fibre”. References of these articles were also searched for additional articles in the reference list. A flow chart showing the included studies is detailed in Fig. 1. For studies to be included in the quantitative meta-analysis, they had to meet the following criteria: (1) written in English; (2) included humans and not animals; (3) employed a chronic resistance training intervention (i.e., not plyometric or endurance training); (4) measured individual muscle fiber force; and (5) measured whole muscle strength. Studies without a measure of muscle size were still included as the primary purpose of this study was to examine differences in strength values at the cellular and whole-body level.

All variability statistics reported as standard error units were converted to standard deviation units using an appropriate formula (i.e., multiplying the standard error by the square root of the sample size). When means and variability statistics were not present in the text but were illustrated in graph form, a graph digitizer (Engauge Digitizer Software, version 10.4) was used to estimate the values. An effect size was calculated as the difference in relative pre-test to post-test changes divided by the pooled standard deviations of these relative changes [relative change 1—relative change 2/pooled standard deviations of the relative changes]. We did not use the standard method of computing effect sizes based off the pre-test standard deviation, as this is not appropriate when analyzing paired data (Dankel et al. 2017b). Relative changes were used because strength and muscle size changes at the individual fiber and whole muscle level are expressed

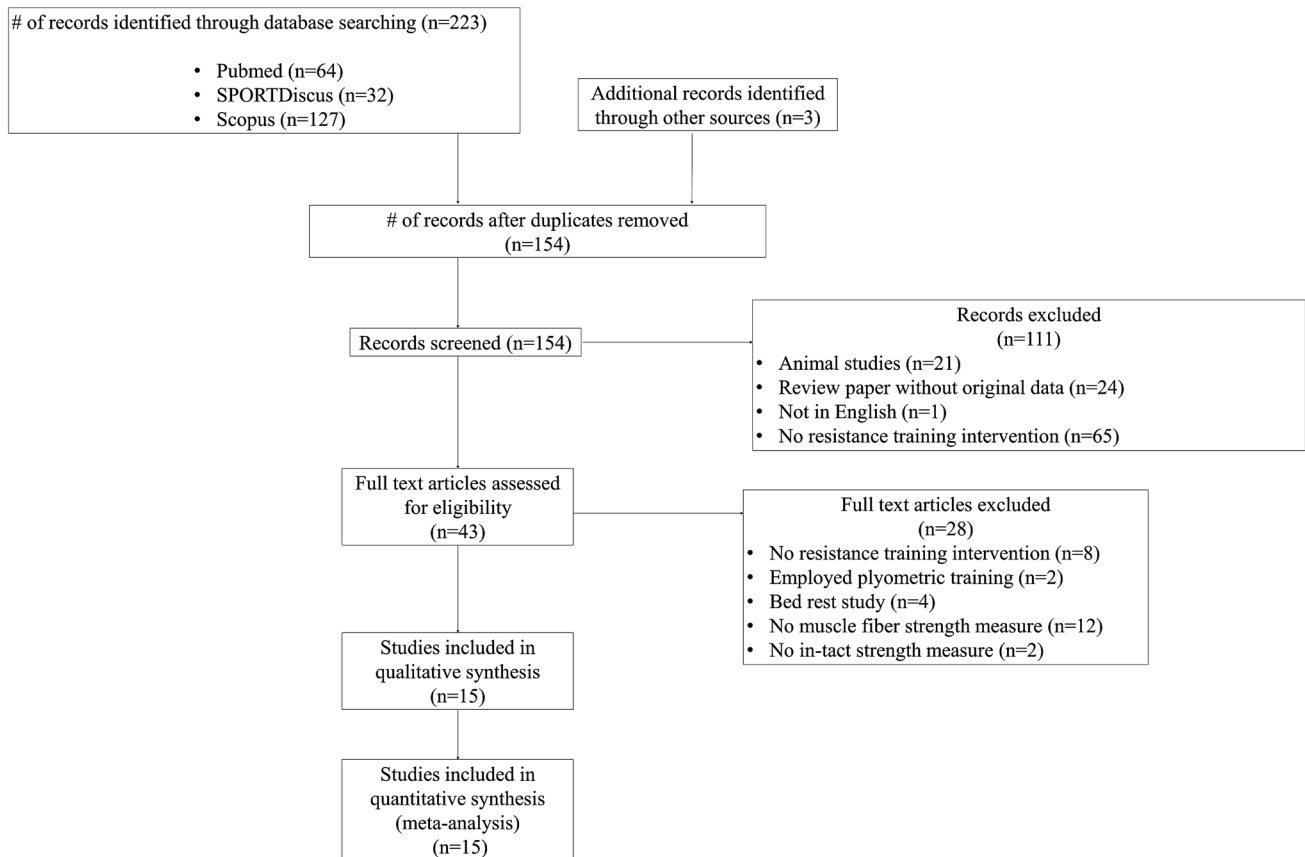


Fig. 1 Flow chart of included studies

in different units. Therefore, relative changes were used to standardize the units and obtain one effect size directly comparing the whole muscle and individual fiber level (as opposed to comparing two independent effect sizes).

