Impact of different mechanical and metabolic stimuli on the temporal dynamics of muscle strength adaptation

Brief Running Head: Temporal dynamics of muscle strength adaptation

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ABSTRACT

A fundamental task in exercise physiology is to determine and ultimately improve the adaptations that take place in the human body, an integrated network of various physiological systems e.g., muscle, tendon and bone. Investigating the temporal dynamics (time-course) of adaptations in these diverse systems may help us gain new knowledge about the functioning of the neuro-motor system in healthy and pathological conditions. The aim of this review was to explore the temporal dynamics of muscular strength adaptations in studies implementing a resistance training intervention. In addition, we categorised these studies under mechanical or metabolic stimuli to identify whether certain stimuli cause faster muscle strength gains. Searches were performed using PubMed and Google Scholar databases. The review comprised 708 participants from 57 training groups within 40 studies that met the inclusion criteria. The results revealed that the mean time point of first significant increase in muscle strength of all studies was 4.3 weeks and the corresponding increase was on average about 17%. A plateau in muscle strength increase (~25%) was found to occur between weeks 8 and 12. Categorisation into stimuli groups revealed that performing training in a hypoxic environment is likely to produce a leftward shift (~25% increase at ~2.8 weeks) in the dose-response relationship compared to blood flow restriction and supplementation. However, stimuli that cause faster muscle strength gains may also induce imbalanced adaptation between the muscle and the surrounding biological structures potentially triggering a degradation in some parts of the network (i.e., leading to an increased risk of injury).

KEY WORDS: dose-response relationship, time-related adaptive response, resistance training

INTRODUCTION

Muscle strength is a prerequisite for improved athletic performance, prevention of injuries and maintenance of a healthy lifestyle (21,65). Hence, increasing muscle strength has become one of the central aspects in sports, clinical and rehabilitation settings (22,61,90). Classical strength training is largely based on the “overload” principle (27), according to which muscle strength can be increased when a minimal loading intensity threshold is exceeded. Correspondingly, moderate to high mechanical loading (≥60% of one repetition maximum; 1RM) has been traditionally regarded as the primary stimulus (i.e., mechanical tension) causing muscle hypertrophy and thus to increases in muscle strength (26,40). It is principally known that muscular strength development is established by a combination of neural and morphological adaptations in a time-dependent order. Firstly, enhanced neural factors explain the larger proportion of the initial muscle strength increments whereas changes in muscle morphology (hypertrophy) form a rather longer-term mechanism behind improved muscle strength (23,56). From the morphological perspective, it has been hypothesized that both mechanical tension and metabolic stress contribute to training-related muscle hypertrophy and hence to an increase in maximal strength (20).

Increased force generation capacity of a muscle has central and peripheral level nervous system origins (2,88). An increased ability to transmit signals (neural drive) between the brain and spinal cord (central nervous system) and the rest of the body (peripheral nervous system) forms a more noticeable component in muscle strength adaptations during the first weeks of exercise compared to muscle hypertrophy. This is indirectly indicated by the higher increase in muscle strength as to muscle size in the early stages of training (28,41). More direct evidence of neural adaptations come

from studies which have shown that following strength training central motor drive and motoneuron excitability increase while presynaptic inhibition of Ia afferent synapses decreases (2,29). Investigations implementing techniques such as surface electromyography, interpolated twitch and evoked spinal reflexes show that the increased motor unit recruitment and firing frequency result in an overall higher agonist muscle activation while the reciprocal inhibition leads to a lower antagonist activation/co-activation, ultimately enabling the muscle to produce a higher moment output at the joint level (6,78).

Following the initial phase of muscle strength increments largely dominated by the adaptations in the nervous system, the peripheral adaptations in muscle morphology and contractility become more prominent. Firstly, changes in contractile function occur on the molecular level as myosin, the key contractile protein, may change its isoform type by adjusting to the intrinsic velocity of force generation (87). For example, radial adaptation in response to higher forces involves the building and addition of more sarcomeres, the force-producing units of muscle, in parallel thus increasing the physiological cross-sectional area (PCSA) of a muscle (35,45,67,68). Secondly, contractile function is enhanced with increases in the pennation angle of a muscle's fibers, which is believed to be a regulating component of the PCSA enabling fibre hypertrophy and inducing further radial muscle growth (1,9). Targeting for higher CSA /size, which in vivo studies in humans have shown is positively correlated with maximum shortening velocity and mechanical power of muscle fibres, may have profound improvements on functional performance (9,24).

Investigating the temporal dynamics (time-course changes) of muscle strength adaptation may provide the practitioner with an advanced understanding of how to most effectively influence these internal networks and ultimately improve performance

by optimising individual exercise prescriptions. In this way, training can be done at a more representative level of the participant's ability and goals, hence providing constantly appropriate stimuli to trigger muscle strength gains (3). Failing to make appropriate adjustments in training intensity/volume can lead to a phase of plateau (not challenging enough and no improvement) or may cause fatigue (too challenging for improvement) and even an increased risk of injury (28). However, the majority of strength and conditioning experiments to date do not consider the temporal dynamics of adaptation and report only overall improvements in muscle strength (usually after 12-14 weeks). As a result, most reviews conducted in the last decades provide us with limited information on which mechanical or metabolic stimuli has the most expedited effect on muscle strength gains. Typical categorisations reviewed include: loading level (66), type of muscle contraction (i.e., eccentric vs concentric; 65), type of training focus (i.e., strength vs power; 8), supplementation (63) and blood flow restriction (BFR; 46); but since the timeline of muscle strength adaptation has not been considered in these reviews, only the overall benefit to exposure (effect of the intervention) is known of selected mechanical and metabolic stimuli.

