Determining the cortical, spinal and muscular adaptations to strength-training in older adults: A systematic review and meta-analysis

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ABSTRACT

There are observable decreases in muscle strength as a result of ageing that occur from the age of 40, which is thought to occur as a result of changes within the neuromuscular system. Strength-training in older adults is a suitable intervention that may counteract the age-related loss in force production. The neuromuscular adaptations (i.e., cortical, spinal and muscular) to strength-training in older adults is largely equivocal and a systematic review with meta-analysis will serve to clarify the present circumstances regarding the benefits of strength-training in older adults. 20 studies entered the meta-analysis and were analysed using a random-effects model. A best evidence synthesis that included 36 studies was performed for variables that had insufficient data for meta-analysis. One study entered both. There was strong evidence that strength-training increases maximal force production and rate of force development and muscle activation in older adults. There was limited evidence for strength-training to improve voluntary-activation, the volitional-wave and spinal excitability, but strong evidence for increased muscle mass. The findings suggest that strength-training performed between 2-12 weeks increases strength, rate of force development and muscle activation, which likely improves motoneurone excitability by increased motor unit recruitment and improved discharge rates.

Keywords: ageing, corticospinal inhibition, force production, motoneurone, rate of force development.

1. Introduction

Strength can be broadly defined as the maximal voluntary force that can be developed by the musculature whilst performing a specific movement (Enoka, 1988). Force production requires the complicated interaction between the nervous and muscular systems (Enoka, 1988; Rutherford and Jones, 1986). Maximal voluntary force production declines with age and contributes to functional limitations, reduced quality of life and mortality (Clark et al., 2015). Although there is a reduction in the maximal force generating capacity of the muscle through ageing, the mechanism accounting for strength loss are less clear. For example, for many years, the age-related loss in strength was due to a loss of muscle mass (sarcopenia), however there is a disproportionate loss of maximal force production (i.e., strength) compared to muscle mass (Metter et al., 1999) and maintaining muscle mass or increasing muscle mass, does not prevent the age-related loss in maximal force production (Delmonico et al., 2009). At a minimum, this suggests that a loss in maximal force production is only somewhat related to the loss muscle mass and reveals that there is a need to develop optimal strategies to ameliorate age-related losses in maximal force production, with a focus on identifying the mechanisms of force/or strength loss, other than simply muscle size or mass.

Age-related changes in the neuromuscular system could be one potential contributor to the reduction in maximal force production (Ward, 2006). Several studies have identified age-related changes in the physiological properties of the spinal motoneurones (Christie and Kamen, 2006; Kido et al., 2004; Scaglioni et al., 2002) as well as the primary motor cortex (Rossini et al., 2015). Further, several studies have examined the influence of ageing on the neuromuscular system's ability to "activate" muscles via transcranial magnetic stimulation (Taube, 2011), voluntary activation (VA) and by the volitional wave (V-wave) (Clark and Taylor, 2011; Clark et al., 2014b). In general, the age-related changes in muscle activation seems to be related to reduced motoneurone excitability (Kido et al., 2004), reduced discharge rates (Dalton et al., 2010), and reduced doublet discharges (Christie and Kamen, 2006). Reduced motoneurone activation has been associated with reduced muscle strength (Kaya et al., 2013) and the ability to activate muscles is important to perform activities of daily living (ADL), such as walking, rising from a chair, and ascending/descending stairs. Experimental evidence showed that the strength of lower limb muscles is positively correlated to walking speed (Suzuki et al., 2001), improved balance (Spink et al., 2011), and reduced risk of falls (Moreland et al., 2004). Similar evidence is also observed in the upper limb where hand grip strength can be used as a proxy for the identification of slow walking speed (Lin et al., 2021).