If the standard deviation of the pre-test to post-test change was not reported, this value was estimated by obtaining the pre-test to post-test correlations from similar studies. These r values for each variable were calculated from multiple studies and were then averaged together. The corresponding r values and studies from which they were obtained are as follows: 1RM (one-repetition maximum) strength: $r=0.76$ (Trappe et al. 2000; Godard et al. 2002; Slivka et al. 2008), isokinetic strength: $r=0.69$ (Pansarasa et al. 2009), MVC (maximal voluntary isometric contraction) strength: $r=0.79$ (Pansarasa et al. 2009), type 1 muscle fiber force: $r=0.79$ (Widrick et al. 2002; Claffin et al. 2011), type 2 muscle fiber force: $r=0.34$ (Widrick et al. 2002; Claffin et al. 2011), type 1 muscle fiber size: $r=0.79$ (Widrick et al. 2002; Claffin et al. 2011), type 2 muscle fiber size: $r=0.33$ (Widrick et al. 2002; Claffin et al. 2011), whole muscle size measured by MRI (magnetic resonance imaging): $r=0.98$ (Erskine et al. 2011), whole muscle size measured by CT (computed tomography) scan: $r=0.98$ (Slivka et al. 2008). For hybrid

fibers, the average of type 1 and type 2 correlations was used. These correlations were then plugged into the formula: $SD_{\text{intervention}} = \text{square root} [(SD_{\text{Pre-test}})^2 \text{ plus } (SD_{\text{Post-test}})^2 \text{ minus } (2r \text{ multiplied by } SD_{\text{Pre-test}} \text{ multiplied by } SD_{\text{Post-test}})]$ which allowed us to estimate the variability in response to the actual intervention itself. If the standard deviation of the change score was already provided this value was used.

There were three studies where the variability for isotonic strength vs. individual muscle size comparisons could not be calculated using the information provided (Claffin et al. 2011; Toth et al. 2012; Miller et al. 2017). For these studies, the average pooled standard deviations for individual muscle fiber and whole muscle strength from the other included studies (22.33%) were used to estimate the variability present. Similarly, for type 1 and type 2A muscle size vs. strength comparisons, four studies did not provide the necessary variability statistics to compute effect sizes (Parente et al. 2008; Pansarasa et al. 2009; Toth et al. 2012; Miller et al. 2017), and thus, the pooled average variability from the other included studies was used (type 1: 25.31%, type 2A: 37.82%). Given that all effect sizes were computed with the variability expressed as a percentage, averaging values from other studies should not be sensitive to different magnitudes

of strength across individuals and/or exercises. Even so, we did not feel it would be appropriate to estimate variability for the computation of effect sizes for whole muscle isometric strength vs. individual fiber strength, whole muscle isokinetic strength vs. individual fiber strength, or type 2X comparisons of size vs. strength as $\leq 50\%$ of the studies reporting means included variability data. Therefore, only relative percentage changes (as opposed to effect sizes) were compared. In the Miller et al. study (2017) where two 1RM strength tests assessing the quadriceps muscles were used (i.e., leg press and leg extension) these percentage changes in strength from pre-test to post-test were averaged together.

Sufficient data were available to compute effect sizes for the following comparisons: (1) whole muscle isotonic strength vs. individual muscle fiber strength; (2) whole muscle size vs. individual muscle fiber size; (3) type 1 muscle fiber size vs. type 1 muscle fiber strength; and (4) type 2A muscle fiber size vs. type 2A muscle fiber strength. To calculate the average muscle fiber size and strength at the individual fiber level, we weighted the strength/size of each fiber by the proportion of each fiber type in the muscle to account for the heterogeneity in muscle fibers, as well as any fiber shifts that would have occurred from pre to post exercise. This was calculated by multiplying the percentage of each muscle fiber by the average force/size of the given fiber. These values were then summed to compute the average strength of an individual muscle fiber. For example, if a muscle biopsy contained 40% type 1 and 50% type 2A, and 10% type 2X fibers, the average strength/muscle size was estimated as [(type 1 strength/size \times 0.40) + (type 2A strength/size \times 0.50) + (type 2x \times 0.10)]. If the percentages of individual muscle fiber types were not reported, it was estimated that 1/3 of the muscle fibers in the vastus lateralis were type 1 and 2/3 were type 2A (Edgerton et al. 1975).

Statistics were computed using SPSS v. 25 (IBM, NY, USA). A random effects model was used to assess if there were differences in relative strength and relative size increases at the whole muscle and individual fiber level. A positive effect size indicated a greater increase in relative strength/size in the whole muscle compared to the individual fiber level. Additional random effects models were computed comparing the relative strength and muscle size increases within type 1 and type 2A muscle fibers such that a greater effect size illustrates a greater increase in muscle strength compared to muscle size. Two dichotomous potential moderator variables were also tested to see if effect sizes differed depending on age (< 45 vs. ≥ 45 years) and/or sex (male vs. female). Additionally, meta-regression was used to assess the influence of the following two continuous variables: (1) training load and (2) total supervised training sessions completed. Eggers test was used to test for publication bias across studies, and the quality assessment tool for pre-post studies without a control group was adapted from

the National Institute of Health (NIH) (Table 1). Sensitivity analyses were performed using the one study removed method to assess changes in point estimates. Statistical significance level was set at 0.05.

Results

A total of fifteen studies met the criteria for inclusion in the meta-analysis (Trappe et al. 2000, 2001; Godard et al. 2002; Widrick et al. 2002; Frontera et al. 2003; Cristea et al. 2008; Slivka et al. 2008; Parente et al. 2008; Raue et al. 2009; Pansarasa et al. 2009; Erskine et al. 2011; Claffin et al. 2011; Toth et al. 2012; Paoli et al. 2016; Miller et al. 2017). The study quality assessment is detailed in Table 1, showing that the studies included in this analysis were of a similar quality. Information on the population and whole muscle measurements of the included studies is detailed in Table 2. Information on the fiber level measurements used in each study are shown in Table 3. Notably, all studies had individuals train with the same isotonic exercises in which they were tested for isotonic 1RM strength. The isometric and isokinetic strength tests assessed the same muscle group that was trained, but the individuals did not train with this mode of exercise. Similarly, with the exception of one study assessing the latissimus dorsi muscle (Paoli et al. 2016), all included studies that assessed the vastus lateralis muscle (Table 2).