The strength adaptations and the extent to which they develop, are not only dependent on the type of stimuli (mechanical vs metabolic), but they are also time as well as loading volume and magnitude dependent (21). Existing literature suggests that muscle strength can adapt as early as 2 weeks after commencing a heavy resistance (75% 1RM) training intervention (11), but conversely can take up to 6 weeks when using a lower intensity (range: 8-20RM) training volume (62). Paradoxically, combining blood flow restriction with low loads results in similar adaptations in muscle strength and hypertrophy (16,74) as training with higher loads. This emphasises that morphological adaptations induced by increased metabolic stress may be as effective

in muscle strength gains (20,49) as increased neural adaptations (i.e. higher intensities). Metabolic mechanisms that can cause muscle hypertrophy include the accumulation of by-products such as lactate, hydrogen ions, inorganic phosphate, adenosine diphosphate and mitogen-activated protein kinase which may induce an anabolic signal (25,60). In addition, even though the direct involvement in hypertrophy of hormones such as growth hormone, insulin-like growth factor-1 and testosterone is unclear, there is evidence that these hormones complement muscle anabolism by optimising the adaptations (69,81,85). This is revealed through facilitation of amino acid transport, activation of satellite cells and improved force transmission, all of which may increase muscular strength (47,89).

It has been argued that any periods of imbalanced strength adaptation between muscles (or other interconnected biological tissues e.g., tendons) which work together simultaneously, such as quadriceps and hamstrings during a (stretch-shortening-cyclic) football kick, may increase the risk of musculoskeletal injuries (48). Therefore, knowledge of the temporal dynamics in muscle strength adaptations in response to different training modalities is important and needed for the development of appropriate training programmes to improve athletic performance, reduce injury risk and maintain the ability of executing everyday activities. Accordingly, the primary aim of this review is to investigate the temporal dynamics of muscle strength adaptations in response to various resistance exercise modalities. More specifically, to define the time points and magnitudes of first significant increase and saturation (plateau) in increase of muscle strength. The secondary aim is to reveal how strength adaptation depends on the type of training stimuli and whether any of these may cause a leftward shift in the dose-response relationship (i.e. time – strength adaptation relationship).

METHODS

The review was conducted according to the search strategy guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; 54). One reviewer performed initial electronic database searches for articles investigating the temporal dynamics of muscle strength adaptations to training intervention in human participants (by September 2021). PubMed and Google Scholar electronic databases were searched for articles written in English. Combinations of the following words and phrases were used as search terms: ‘muscle strength’, ‘temporal dynamics’, ‘training intervention’, ‘resistance training’, ‘time-course adaptations’, ‘strength training programme’, ‘muscular adaptation’, ‘muscular output’, ‘dose-response relationship’ and ‘strength monitoring’. Additionally, references from the chosen papers were also crosschecked manually by the reviewer to identify relevant studies that might have been missed in the primary search and to eliminate duplicates.

A study was included in the review if the following selection criteria were fulfilled: (1) was a controlled trial with healthy adults as participants; (2) involved a training intervention that targeted strength improvement and lasted more than six weeks with at least two training sessions per week (adequate time and training volume for significant gains to be recorded); (3) measured muscular strength in terms of 1 repetition maximum (1RM) or maximum voluntary contraction (MVC) at least once during the intervention other than pre and post measurements and (4) was published in a peer-reviewed journal after 1980 (conference abstracts and unpublished studies were excluded). The initial search process yielded 174 studies after duplicates were removed. Then, titles and abstracts of the remaining papers were read, from which 132 were excluded. The remaining 42 studies were fully read and 40 studies were considered eligible according to the criteria mentioned earlier (Fig. 1). Statistical

significance level was set at $p \leq 0.05$ and the data were analysed in Matlab software (Mathworks, Inc., Natick, MA, USA).

----- Figure 1 about here -----

RESULTS

Across the 40 studies included, 57 training groups were analysed and reported in this review. 708 participants (194 females: 27% and 514 males: 73%) with a range of age of 18-88 years were recruited. More than half of the studies (n=26; 65%) recruited just male participants, ten (25%) recruited participants of both genders and only four recruited just females (10%). More than half of the studies (n=21; 53%) involved interventions that lasted at least ten weeks (See Table 1 for details of each study). The participants in the majority of studies (n=33; 82.5%) were not regularly trained nor experienced with resistance training, while four studies (10%) had regularly trained participants and another three studies (7.5%) examined elite athletes. In addition, more than half the studies (n=24; 60%) recruited participants under the age of 30. Nine studies (n=9; 22.5%) recruited participants between the ages of 30 and 60 years and the remaining seven studies (17.5%) recruited participants over 60 years. For thirty-six studies (n=36; 90%) lower limb muscle groups strength is reported in this review with the remaining studies (n=4; 10%) being upper limb strength.

----- Table 1 about here -----

Most of the studies (n=32; 80%) involved resistance/weight training exercises and the remaining eight studies (20%) implemented isometric/isokinetic training. More than half of the studies (n=26; 65%) investigated a training group against control, three studies (7.5%) examined the effect of training in hypoxic versus control environment, and another three studies (7.5%) examined the effect of blood flow restriction with low-

load intensity training (<30% 1RM) against a control of high intensity (>70% 1RM). In addition, six studies (15%) examined the effect of supplementation against control/placebo and the remaining two studies (5%) compared various training intensities.

The mean time point of all studies (n=40) / training groups (n=57), at which the first significant increase in muscle strength (experimental group) was recorded, was 4.3 ± 2 (range=1-12) weeks after the beginning of the training intervention (Fig. 2) while the mean testing frequency was 3.3 ± 1.5 (range=1-6) weeks. The mean level of the first significant increase was 17.3 ± 9.6 (range=3.7-45%). For training groups that data was available (n=48) to calculate the increase in the following equivalent period (i.e., if first increase was at week 4, the comparison would be with the increase at week 8) it was found that the first significant increase (16.3%) was significantly higher ($Z=5.60$, $p<0.05$) than the increase in the following equivalent period (7.6%; Fig. 3). The majority of training groups (n=44; 77%) performed the first mid-intervention test not later than four weeks (range=1-4 weeks) after the start of the training intervention and in 80% of these groups (n=35), the first significant increase was recorded within this period. In addition, a phase of plateau in muscle strength increments (~25%) seemed to begin between weeks 8 and 12 in training programmes that did not make adjustments in intensity levels throughout.