Several studies have reported impairments in VA with age; however, the results are inconsistent, which might be due to methodological differences across studies (Harridge et al., 1999; Jakobi and Rice, 2002; Shinohara et al., 2003). In light of this, identifying VA seems important as it may isolate to what extent a loss in maximal force production is due to neuromuscular factors and more importantly, what interventions could be prescribed to improve force production in older adults. For example, strength-training is a simple, cost effective and easily translated intervention to increase force production in most people and is recommended for older adults (Fragala et al., 2019). However, despite several strength-training studies reporting increased VA in older adults, (Knight and Kamen, 2001; Scaglioni et al., 2002; Walker and Häkkinen, 2014), the results are conflicting (Clark and Taylor, 2011) and hence a systematic evaluation of the literature is required to determine consensus. In addition, measuring VA provides limited insight into the specific site and or neural mechanism underpinning maximal force production, thus transcranial magnetic stimulation (TMS) may provide greater insight into the neurological mechanisms underpinning strength gain and strength loss. TMS can be used to determine synaptic activity of the corticocortical circuitry of the motor cortex and of the corticospinal-motoneuronal pathway (Oliviero et al., 2006). TMS of the motor cortex induces muscle responses, recorded in the target muscle by surface electromyography (sEMG) and are termed motor evoked potentials (MEPs). Changes in the amplitude of MEPs have been examined to study the physiology of the corticospinal-motoneuronal pathway after strength-training (Carroll et al., 2002). Typically, a variety of parameters of the MEP can be investigated, including MEP amplitude, motor threshold, corticospinal silent period duration, and facilitation of the intracortical circuits of the motor cortex (Carroll et al., 2002; Christie and Kamen, 2014; Mason et al., 2017; Pearce et al., 2013). Interestingly, ageing has shown to reduce motor cortex excitability (Bernard and Seidler, 2012), increase intracortical inhibition and reduce intracortical facilitation (McGinley et al., 2010). Therefore, interventions known to increase motor cortex excitability and reduce intracortical inhibition could be prescribed and provide insight into the mechanisms of strength gain and or loss in older adults (Siddique et al., 2020; Taube, 2011).

In light of the above, strength-training is one the most effective and recognized modes of exercise for improving neuromuscular function and increasing muscle strength and size (Barry et al., 2005; Caserotti et al., 2008; Hakkinen et al., 1998b; Häkkinen et al., 1998a; Häkkinen et al., 2001; Hortobagyi et al., 2001; Suetta et al., 2004). Further, strength-training induces plasticity in both the skeletal muscles (a peripheral adaptation) as well as the nervous system to compensate for the age-related loss in muscle size and neuronal function, which is thought to underpin the improvements in functional capacity in older adults (Caserotti et al., 2008; Fiatarone et al., 1994; Suetta et al., 2004). Early changes in maximal force production have been attributed to changes within the neuromuscular system, with particular emphasis on improved “neural drive” to the trained muscle (Walker, 2021). Long-term strength-training can reduce the rate of decline in maximal force production, power and rate of force development (RFD) with ageing (Caserotti et al., 2008; De Vos et al., 2005; Hakkinen et al., 1998b; Häkkinen et al., 1998a; Häkkinen et al., 2001; Hortobagyi et al., 2001). Similar increments in RFD and maximal force production following strength-training have also been reported along with increased sEMG amplitude reflecting elevated neuromuscular activity (Barry et al., 2005; Caserotti et al., 2008; Häkkinen et al., 1998a; Häkkinen et al., 2001; Hortobagyi et al., 2001; Suetta et al., 2004). Maximal force gains in the elderly have also been observed as a consequence of heavy-load strength-training (Barry et al., 2005; Caserotti et al., 2008; Hakkinen et al., 1998b; Häkkinen et al., 1998a; Häkkinen et al., 2001; Hortobagyi et al., 2001; Suetta et al., 2004). Some studies have reported greater increments in maximal force production and muscle mass in older adults (Kraemer et al., 1999; Welle et al., 1996). However, several large-scale studies and meta-analyses do not support this view and contend the results have comparable increase in maximal force production, irrespective of age with the exception of very old adults (>80years) (Ahtiainen et al., 2016; Grgic et al., 2020; Guizelini et al., 2018). However, this increment may also be affected by several other factors residing in an individual other than age. In order to clarify the discrepant findings in the extant literature regarding the neuromuscular adaptations to strength-training in older adults, we feel a systematic review with meta-analysis and best evidence synthesis is required.