Whole muscle isotonic strength vs. individual fiber strength

Twelve studies were included in the comparison (Trappe et al. 2000, 2001; Godard et al. 2002; Widrick et al. 2002; Frontera et al. 2003; Cristea et al. 2008; Slivka et al. 2008; Raue et al. 2009; Claffin et al. 2011; Toth et al. 2012; Paoli et al. 2016; Miller et al. 2017) which allowed for the computation of 16 effect sizes. There was a greater relative increase in whole muscle isotonic strength when compared to individual muscle fiber strength [ES: 1.14 (95% CI 0.63–1.64); $p < 0.001$; Fig. 2a]. The average relative increase in isotonic strength was 43.3% and the average relative increase in individual muscle fiber strength was 19.5%. When examining moderator variables, there was no effect of age ($p = 0.45$) or sex ($p = 0.33$), but there was an effect of training load [β : -0.04 (95% CI $-0.08, 0.00$); $p = 0.002$] and total number of supervised sessions [β : 0.07 (95% CI 0.03, 0.10); $p < 0.001$] on the overall effect size. This indicates that an increase in the training load resulted in a greater individual muscle fiber strength relative to whole muscle strength, and an increase in the total number of sessions favored an increase in whole muscle strength over individual muscle fiber strength. There was no evidence of publication bias ($p = 0.569$).

Table 1 Study Quality Assessment Adapted from the National Institute of Health (NIH)

	Claflin et al. (2011)	Cristea et al. (2008)	Erskine et al. (2011)	Frontera et al. (2003)	Godard et al. (2002)	Miller et al. (2017)	Pansarasa et al. (2009)	Paoli et al. (2016)	Parente et al. (2008)	Raue et al. (2009)	Silvka et al. (2008)	Toth et al. (2012)	Trappe et al. (2001)	Trappe et al. (2000)	Widrick et al. (2002)	
1. Was the study question or objective clearly stated?	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2. Were eligibility/selection criteria for the study population pre-specified and clearly described?	0	0	1	0	1	1	0	0	0	1	1	1	0	0	0	0
3. Were all eligible participants that met the pre-specified entry criteria enrolled?	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4. Was the sample size sufficiently large to provide confidence in the findings?	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5. Was the test/service/intervention clearly described and delivered consistently across the study population?	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6. Were the outcome measures pre-specified, clearly defined, valid, reliable, and assessed consistently across all study participants?	1	1	0	1	1	1	1	0	1	1	1	1	1	1	1	1
7. Was the loss to follow-up after baseline 20% or less?	0	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1
8. Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p values for the pre-to-post changes?	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Total	5	5	6	6	7	7	6	5	6	7	7	6	6	6	6	6

Studies were score as 0 (No) or 1 (Yes) for a possible total score of 8 points. If there was insufficient information a 0 was given

Table 2 Information on population and whole muscle measurements in included studies

Population and exercise protocol	Strength tests assessing the same muscle biopsied	Muscle biopsied	Muscle size measure	Interpolated twitch performed
Claffin et al. (2011) 15 untrained younger men (mean age: 24 years) completed 42 supervised sessions of leg press and hip flexion exercises using machines. Performed two sets of 10 and a third set to failure	Leg press 10RM (IRMs were performed but this data is not reported)	Vastus lateralis	N/A	No
Claffin et al. (b) (2011) 18 untrained younger women (mean age: 24 years) completed 42 supervised sessions of leg press and hip flexion exercises using machines. Performed two sets of 10 and a third set to failure	Leg press 10RM (IRMs were performed but this data is not reported)	Vastus lateralis	N/A	No
Claffin et al. (c) (2011) 14 untrained older men (mean age: 76 years) completed 42 supervised sessions of leg press and hip flexion exercises using machines. Performed two sets of 10 and a third set to failure	Leg press 10RM (IRMs were performed but this data is not reported)	Vastus lateralis	N/A	No
Claffin et al. (d) (2011) 16 untrained older women (mean age: 75 years) completed 42 supervised sessions of leg press and hip flexion exercises using machines. Performed two sets of 10 and a third set to failure	Leg press 10RM (IRMs performed but this data is not reported)	Vastus lateralis	N/A	No
Cristea et al. (2008) 11 untrained older men (mean age: 66 years) completed 32 supervised sessions of leg press, half squats, clean pulls, and Romanian deadlifts. Involved either 3–4 sets at 50–70% 1RM, 2–3 sets at 70–85% 1RM, or 2–3 sets at 35–60% 1RM	Knee extension 1RM, isometric knee extension	Vastus lateralis	N/A	No
Erskine et al. (2011) 17 untrained younger men (mean age: 20 years) completed 27 supervised sessions of unilateral knee extensions. 4 sets of 10 @ 80% 1RM	Isometric knee extensions	Vastus lateralis	MRI	Yes
Frontera et al. (2003) 7 untrained older women (mean age: 73 years) completed 36 supervised sessions of knee extensions and knee flexions. 4 sets of 8 repetitions at 65–80% 1RM	Knee extension 1RM, and isokinetic knee extension at 60°/s	Vastus lateralis	CT	No
Godard et al. (2002) 6 untrained older women (mean age: 73 years) completed 36 supervised sessions of knee extensions. 3 sets at 80% 1RM	Knee extension 1RM	Vastus lateralis	N/A	No
Miller et al. (2017) 17 untrained older men and women with knee osteoarthritis (mean age: 70 years) completed 42 supervised sessions of leg press, knee extensions, knee flexions, calf raises, hip extensions, hip flexions. 1 set of 8 at 30% 1RM	Leg press 1RM, knee extension 1RM, isometric knee extension, isokinetic knee extension at 60 and 180°/s	Vastus lateralis	CT	No
Pansarasa et al. (2009) 5 untrained younger women (mean age: 25 years) completed 104 supervised sessions of leg press and calf raises. 1 set of 12 at 60% 1RM	Isometric knee extension	Vastus Lateralis	N/A	No
Paoli et al. (2016) 18 untrained (with the exception of a few individuals with ≤3 months training) younger men (mean age: 24 years) completed 24 supervised sessions of bench press, latissimus pull-downs, seated rows, shoulder press, biceps hammer curls, dumbbell lying external rotation. 2–3 sets of 9–11 repetitions at 75–80% 1RM or 6–8 repetitions at 80–85% 1RM	Latissimus pull-down 1RM	Latissimus Dorsi	N/A	No