----- Figure 2 about here -----

Similar muscle strength adaptations were seen in studies implementing resistance training of high (>65% of 1RM; 11,16,28,31,33,59,70,72,80) and low (<60% of 1RM; (3,31) constant intensity (n=11). The mean time point after the initial testing that the first significant increase of muscle strength was recorded was not significantly different

(z=0.895, p=0.37); 3.9 ± 1.5 (range=1-8) and 4.8 ± 2.4 (range=2-8) weeks, respectively. The mean strength increase at this time point was not significantly different either (z=0.039, p=0.97): 16.3 ± 5.4 (range=9.2-24.2%) for low-intensity and 17.6 ± 10.2 (range=4.3-45%) for high-intensity.

The small number of studies (n=3) that examined the effect of hypoxia on muscle strength adaptation produced faster results compared to the mean of all studies concerning the time point of first significant increase (2.8 ± 0.6; range=2-3.5 weeks). In addition, muscle strength increase (24.9 ± 14.3; range=13.8-45%) at this time point was significantly higher than the respective control (normoxia) groups (15.8 ± 5.5; range=8.1-36.4%); and the mean strength gain of all the papers included in this review. Similarly, in another small sample of studies (n=3) that investigated the effect of blood flow restriction in parallel with low intensity (<30% 1RM) resistance training, it was revealed that the mean first significant increase of muscle strength occurred at 3.3 ± 1.9 (range=2-6) weeks and this increase (19.5 ± 6.5; range=10.3-24.2%) was slightly higher than the mean strength gain of all the papers included in this review. Finally, the six studies that investigated the effect of supplements (creatine and/or protein) all recorded a first significant increase in muscle strength (14.6 ± 11.8; range=3.7-40.3%) after five weeks.

----- Figure 3 about here -----

In summary, the mean time point of first significant increase in muscle strength of all 40 studies included in this review was four weeks and the corresponding increase value was 17.3%. Categorisation of the studies into training modalities revealed that only a hypoxic environment could possibly produce a leftward shift in the dose-response relationship. Other types of stimuli such as training intensity, blood flow

restriction and supplementation were not found to cause increased temporal dynamics in muscle strength gains.

DISCUSSION

To the knowledge of the authors the present review is the first to specifically focus on the temporal dynamics of muscle strength adaptations. This review aimed to investigate the effect of different mechanical and metabolic modalities and stimuli on the time course and magnitude of muscular strength adaptations during resistance training interventions.

The main results revealed that irrespective of the stimulus, muscle strength - in terms of 1RM or MVC, increased significantly within four weeks of starting a resistance training intervention (~17%). In addition, even earlier (e.g. week 1) significant increases were observed in interventions which tested more frequently (n=13), showing that more regular monitoring and corresponding adjustments of training intensity may lead to enhanced strength adaptations.

Another important finding of this review was that in interventions involving high- or low-constant intensities throughout the training period (i.e. which did not involve frequent adjustments of the training intensity based on a new true 1RM or MVC value), a plateau (or smaller non-significant improvement) was recorded in the last weeks of the training programme (28). On the other hand, more recent studies which adjusted the intensity regularly (30,41,57) showed significant improvements in muscle strength throughout the duration of intervention, (i.e. no saturation of increase). These studies implemented the theory of periodization in their training intervention which promotes the design of progressive training programmes specific to the participants with the aim to maintain high efficiency throughout and overall effectiveness of interventions (40).

An indication observed from the results of this review regarding the effect of initial training level on the temporal dynamics of muscular strength gains concurs with the conclusions of recent meta-analytical reviews suggesting that it is not significant (66). To elaborate, it has been well established that muscle strength improves early in untrained people even with lower training intensities, which as shown in the studies of Radaelli et al. (62) and Tanimoto & Ishii (77) mainly results from neurological adaptations such as coordinated changes in muscle activation, more specifically increased agonist and decreased antagonist muscle activation (78). However, even elite/regularly trained athletes, who have been training consistently before the beginning of the intervention, seem to be able to increase their muscle strength at similar time points (39,86), arguably due to the appropriate selection of their training programme and intensity (>80% 1RM).

The third main finding of the review was that hypoxic training seems to be more effective at eliciting strength gains when compared to traditional training modalities and other ergogenic aids. Although the number of studies that satisfied inclusion in this review was low, the indication is that training in an environment where the partial pressure of oxygen increases the magnitude of strength improvement and reduces the time course in its first significant development. Mechanistically, performing exercise in an hypoxic environment increases metabolite accumulation such as blood lactate and growth hormone (75). This can potentially lead to a greater recruitment of higher threshold motor units and an increased hypertrophy (84). As a result, a load which under normal conditions would require the same amount of work from the muscles and/or muscle activation now imposes a greater systemic demand and corresponds to a higher percentage of maximal oxygen uptake. Thus, training in these conditions is an increased stimulus for many biological functions such as endocrine response

which can in turn induce muscle strength gains by controlling the metabolism more efficiently (10). Therefore, this review recommends hypoxic training to not only be incorporated in a training programme as an effective alternative for individuals with physical limitations to engage in high-intensity training (46) but also to healthy individuals for higher and faster muscle strength gains.