The increase in maximal force production following strength-training in older adults might emanate as a result of several subtle adaptations within the elements of the neuromuscular system (e.g., supraspinal, spinal and muscular). However, the body of evidence is mixed for potential mechanism of adaptation and a systemic review and meta-analysis is required to determine the neuromuscular responses to strength-training in older adults. To our knowledge, there are no systematic reviews that have examined the potential sites of adaptation in the neuromuscular system (muscle, spinal and supraspinal) following strength-training in older adults. Therefore, the aim of this systematic review was to determine the potential neuromuscular mechanisms for improved maximal force production and RFD in older adults following strength-training. We hypothesised that the neuromuscular adaptations to strength-training in older adults will involve subtle changes in the neuromuscular system (e.g., increased cortical and spinal excitability, neural drive and increased muscle mass) that will underpin the increase maximal force production and RFD.

2. Methods:

2.1 Search Strategy

This review was conducted in accordance with the latest Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021). Relevant articles were identified through a standardized search strategy using the following electronic databases: PubMed, Science Direct, Ovid Medline, Embase, APA PsycInfo and Google Scholar. The search strategy included the following keywords: “strength-training” combined with its synonyms (“resistance-training” and “weight training”), and “ageing” or “old adults”. The following key terms were used in combination with the above terms: “neuronal plasticity”, “transcranial magnetic stimulation”, “motor-evoked potential”, “cortical silent period”, “H-reflex”, “M wave”, “V-wave”, “voluntary activation”, “electromyography”, “motor unit”, “discharge rate”, “muscle hypertrophy”, physiological CSA”, “muscle fiber”, “muscle mass”, “muscle size”. Each database was searched from inception until 10 March 2022. References found from published literature were also searched for similar articles. Figure 1 illustrates the flow of search strategy for studies that entered into the meta-analysis.

Insert Figure 1 here.

2.2 Study Selection

During the initial search, all study titles and abstracts of retrieved articles were reviewed and screened for eligibility. Any duplicates or articles considered outside the scope of this meta-analysis were excluded. Following initial screening, two authors (US & DJK) independently screened, reviewed, and selected articles to be included. Disagreement between the two assessors regarding any study selection was resolved with the help of a third assessor (AKF). The decision of the third author was deemed final.

2.3 Eligibility Criteria-Inclusion and Exclusion

Studies were considered for review if they fulfilled the following criteria: **(1)** Full text articles available in English; **(2)** Untrained healthy adults of either sex with a mean age of 60 and above **(3)** Training must have been strength-training of the upper- or lower-limbs and greater than 50% of the maximal load aimed at increasing maximal force production, muscle activity, efferent drive and muscle mass; **(4)** Included studies must have a had a training intervention duration between 2-12 weeks (this was primarily based upon evidence showing that the minimum number of training sessions required to increase strength is between 3-5 training sessions; Hortobágyi et al., 2011; Mason et al., 2020); for articles where the training duration was more than 12 weeks, data was extracted if available for up to 12 weeks; **(5)** randomized controlled trials or non-randomized controlled trials were also included. Exclusion criteria included: **(1)** non-English publications; **(2)** disease populations; **(3)** non-peer reviewed proceedings and theses; **(4)** conference abstracts.