Table 2 (continued)

	Population and exercise protocol	Strength tests assessing the same muscle biopsied	Muscle biopsied	Muscle size measure	Interpolated twitch performed
Parente et al. (2008)	4 untrained older women (mean age: 78 years) completed 104 supervised sessions of seated leg press and calf press. 1 set of 12 at 60% 1RM	Isometric knee extension	Vastus lateralis	N/A	No
Raue et al. (2009)	6 untrained older women (mean age: 85 years) completed 36 supervised sessions of knee extensions. 3 sets of 10 repetitions at 70–75% 1RM	Knee extension 1RM	Vastus lateralis	CT	No
Raue et al. (b) (2009)	9 untrained younger women (mean age: 21 years) completed 36 supervised sessions of knee extensions. 3 sets of 10 repetitions at 70–75% 1RM	Knee extension 1RM	Vastus lateralis	CT	No
Silvka et al. (2008)	6 untrained older men (mean age: 82 years) completed 36 supervised sessions of knee extensions. 3 sets of 10 at 70% 1RM	Knee extension 1RM	Vastus lateralis	CT	No
Toth et al. (2012)	14 untrained older men and women (mean age: 71 years) completed 54 supervised sessions of knee extensions, leg press, knee flexions, shoulder press, bench press, biceps curls, and latissimus pull-downs. 3 sets of 8 at 50–80% 1RM	Isometric knee extension and isokinetic knee extension at 60, 120, and 180°/s	Vastus lateralis	N/A	No
Toth (b) (2012)	10 untrained older men and women with heart failure (mean age: 73 years) completed 54 supervised sessions of knee extensions, leg press, knee flexions, shoulder press, bench press, biceps curls, and latissimus pull-downs. 3 sets of 8 at 50–80% 1RM	Isometric knee extension and isokinetic knee extension at 60, 120, and 180°/s	Vastus lateralis	N/A	No
Trappe (2001)	7 untrained older women (mean age: 74 years) completed 36 supervised sessions of knee extensions. 2 sets of 10 repetitions and a third set to failure at 80% 1RM	Knee extension 1RM	Vastus lateralis	N/A	No
Trappe et al. (2000)	7 untrained older men (mean age: 74 years) completed 36 supervised sessions of knee extensions. 2 sets of 10 repetitions and a third set to failure at 80% 1RM	Knee extension 1RM	Vastus lateralis	N/A	No
Widrick et al. (2002)	6 untrained younger men (mean age: 27 years) completed 36 supervised sessions of squats, knee extensions, knee flexions, calf raises, bench press, latissimus pull-downs, shoulder press, triceps press, biceps curls, and seated rows. 3 sets of a 6–12 RM	Leg press 6RM	Vastus lateralis	N/A	No

Different letters listed within the citations after the author indicate a different sub-sample of individuals within each study
 CT computed tomography, MR magnetic resonance imaging, N/A not available

Whole muscle isokinetic strength vs. individual fiber strength

Three studies included a measure of isokinetic strength tests (Frontera et al. 2003; Toth et al. 2012; Miller et al. 2017), reporting similar increases in both whole muscle isokinetic (6.3%) and individual muscle fiber (5.0%) strength. No effect sizes were computed since variability statistics were only reported for one of the three studies.

Whole muscle isometric strength vs. individual fiber strength

Six studies included a comparison of whole muscle isometric strength to individual muscle fiber strength (Cristea et al. 2008; Parente et al. 2008; Pansarasa et al. 2009; Erskine et al. 2011; Toth et al. 2012; Miller et al. 2017). Similar to isokinetic testing, the strength increase was similar in both whole muscle isometric (16.8%) and individual muscle fiber (20.6%) strength. No effect sizes were computed since variability statistics were only reported for two of the size studies.