The deteriorating effect of ageing on muscle strength has been widely evidenced in literature (51). However, its effect on the temporal dynamics of muscle strength gains during training interventions seems equivocal. Additional analysis of the results from this review revealed similar time points of the first significant increase (4.6 ± 1.8, range=2-8 weeks vs 4.2 ± 2, range=1-12 weeks) and relative magnitude of the increase (18.4 ± 6.7, range=8-33.4% vs 17.0 ± 10.3, range=3.7-45%) in persons aged above versus below 50 years, respectively. Similarly, the effect of sex on the time course of muscle strength adaptations is not clear. Upon additional analysis of the effect of sex on temporal dynamics of muscle strength increase, it was found that female training groups had a higher gain in muscle strength (22.2 ± 9.4; range=11.5-40.3%) compared to male groups (15.2 ± 8.7; range=3.7-45%) but at a slightly later time point too (4.7 ± 0.7, range=4-6 weeks vs 4.1 ± 2.1, range=1-12 weeks). However, the female groups performed the first testing session later (week 4 ± 1.5; range=2-6) compared to the male groups (week 3 ± 1.2; range=1-6). Therefore, the fact that the mean first significant strength increase in females was higher than the males allows the speculation that had the first testing session been performed earlier in the female studies too, a significant increase could still be recorded. Even though evidence points to differences in the muscle functional improvements following strength training between females and males (e.g. hormonal mechanisms; (53,73) and young and older adults, there is lack of knowledge regarding the effect of sex and ageing on the

temporal dynamics of muscle strength adaptation. Similarly, although it has been postulated that the time course of adaptations in various contributors to muscle strength increases in response to mechanical loading (e.g. neural, metabolic and morphological changes) is different (20), there are limited studies assessing the time course of these different contributors in humans. For example, whether radial growth and hence muscle PCSA is triggered first via building of additional sarcomeres in parallel or via changes in pennation angle of muscle fibers is currently not established (1).

An important point to consider when interpreting the results of this review is that all included studies, even those categorised together to represent a specific stimulus, had inherent differences between them in the manipulation of variables such as training volume and testing frequency. For example, studies included in the hypoxic category not only had different exercise selection and intensity level but even the fraction of inspired oxygen (FiO_2) during the training of their experimental group was different (14.3%, 12.7% and 16%). Additionally, test-specificity is another factor that has been argued to cause bias in muscle strength adaptation results across the different interventions (12). However, its effect on the results of this review seems not as adverse. Indeed, a couple of studies (55,58) used a test of muscle strength adaptation different to the exercise in their training protocol and the results produced higher and faster muscle strength gains in contrast to the means of all studies included in the review. On the other hand, in the study of Tanimoto and Ishii (77) where the intervention involved isotonic knee extension at 50 and 80% of 1RM while the testing was an isometric MVC, the results were similar to the mean of all studies. Consequently, as pooling of data may not necessarily represent these

differences/sources of bias and their potential effect on results, the findings of this review should be considered as trends/indications and not conclusive statements.

Overall, the results of this review reveal that muscle responds well to a wide range of exercise modalities and stimuli with a clear increase in its strength. Hence, it is reasonable and achievable for an athlete or an individual rehabilitating from injury/pathology to aim towards faster and higher muscle strength gains in order to improve athletic performance or regain ability to carry out everyday tasks, respectively. However, from a clinical perspective the other tissues connected to the muscle e.g., tendons are known to show a lower metabolic response to mechanical stimuli (42). Contrary to muscle, tendon appears to respond only to high magnitude loading and repetitive loading cycles with long tendon strain durations (4). There is growing evidence in current literature suggesting that muscle and tendon adaptation do not always progress in a balanced manner (34,37,42,52). This shows that in the effort to promote high muscle strength gains faster, some training programmes might in fact cause more harm than benefit as shown by the increased cases of tendinopathy, especially in athletes experiencing high amount of jumping (e.g. high jumpers and volleyball players; 44,52). Recommended training, which can simultaneously increase muscle strength and lead to tendon adaptation involves high muscular output (80-90% MVC) inducing high enough cyclic tendon strain (5). Thus, despite some indications that low-load blood flow restriction training (20-35% of 1RM) over 14 weeks <u>can</u> lead to an increase in tendon stiffness (15), caution should be taken when training with low muscular output as the effectiveness of tendon adaptation to mechanical loading is reduced (4). This can potentially lead to an imbalanced adaptation between muscle and tendon and hence an increased mechanical demand placed on the tendon (i.e. higher strain) during physical activity and sports (5).

PRACTICAL APPLICATIONS

In conclusion, the results from the present review demonstrate that generally muscle strength can be significantly improved (~17%) within the first month of strength training. This increase is significantly higher than the following increase (7.6%) of the second month as gradually a plateau in muscle strength increments (~25%) occurs between weeks 8 and 12 in training programmes which do not make adjustments in intensity levels throughout. In addition, hypoxic training causes a leftwards shift (faster gains) in the dose-response relationship compared various mechanical and metabolic stimuli. From a practical standpoint, these findings suggest that strength and conditioning coaches and physiotherapists should use more frequent testing in order to regularly adjust to true new intensity level considering the situation and needs of their athletes and clients. Additionally, individuals who may need fast muscle strength gains could benefit from implementing hypoxic training as part of their overall programme. However, caution should be taken when targeting for such rapid muscle strength gains as the in series connected tendon requires more time for adequate adaptation of its stiffness. Therefore, the potential imbalanced adaptation between muscle and tendon should be avoided by implementing suitable training programmes (4) in order to reduce the risk of tendon overload injuries (34,52). More investigations are needed for females and future studies should investigate the temporal dynamics of muscle and tendon together, as this could allow to optimize training variables for balanced adaptations in the effort to improve performance and minimise the risk of musculotendinous overuse injuries.

KEY POINTS

- Generally, muscle strength can be significantly improved (~17%) by various stimuli within the first month of training while a phase of plateau (~25%) seems to occur between the second and third month.
- Hypoxic training can induce faster and higher gains compared to other stimuli.
- More research on temporal dynamics is needed to promote a balanced rate of adaptation between muscle strength and the connected biological systems.