2.4 Assessment of Quality and Risk of Bias

The quality of included studies was assessed using a modified version (Table 2) of the Downs and Black checklist (Downs and Black, 1998) by two authors (US and DJK). Seventeen items (1, 2, 3, 5, 6, 7, 10, 11, 12, 14, 16, 18, 20, 21, 25, 26, 27) out of a total of 27 were included to measure study quality as they were the most relevant items for this systematic review. These items were selected based on previously conducted studies (Alibazi et al., 2021; Maniar et al., 2016) and were used to assess reporting, external validity, internal validity bias and internal validity confounders. Disagreement between the assessors regarding any individual item was resolved by a third assessor (AKF) to reach consensus. The Cochrane Collaboration Risk of Bias tool (Higgins, 2011) was used to assess the methodological quality of all included studies (Figure 2). This tool rates quality on six domains: sequence allocation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting and other sources of bias. A rating of either “high” or “low” was given based on the number of criteria fulfilled. An “unclear” risk of bias was reported for a domain where inadequate details were provided. Any disagreement between authors regarding risk of bias assessment was resolved by discussion.

2.5 Data Extraction

Data was extracted from all included studies by two authors (US and DJK) in a customized manner. To check for accuracy, data extraction of all articles was independently assessed by both authors. Study characteristics (year, author, sample size and sample design), participants demographics (age, sex) and strength-training protocol (isometric, dynamic, eccentric, concentric, upper body, lower body) were retrieved from studies that entered the meta-analysis. Information about the following outcome measures were also extracted from the available text of included studies: strength (expressed as Newton, kilogram, percentage, torque [N·m]), MEP amplitude (peak-to-peak waveform and expressed either as a raw amplitude, percentage of peripheral M-wave amplitude relative to motor threshold, MEP_{MAX} or arbitrary units obtained from a stimulus–response curve), silent period (duration from the onset of MEP waveform to the return of uninterrupted sEMG activity), RFD (early or late phase, expressed as $N \cdot s^{-1}$) and CSA (expressed as cm^2). Changes in VA (using single or double pulses), M-wave, V-wave (normalised to M-wave), H-reflex (normalised to the M-wave and recorded in resting and/or active muscle activity as a percentage of maximal voluntary contraction) and sEMG following strength-training were also retrieved from the included studies. All extracted data were entered into an Excel spreadsheet. If the reported data did not provide mean ± SD or SE values for post-intervention measures, raw data (means and SD) were derived or calculated from SE, 95% confidence intervals (CI), P values, t values, or F values. In addition, when only figures were available in text, data were extracted using Plot Digitizer software (Rohatgi, 2015).

2.6 Statistical Analysis

The post-strength-training data of the trained older and untrained older control group from included studies were used for the following outcome variables: strength, MEP, silent period, RFD, voluntary activation, M-wave, H-reflex, V-wave, cross-sectional area/muscle mass and sEMG amplitude. Data from included studies were pooled for meta-analysis using RevMan 5.4.1 (Higgins et al., 2019). Meta-analysis was performed using a random effects model to eliminate systematic influences and random error present between study effect sizes. Emerging evidence suggests that estimating the size of intervention effects is more reliable than using *P* values as they only to determine the existence of effects (Herbert, 2019). Therefore, standardized mean difference (SMD) with 95% confidence intervals (CI) was used to measure the intervention effects as the included studies presented the same outcome measures differently. The SMD values of 0.20 ≤ 0.49, 0.50 ≤ 0.79 and ≥ 0.80 indicated small, medium and large effect sizes, respectively (Cohen, 1988). However, the results are reported with the SMD value, followed by their 95% CI and, finally, the corresponding *P* value. For analysis of single studies with the same unit of measurement and consistent methodology, the mean difference (MD) with 95% CI was used to report the outcome measures. SMD and MD were used to report post-strength-training outcomes measures that involved strength-training of older adults compared to age-matched controls. To examine heterogeneity between studies, the Chi-squared test, along with the I^2 analysis were used. The inconsistency (I^2) statistic was used to indicate the percentage variance between studies where <25%, 25% - 75% and >75% indicated low, moderate and high heterogeneity, respectively (Higgins et al., 2003; Siddique et al., 2020). In case of heterogeneity exceeding this threshold, a leave-one-out sensitivity analysis was performed to check whether our findings were driven by a single study (Manca et al., 2017).