Whole muscle size vs. individual muscle fiber size

Five studies were included in the comparison (Frontera et al. 2003; Slivka et al. 2008; Raue et al. 2009; Erskine et al. 2011; Miller et al. 2017) which allowed for the computation of six effect sizes. Of these studies, four used CT (Frontera et al. 2003; Slivka et al. 2008; Raue et al. 2009; Miller et al. 2017) to measure whole muscle size and one used MRI (Erskine et al. 2011). There was no difference in the change between whole muscle size and individual muscle fiber size [ES: -0.03 (95% CI $-0.39, 0.323$); $p=0.88$; Fig. 2b]. The average relative increase in whole muscle size was 4.6% and the average increase in individual muscle fiber size was 7.0%. When examining moderator variables, there was no impact of age ($p=0.41$), sex ($p=0.20$), training load ($p=0.10$), or total supervised sessions completed ($p=0.42$). There was no evidence of publication bias ($p=0.302$).

Type 1 individual fiber strength vs. size

A total of 15 studies (Trappe et al. 2000, 2001; Godard et al. 2002; Widrick et al. 2002; Frontera et al. 2003; Cristea et al. 2008; Slivka et al. 2008; Parente et al. 2008; Raue et al. 2009; Pansarasa et al. 2009; Erskine et al. 2011; Claffin et al. 2011; Toth et al. 2012; Paoli et al. 2016; Miller et al. 2017) were included which allowed for the computation of 20 effect sizes. There were differences in the relative increase in muscle size and strength that was observed in type 1 muscle fibers [ES: 0.39 (95% CI $0.08, 0.69$); $p=0.013$] indicating that the relative increase in type 1 fiber strength (17.5%) was greater than the relative increase in type 1 fiber size

(6.7%). This effect did not differ based on age ($p=0.29$) sex ($p=0.45$), training load ($p=0.35$), or total supervised sessions completed ($p=0.59$). Egger's test was statistically significant indicating the possibility of publication bias ($p=0.002$). When rerunning the analysis to exclude the Trappe et al. study (2001) which was >3 standard deviations above the other included studies, the magnitude of the effect was reduced but still statistically significant [ES: 0.28 (95% CI $0.06, 0.50$); $p=0.012$; Fig. 3a]. Figure 3a depicts the results with the Trappe et al. study (2001) removed.

Type 2A individual fiber strength vs. size

A total of 14 studies (Trappe et al. 2000, 2001; Godard et al. 2002; Widrick et al. 2002; Cristea et al. 2008; Slivka et al. 2008; Parente et al. 2008; Raue et al. 2009; Pansarasa et al. 2009; Erskine et al. 2011; Claffin et al. 2011; Toth et al. 2012; Paoli et al. 2016; Miller et al. 2017) were included which allowed for the computing of 19 effect sizes. There was no difference in the relative increase in type 2A muscle fiber size or strength [ES: 0.13 (95% CI $-0.08, 0.34$); $p=0.24$; Fig. 3b]. Specifically, the average increase in type 2A muscle strength was 17.7% while the increase in type 2A muscle size was 12.1%. There was no moderating effect of age ($p=0.61$), sex ($p=0.58$), training load ($p=0.56$), or total supervised sessions completed ($p=0.31$). Egger's test was statistically significant indicating the possibility of publication bias ($p=0.001$).

Type 2X individual fiber strength vs. size

Four studies (Widrick et al. 2002; Pansarasa et al. 2009; Paoli et al. 2016; Miller et al. 2017) included a measure of type 2X muscle size illustrating a 31.0% increase in relative strength and a 18.4% increase in relative size. No effect sizes were computed as only two of the four studies included variability statistics.

Sensitivity analyses

When examining changes in point estimates for effect sizes using the one study removed method, the most extreme effect sizes on both the higher and lower end of the estimate were as follows: whole muscle vs. individual fiber strength (lowest: 1.01, highest: 1.27); whole muscle vs. individual fiber size (lowest: -0.21 , highest: 0.05); type 1 strength vs. size (lowest: 0.27, highest: 0.44); and type 2A strength vs. size (lowest: 0.06, highest: 0.16).

Table 3 Information on fiber-level assessments in included studies

	Number of fibers analyzed per biopsy	Temperature analyzed at (°C)	Length of sarcomere
Clafflin et al. (2011)	~ 19.3 for both fiber force and size	15	2.5–2.6 μm
Clafflin et al. (b) (2011)	~ 20.1 for both fiber force and size	15	2.5–2.6 μm
Clafflin et al. (c) (2011)	~ 19.0 for both fiber force and size	15	2.5–2.6 μm
Clafflin et al. (d) (2011)	~ 20.0 for both fiber force and size	15	2.5–2.6 μm
Cristea et al. (2008)	~ 19.9 for fiber force and ~ 42.7 for fiber size	15	2.72–2.84 μm
Erskine et al. (2011)	~ 4.2 for both fiber force and size	15	2.6 μm
Frontera et al. (2003)	~ 17.8 for both fiber force and size	15	2.75–2.85 μm
Godard et al. (2002)	~ 22.8 for both fiber force and size	15	2.5 μm
Miller et al. (2017)	~ 13 for both fiber force and size	15	N/A
Pansarasa et al. (2009)	~ 35.8 for both fiber force and size	12	2.5 μm
Paoli et al. (2016)	N/A	12	N/A
Parente et al. (2008)	~ 38.8 for both fiber force and size	12	2.5 μm
Raue et al. (2009)	~ 19.5 for both fiber force and size	15	2.5 μm
Raue et al. (b) (2009)	~ 19.5 for both fiber force and size	15	2.5 μm
Silvka et al. (2008)	~ 22.3 for both fiber force and size	15	2.5 μm
Toth et al. (2012)	~ 5.6 for both fiber force and size	15	2.65 μm
Toth et al. (b) (2012)	~ 6.7 for both fiber force and size	15	2.65 μm
Trappe (2001)	~ 22.4 for both fiber force and size	15	2.5 μm
Trappe et al. (2000)	~ 24.6 for both fiber force and size	15	2.5 μm
Widrick et al. (2002)	~ 24.6 for both fiber force and size	15	2.5 μm