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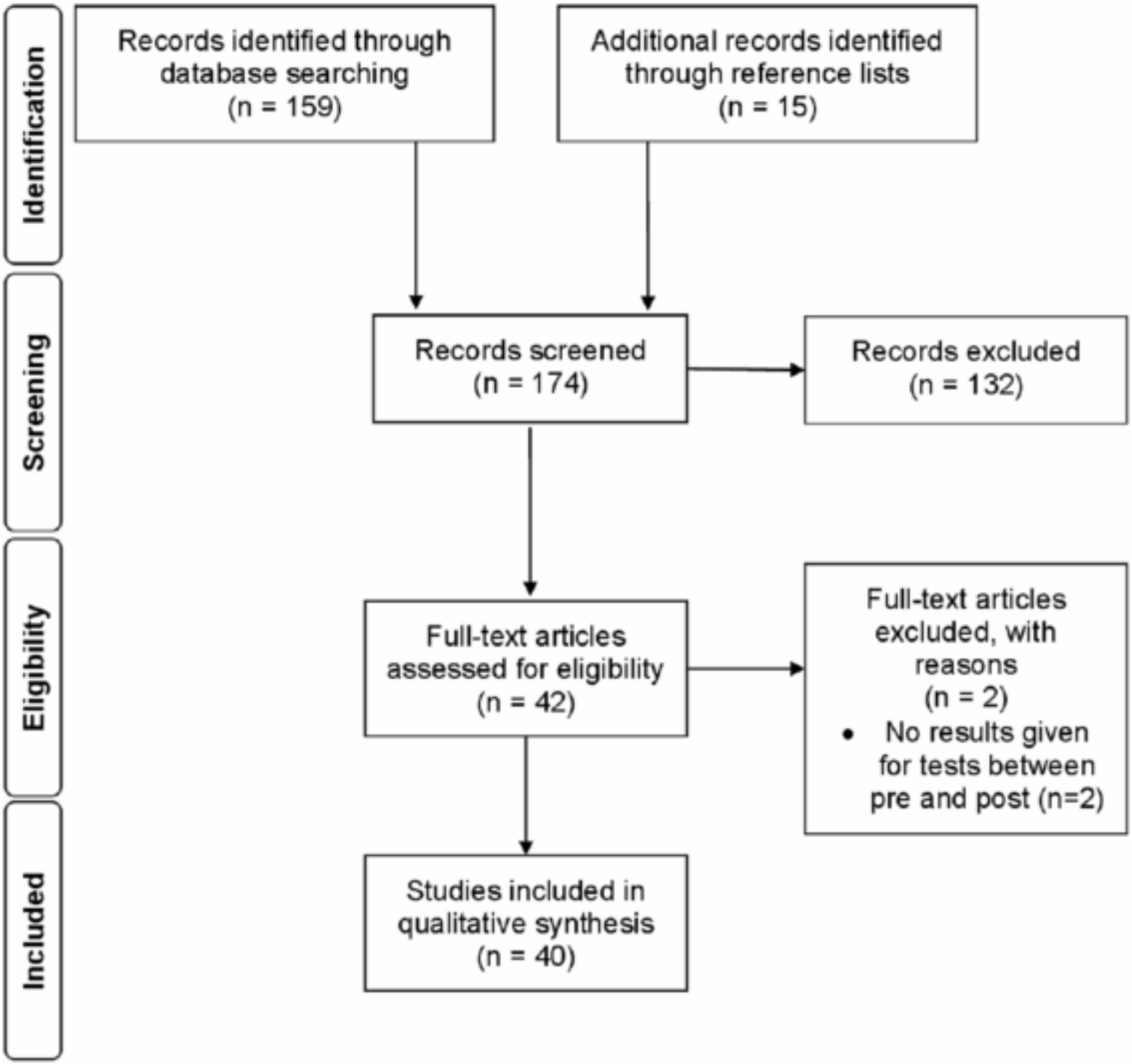
Figure Legends:

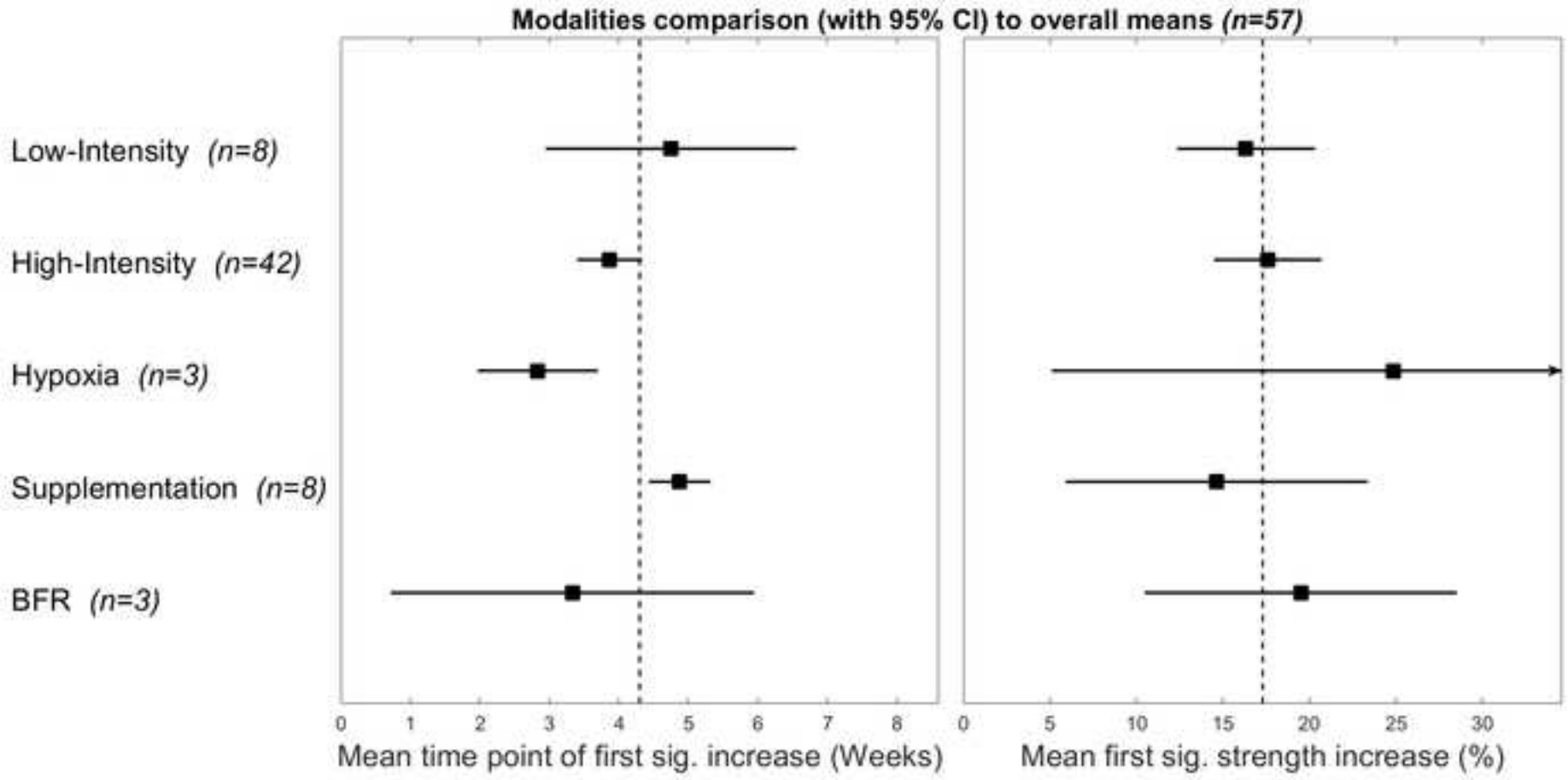
Figure 1. PRISMA search flow diagram.