Different letters listed within the citations after the author indicate a different sub-sample of individuals within each study

Discussion

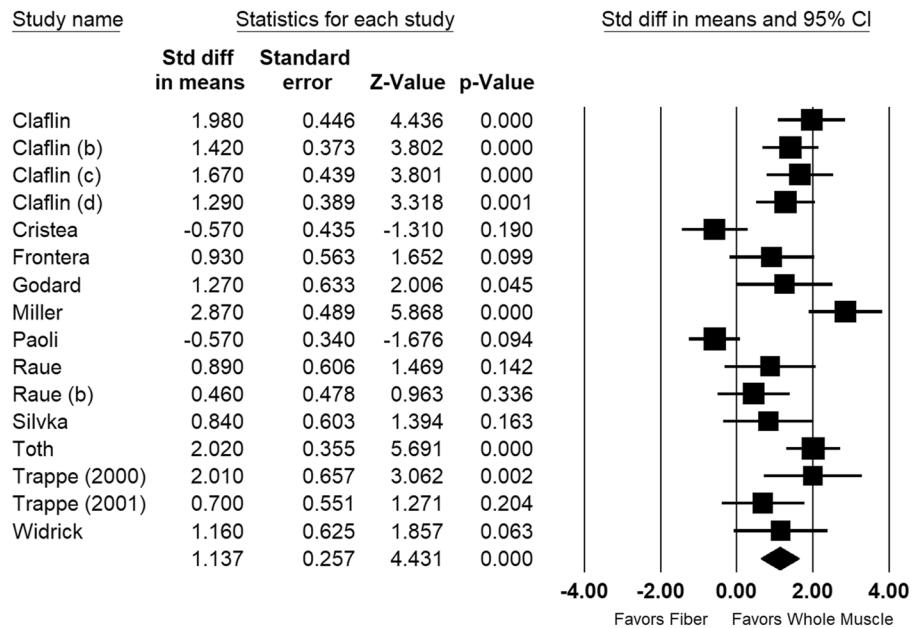
The primary findings of the present study were as follows: (1) the relative increase in whole muscle isotonic strength was over twice as large as the relative increase in individual muscle fiber strength (43.3 vs. 19.5%); (2) voluntary isometric and isokinetic strength increases were similar to that of the individual muscle fiber; (3) increases in whole muscle and individual fiber size were relatively similar (4.6 vs. 7.0%); and (4) there was an apparent increase in the specific tension of muscle fibers, and this was the most pronounced in type 1 muscle fibers. Collectively, these results suggest that the nervous system likely plays a large role in increasing voluntary isotonic strength, but the quality of the muscle fiber also appears to improve and contribute to strength increases.

Increases in strength that occur with resistance training are thought to be at least partially the result of neurological adaptations (Sale 1988; Carroll et al. 2001). In the present study, we found that the relative improvements in whole muscle isotonic strength were approximately twice as great as the relative improvements in individual muscle fiber strength suggesting a large contribution of the nervous system in increasing isotonic strength. Interestingly, when examining the impact of the training loads used,

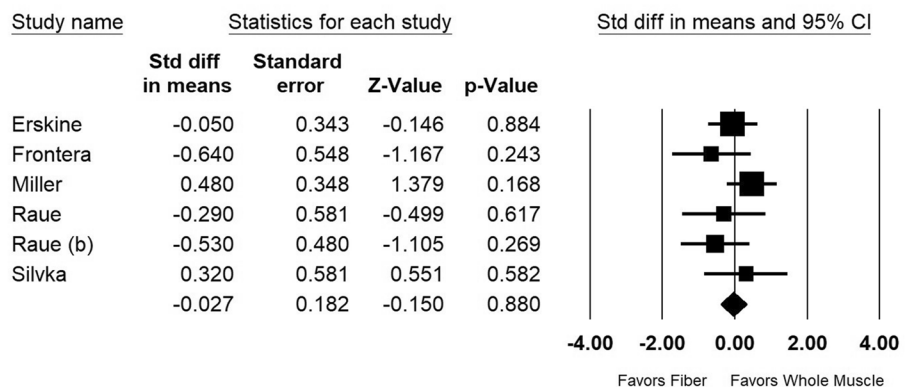
we observed that each 10% increase in 1RM training load actually resulted in a 0.4% greater increase in individual muscle fiber strength relative to that of whole muscle isotonic strength. We feel this may be a spurious finding given the small magnitude of effect, and previous studies showing that greater isotonic training loads typically produce greater increases in voluntary isotonic strength (Mitchell et al. 2012; Ogasawara et al. 2013a; Schoenfeld et al. 2015). It is commonly stated that increases in strength are primarily due to neurological adaptations early on before being driven primarily by increases in muscle size (Moritani and deVries 1979), but our results did not seem to support this hypothesis. This hypothesis would have predicted that longer training interventions would have yielded greater increases in individual fibers strength when compared to whole muscle strength (given the attenuated neurological improvements), but our moderator analysis revealed the opposite. Specifically, our analysis revealed that each additional training session produced a 0.07% greater increase in whole muscle strength when compared to individual muscle fiber strength. This may suggest that the neurological adaptations occurring with resistance exercise are still present at the later stages of a training program, although this finding by itself provides only minimal support for this hypothesis. Only one study included in this analysis used the interpolated twitch technique (Erskine et al. 2011) and the results suggest that