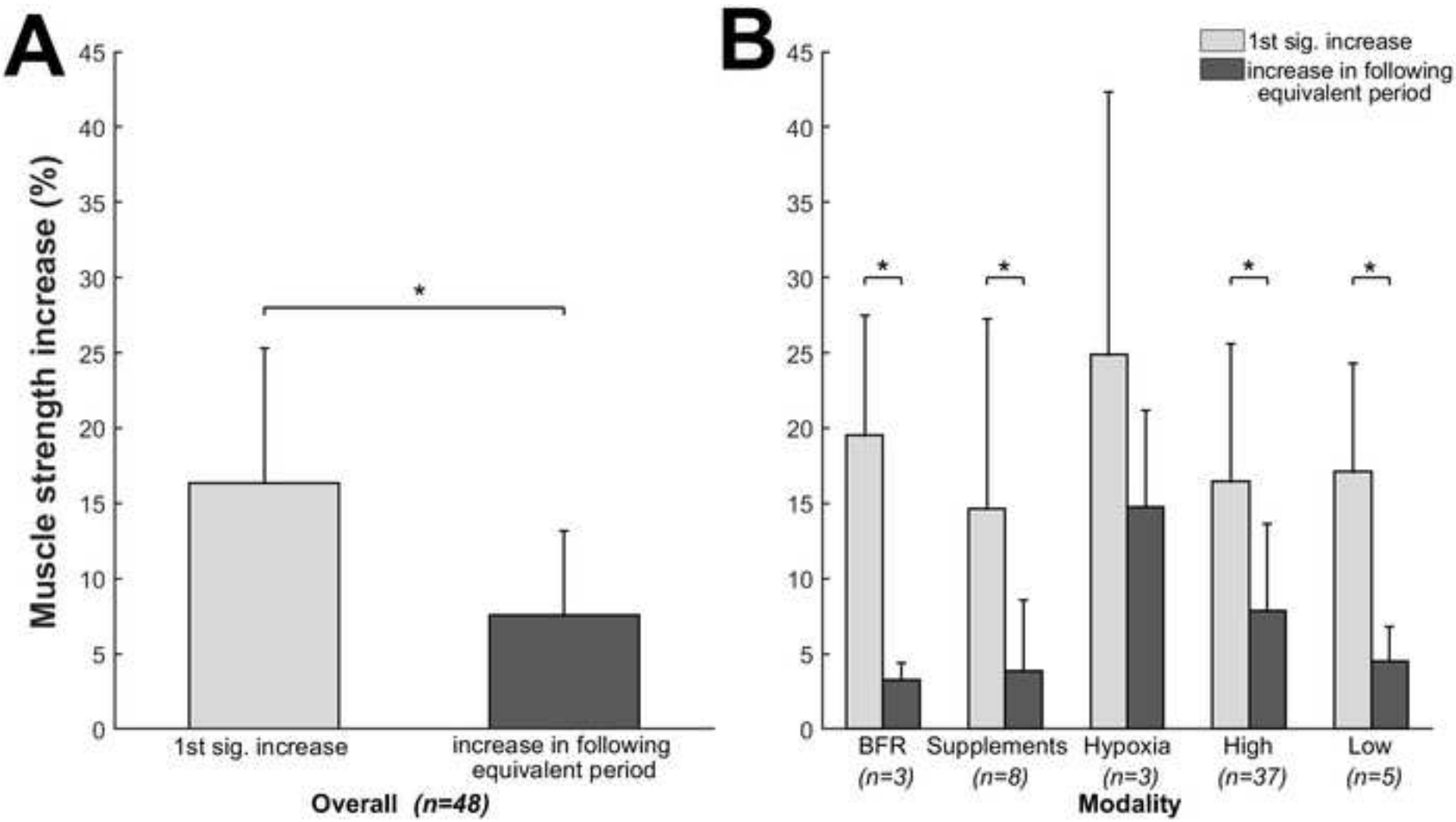
Figure 2. Forest plot of various subgroups/stimuli (mean ± 95% CI) compared to overall means (vertical lines) of time point of first significant increase (weeks) and respective value of increase (%)

Figure 3. A. Comparison between first significant increase and increase in following equivalent period for all training groups with available data (n=48). B. Comparison between first significant increase and increase in following equivalent period in different modalities.

Table 1. N: number of participants who completed the training intervention; M: Males; F: Females; Tr: Training Status; T: Trained; U: Untrained; Wks x Freq; Weeks of intervention x weekly sessions; TP: Timepoint of first significant increase; 1st sig incr:


Identification
Screening
Eligibility
Included
Records identified through database searching (n = 159)
Additional records identified through reference lists (n = 15)
Records screened (n = 174)
Records excluded (n = 132)
Full-text articles assessed for eligibility (n = 42)
Full-text articles excluded, with reasons (n = 2)
• No results given for tests between pre and post (n=2)
Studies included in qualitative synthesis (n = 40)





Table

Table 1. Overview of the studies included in the review.

Study (year)	N	Sex	Tr	Age range	Wks x Freq	Training Exercises	Sets x reps	Intensity	Modality	Assessment Exercise	Test	Test Freq (wk)	TP 1st sig incr (wk)	1st sig incr	2nd incr
Abe (1999) (3)	17	M	U	25-50	12 x 3	various exercises incl. knee extension	3 x 8-12	70% 1RM	high	knee extension	1RM	2	2	11.7 %	4.7%
	20	F	U	25-50	12 x 3	various exercises incl. knee extension	3 x 8-12	70% 1RM	high	knee extension	1RM	2	4	13.8 %	6.5%
Baroni (2013) (7)	20	M	U	20-35	12 x 2	eccentric knee extension 60°/s	3-5 x 10	100% MVC	high	knee extension	MVC	4	4	15.8 %	7.4%
Blazevich (2007) (9)	12 & 12	M & F	U	19-30	10 x 3	concentric or eccentric knee extension 30°/s	4-6 x 6	100% MVC	high	knee extension	MVC	5	5	16.4 %	6.4%
Brook (2015) (11)	10	M	U	22-24	6 x 3	unilateral knee extension	6 x 8	75% 1RM	high	knee extension	1RM	1.5	1.5	14.5 %	9.3%
Cannon & Marino (2010) (13)	16	F	U	20-30	10 x 3	knee extension & flexion	3 x 10	75% 1RM	high	knee extension	1RM	2	4	11.5 %	6.9%

Carolan (1992) (14)	10	M	U	20-23	8 x 3	unilateral isometric knee extension	1 x 30	100% MVC	high	knee extension	MVC	1	1	10.0%	6.5%
Cook (2017) (16)	5 & 7	M & F	U	72-82	12 x 2	knee extension, leg curl and press	3 x fail	30% 1RM with BFR	low & BFR	knee extension	1RM	6	6	24.0%	2.1%
	5 & 7	M & F	U	72-82	12 x 2	knee extension, leg curl and press	3 x fail	70% 1RM	high	knee extension	1RM	6	6	33.4%	20.4%
Cooke (2014) (17)	10	M	U	55-70	12 x 3	various resistance exercises incl. leg press	3 x 10	75% 1RM	supp & high	leg press	1RM	4	4	16.4%	1.6%
	10	M	U	55-70	12 x 3	various resistance exercises incl. leg press	3 x 10	75% 1RM	high	leg press	1RM	4	4	15.8%	1.8%
Cormie (2014) (18)	8	M	T	19-30	10 x 3	squat	3 x 3-6	75-90% 1RM	high	squat	1RM	5	5	25.0%	7.0%
DeFreitas (2011) (19)	25	M	U	18-25	8 x 3	leg press, knee extension & bench press	3 x 8-12	80% 1RM	high	knee extension	MVC	1	4	14.6%	9.3%

DeSouza (2018) (71)	9	M	U	19-33	12 x 2	squat & knee extension	2-4 x 4-12	70-90% 1RM	high	squat	1RM	6	6	7.7%	9.4%
Hickson (1994) (28)	5 & 5	M & F	U	25-30	8 x 3	various exercises incl. squat & bench press	5 x 5	80% 1RM	high	squat	1RM	1	1	6.2%	4.7%
Inness (2016) (30)	10	M	T	18-34	7 x 3	squats, deadlifts & lunges	2-4 x 3-6	75% 1RM; FiO2 = 0.143	high & hyp	squat	1RM	3.5	3.5	13.8%	7.4%
	10	M	T	18-34	7 x 3	squats, deadlifts & lunges	2-4 x 3-6	75% 1RM; FiO2 = 0.20	high	squat	1RM	3.5	3.5	8.1%	4.5%
Jenkins (2017) (31)	13	M	U	19-35	6 x 3	knee extension	3 x fail	80% 1RM	high	knee extension	MVC	3	3	11.8%	14.5%
	13	M	U	19-35	6 x 3	knee extension	3 x fail	30% 1RM	low	knee extension	MVC	3	6	13.4%	n/a
Kalapotharakos (2010) (32)	7	M	U	80-88	8 x 2	various exercises incl. knee extension	3 x 10	70% 3RM	high	knee extension	3RM	2	2	20.5%	8.5%
Karabulut (2010) (33)	13	M	U	50-64	6 x 2	leg press & knee extension	3 x 15-30	20% 1RM with BFR	low & BFR	knee extension	1RM	2	2	10.3%	4.4%
	13	M	U	50-64	6 x 2	leg press & knee extension	3 x 8	80% 1RM	high	knee extension	1RM	2	2	15.7%	8.6%

Kerksick (2006) (36)	10	M	T	18-50	10 x 4	various exercises incl. leg press	3 x 6-10	75-85% 1RM	supp & high	leg press	1RM	5	5	5.9%	1.0%
	15	M	T	18-50	10 x 4	various exercises incl. leg press	3 x 6-10	75-85% 1RM	supp & high	leg press	1RM	5	5	8.8%	-2.3%
Kraemer (1995) (39)	9	M	T	19-30	12 x 4	various exercises incl. knee extension	3-5 x 5-10	70-85% 1RM	high	knee extension	1RM	4	4	18.8 %	10.5 %
Kraemer (2009) (38)	8	M	U	18-30	12 x 3	various exercises inlc. squat	3-5 x 3-14	65-90% 1RM	supp	squat	1RM	2	6	25.8 %	13.3 %
	9	M	U	18-30	12 x 3	various exercises inlc. squat	3-5 x 3-14	65-90% 1RM	-	squat	1RM	2	12	26.3 %	n/a
Kubo (2010) (42)	8	M	U	20-25	12 x 4	unilateral isometric knee extension (15s contractions)	1 x 10	70% MVC	high	knee extension	MVC	4	8	27.8 %	n/a
Kubo (2012) (41)	9	M	U	22-26	12 x 4	unilateral isometric plantar flexion (15s contractions)	1 x 15	80% MVC	high	plantar flexion	MVC	4	4	12.3 %	6.2%