Fig. 2 Relative changes at the whole muscle and individual muscle fiber level. **a** The difference in the relative increase in voluntary whole muscle isometric strength compared to the relative increase in individual muscle fiber strength. **b** The difference in the relative increase in whole muscle size compared to the relative increase in individual muscle fiber size

A Changes in Muscle Strength



B Changes in Muscle Size



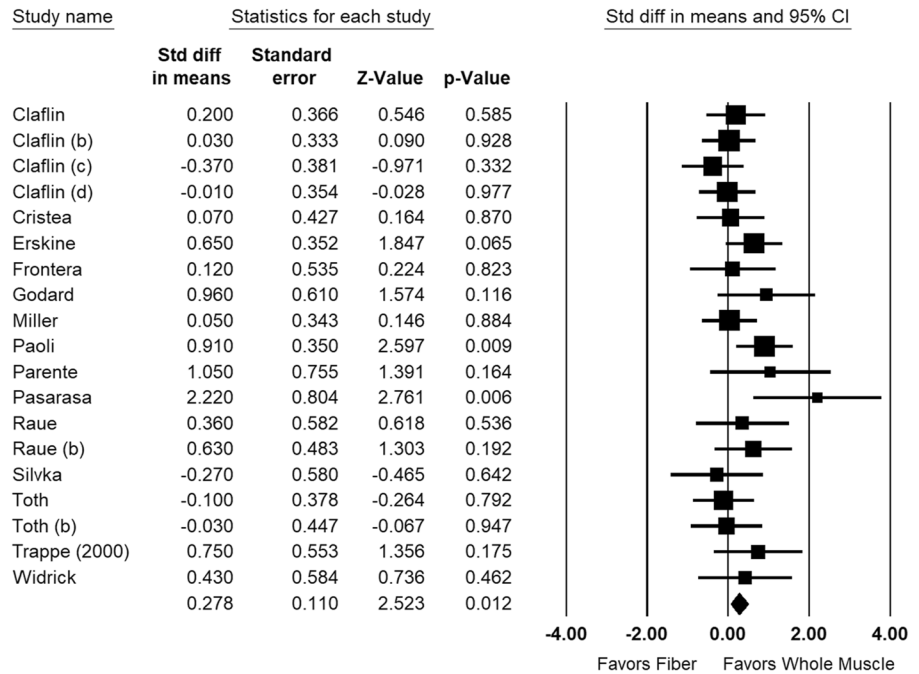
voluntary activation is increased with resistance exercise. This may suggest that a greater activation of agonist muscles and a greater inhibition of antagonist muscles may contribute to increases in voluntary strength occurring in response to resistance exercise.

The idea that voluntary isometric and isokinetic strength more so resembled that of the individual muscle fiber is likely to illustrate the importance of task specificity (Buckner et al. 2017b) given that all of the studies included in this analysis employed an isotonic training intervention. The component of task specificity is likely to play a substantially larger role when assessing voluntary strength given that comparing two distinct protocols (i.e., high vs. low velocity training) produces similar changes at the fiber level despite producing differences in voluntary power measures (Clafflin et al. 2011). Similarly, previous studies have shown that

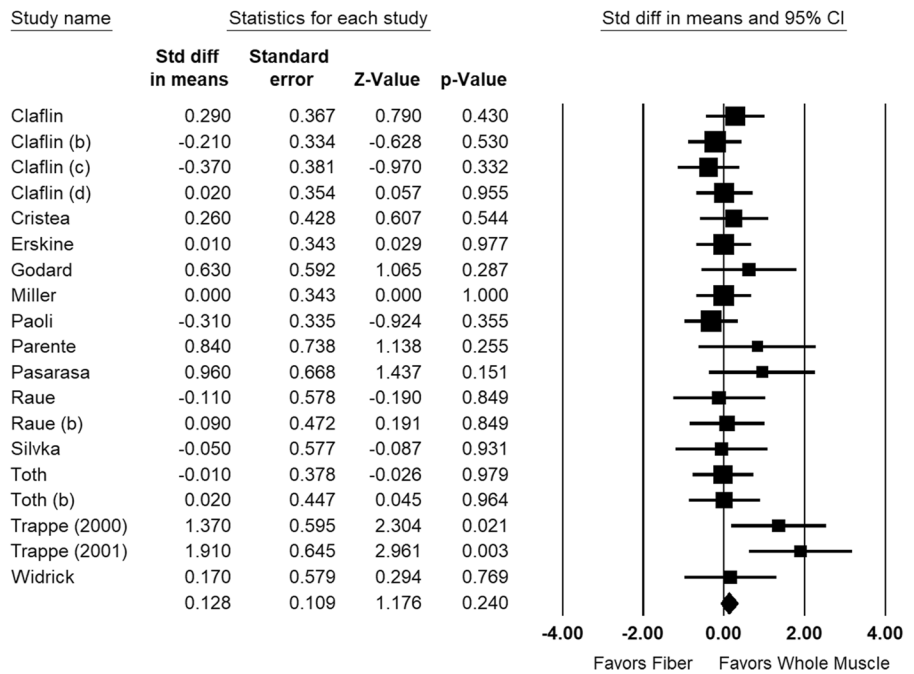
males and females appear to have unique changes to resistance training that occur at the individual muscle fiber level, but this may be less apparent when comparing changes in voluntary whole muscle measures (Trappe et al. 2000, 2001; Miller et al. 2017). Therefore, careful interpretation should be used when making inferences on whole muscle voluntary strength using data collected on individual muscle fibers. When examining the changes in voluntary isokinetic and isometric strength tests, it is tempting to suggest that these measurements may provide a more representative estimate of fiber level adaptation. Although the means were not different, the results of each study were not necessarily similar. To determine the level of agreement within an individual study, we calculated the relative minimal difference between fiber level strength and voluntary isokinetic strength, as well as fiber level strength and voluntary isometric strength. The