Kurobe (2015) (43)	7	M	U	22-25	8 x 3	unilateral elbow extension	3 x fail	75% 1RM; FiO2 = 0.127	high & hyp	elbow extension	10RM	2	2	15.8%	18.1%
	6	M	U	22-25	8 x 3	unilateral elbow extension	3 x fail	75% 1RM; FiO2 = 0.20	high	elbow extension	10RM	2	2	21.1%	13.0%
McCartney (1995) (50)	39 & 37	M & F	U	60-80	42 x 2	various exercises incl. leg press	2-3 x 10-12	50-80% 1RM	-	leg press	1RM	6	6	8.0%	2.0%
Monti (2020) (55)	8	M	U	18-30	6 x 3	Trampoline-Trainer' exercise (similar to leg press)	4-5 x 30	30RM	low	knee extension	MVC	2	2	17.8%	4.4%
Nichols (2008) (57)	13	F	T	18-22	12 x 3	various exercises incl. knee extension	2-3 x 4-15	50-80% 1RM	-	knee extension	10RM	4	4	25.0%	15.5%
Nishimura (2010) (58)	7	M	U	19-24	6 x 2	standing french press & arm curl	4 x 10	70% 1RM; FiO2 = 0.16	high & hyp	french press	1RM	3	3	45.0%	18.8%
	7	M	U	19-24	6 x 2	standing french press & arm curl	4 x 10	70% 1RM; FiO2 = 0.20	high	french press	1RM	3	6	36.4%	n/a
Ogasawara (2012)	7	M	U	22-28	24 x 3	bench press	3 x 10	75% 1RM	high	bench press	1RM	3	3	8.4%	10.7%

(59)															
Ozaki (2017) (60)	6	M	U	24-47	8 x 3	elbow flexion	3 x fail	80% 1RM	high	elbow flexion	1RM	4	4	6.7%	12.5 %
	6	M	U	24-47	8 x 3	elbow flexion	3 x fail	30% 1RM	low	elbow flexion	1RM	4	8	13.3 %	n/a
Radaelli (2014) (62)	12	F	U	60-74	20 x 2	various exercises incl. knee extension	3 x 6-20	50-85% 1RM	-	knee extension	1RM	6	6	21.9 %	13.3 %
Sousa (2017) (70)	7 & 3	M & F	U	18-30	6 x 2	unilateral knee extension	4 x fail	30% 1RM with BFR	low & BFR	knee extension	MVC	2	2	24.2 %	3.3%
	5 & 6	M & F	U	18-30	6 x 2	unilateral knee extension	4 x fail	80% 1RM	high	knee extension	MVC	2	6	43.0 %	n/a
Spillane (2009) (72)	10	M	U	18-22	7 x 4	various exercises incl. leg press	3 x 8-10	70-80% 1RM	high	leg press	1RM	1*	1	4.5%	n/a
Staron (1994) (73)	13 & 8	M & F	U	18-30	8 x 2	squat, leg press & knee extension	3 x 6-12	70-85% 1RM	high	squat	1RM	2	4	28.6 %	22.2 %
Taipale (2013) (76)	11	M	T	21-45	8 x 2	squats & leg press	3 x 4-6	80-85% 1RM	high	leg press	1RM	4	4	4.3%	-1.2%
Tanimoto (2006) (77)	8	M	U	18-22	12 x 3	knee extension	3 x fail	80% 1RM	high	knee extension	1RM	4	4	16.3 %	8.9%
	8	M	U	18-22	12 x 3	knee extension	3 x fail	50% 1RM	low	knee extension	1RM	4	4	9.2%	8.3%

Urlando & Hawkins (2007) (79)	10	M	U	20-30	8 x 3	plantar flexion	3 x 10	70% MVC	high	plantar flexion	MVC	2	4	20.0 %	1.4%
Van Roie (2013) (64)	8 & 10	M & F	U	60-75	12 x 3	leg press & knee extension	2 x 10-15	80% 1RM	high	leg press	1RM	4	4	28.2 %	10.1 %
	9 & 10	M & F	U	60-75	12 x 3	leg press & knee extension	1 x 80-100	20% 1RM	low	leg press	1RM	4	8	18.5 %	n/a
Vandenberghe (1997) (80)	10	F	U	19-22	10 x 3	various exercises incl. squat	5 x 12	70% 1RM	supp & high	squat	1RM	5	5	40.3 %	3.8%
	9	F	U	19-22	10 x 3	various exercises incl. squat	5 x 12	70% 1RM	high	squat	1RM	5	5	19.3 %	4.4%
Watanabe (2020) (82)	8 & 2	M & F	U	69-84	8 x 2	unilateral isometric knee extension	3 x 10	80% MVC	supp & high	knee extension	MVC	2	4	10.2 %	6.9%
	8 & 2	M & F	U	69-84	8 x 2	unilateral isometric knee extension	3 x 10	80% MVC	high	knee extension	MVC	2	6	19.0 %	n/a
Watanabe (2020) (83)	7 & 5	M & F	U	63-84	8 x 2	unilateral isometric knee extension	3 x 5	80% MVC	high	knee extension	MVC	2	4	15.6 %	-0.5%

Wilder (2001) (86)	8	M	T	18-22	10 x 4	various exercises incl. squat	1-6 x 1-20	50-100% 1RM	supp	squat	1RM	5	5	6.0%	4.9%
	8	M	T	18-22	10 x 4	various exercises incl. squat	1-6 x 1-20	50-100% 1RM	supp	squat	1RM	5	5	3.7%	1.7%