Fig. 3 Changes in individual muscle fiber specific tension. **a** The relative change in the muscle size and muscle strength of type I muscle fibers. **b** The relative change in the muscle size and muscle strength of type 2A muscle fibers

A Changes in Size and Strength of Type I Fibers



B Changes in Size and Strength of Type IIA Fibers



relative minimal difference was 243.4 and 102.1% for voluntary isokinetic and isometric tests, respectively. In other words, if there was a 10% increase in voluntary isokinetic strength, the 95% limits of agreement for estimating relative fiber strength would be between -14.3 and 34.3%. Similarly, if there was a 10% increase in voluntary isometric strength,

the 95% limits of agreement for estimating relative fiber strength would be between -0.2 and 20.2%. Therefore, one should use caution when trying to infer relative fiber strength from a voluntary isokinetic/isometric strength test.

The relative increase in muscle size did not differ when comparing changes at the individual fiber and whole muscle

level. This would support the idea that resistance exercise induces increases in muscle mass that are primarily the result of muscle hypertrophy (as opposed to hyperplasia) (McCall et al. 1996). While this resulted in a much greater specific tension at the whole muscle level relative to the individual muscle fiber, there still did appear to be increases in specific tension at the fiber level, particularly in type 1 fibers. This resulted from a greater hypertrophy of type 2 fibers (changes were as follows: type 1: 6.7%, type 2A: 12.1%), despite similar strength changes across these fiber types (type 1: 17.5%, type 2A: 17.7%,). While there was no effect of training load on altering specific tension, this may also have been due to the rather homogenous training load used across studies (Table 2). It has been suggested that the preferential increase in type 2 fibers may be related to a greater stress placed on these fibers as it common for individuals to use relatively higher training loads (i.e., $\geq 60\%$ 1RM) (Ogborn and Schoenfeld 2014). Interestingly, it appears that the greater increase in type 2 muscle fiber size (compared to type 1 fibers) does not promote greater relative strength gains. The lack of a moderating effect of age for any of the outcome variables is somewhat surprising given some of the fiber type changes that accompany aging (e.g., fiber type shifts, fiber number, etc.) (Miljkovic et al. 2015). This may indicate that the relative changes (whole muscle changes relative to individual fiber level changes) in response to resistance exercise are not drastically different between younger and older individuals.

Within the individual studies included in this meta-analysis, there appears to be a discrepancy as to whether specific tension increases with resistance exercise (Fig. 3). Based on our moderator analysis, the discrepant findings did not appear to be driven by age or sex, and may be related to whether or not the calculation of specific tension is adjusted for reductions in myofibril area occurring with exercise (Toth et al. 2012), although this is not a universal finding (Alway et al. 1989). The significant increase we observed in specific tension of type 1 muscle fibers in response to resistance exercise suggests that some property intrinsic to the muscle fiber and independent of muscle hypertrophy is contributing to increases in strength. It remains unknown what intrinsic property may be increasing muscle strength, but some hypothesized mechanisms include shifts in fiber types (Parente et al. 2008), increases in calcium sensitivity (Godard et al. 2002), and increases in strongly bound cross-bridges (Miller et al. 2017).

Our study is not without limitations. First, all but one of the studies in this included analysis examined the influence of resistance exercise on the vastus lateralis muscle, and thus these results may not necessarily generalize to other musculature. Additionally, we found evidence of possible publication bias for the comparison of specific tension at the fiber level, and thus these results should be interpreted with caution. Furthermore, we would like to mention that an

increase in specific force at the individual fiber level does not rule out the possibility that increases in muscle size are playing a role with increases in strength, but rather, points to additional mechanisms that are also likely contributing. Likewise, a lack of change in specific tension at the fiber level does not rule out that peripheral (i.e., muscle level) mechanisms other than muscle hypertrophy are contributing to strength gains.

Conclusion

Collectively, our findings illustrate that, despite similar relative increases in muscle size, resistance exercise results in substantially larger improvements in voluntary whole muscle isotonic strength when compared to individual muscle fiber strength. Additionally, our results appear to demonstrate that increases in specific tension are present at the individual muscle fiber level which suggests that mechanisms independent of neurological adaptations and independent of increases in muscle size are contributing to the strength increases occurring from resistance exercise. Furthermore, the changes in voluntary strength appear to be much more dependent on task specificity, whereas the strength of individual muscle fibers may respond more uniformly to different types of resistance exercise. Therefore, our results suggest that changes that occur at the fiber level do not necessarily provide a good indication of the changes that occur at the voluntary whole muscle level.

Author contribution SJD drafted the manuscript and performed the statistical analysis; JPL designed the study and revised the manuscript for intellectual content; MK assisted with the analysis and revised the manuscript for intellectual content; TA revised the manuscript for intellectual content.

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Compliance with ethical standards

Conflict of interest The authors declares that they have no conflict of interest.

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