A best evidence synthesis (Slavin, 1995) was conducted for studies that did not have a comparison group. Such data could not enter the meta-analysis. The following criteria, which have already been used in previous literature (Alibazi et al., 2021; Maniar et al., 2016), were used to rank the level of evidence for these studies:

- No evidence: no supportive findings in the literature
- Conflicting evidence: inconsistent findings (<75% of studies showing consistent results)
- Limited evidence: one low-quality study
- Moderate evidence: one high-quality study and/or two or more low-quality studies and generally consistent findings (≥75% of studies showing consistent results)
- Strong evidence: two or more studies of a high quality and generally consistent findings (≥75% of studies showing consistent results)

Studies were defined as high (≥70%) and low (<70%) quality based on their risk-of-bias assessment scores (Alibazi et al., 2021; Maniar et al., 2016). Cohen's *d* (Cohen 1988) effect size and 95% confidence intervals were calculated and displayed in forest plots using Prism 9 for Windows (GraphPad Software Inc, La Jolla, CA, USA) for visualisation purposes only. Effect sizes of 0.2 indicated small, 0.5 medium and 0.8 large comparative effects (Cohen's *d*).

3. Results

3.1 Study Selection

The PRISMA flow chart (Figure 1) demonstrates the process of study identification, screening and evaluation of eligibility of included studies. The initial search yielded a total of 5380 studies from the different databases. After removing duplicates, the titles and abstract of 4469 studies were screened. A further 3960 were removed for not meeting the eligibility criteria. In total, 510 full text articles were assessed, out of which, 453 studies were excluded (reasons outlined in Figure 1), leaving 57 studies that were included, with 21 studies only entering the meta-analysis and 35 studies entering the best evidence synthesis. One study (Lixandrao et al., 2016) entered both the meta-analysis and the best evidence synthesis. Table 1 displays the characteristics of the included studies.

Insert Table 1 here.

3.2 Risk of Bias Assessment

Table 2 displays the results from the modified version of the Downs and Black checklist which was used to assess the quality of included studies. Out of 57 included studies, 34 were of high quality (>70%) and 23 were of low quality (<70%) with a mean score of 11.9 ± 2.2. The Cochrane Collaboration Risk of Bias Tool was used to categorize studies based on "high risk", "low risk" and "unclear risk". Most studies were exposed to high risk for sequence generation, allocation concealment, participant and personnel blinding. Low risk was observed for blinding of outcomes and selective reporting. One study was exposed to "high risk" for incomplete outcome data and selective reporting (Figure 2).

Insert Table 2 & Figure 2 here

3.3 Strength-training Variables

The average training intensity ranged from 40-90% of 1RM for all included studies. Low intensities were used at the beginning of the training regime to avoid fatigue and was increased progressively towards the maximum. The average number of sets for the strength-training protocols were 3 sets of 10 repetitions for every exercise performed. The average frequency of training for included studies was 3 times per week for 2-12 weeks duration. Two studies trained isometrically for the dorsiflexor (Christie and Kamen, 2014; Jiang et al., 2016) and the right elbow flexors whereas three studies (Slivka et al., 2008; Trappe et al., 2001; Trappe et al., 2000) performed isotonic leg extension. The remaining studies trained dynamically. The main muscles trained in the included studies were the quadriceps, first dorsal interosseus (FDI), elbow flexors, tibialis anterior, ankle dorsiflexors and plantar flexors.

3.4 Changes in Strength

Complete strength data were extracted from 20 studies (Bellew, 2002; Beurskens et al., 2015; Caserotti et al., 2008; De Vos et al., 2005; Earles et al., 2001; Gurjão et al., 2012; Henwood and Taaffe, 2005; Hortobagyi et al., 2001; Hvid et al., 2016; Jiang et al., 2016; Judge et al., 1994; Kalapotharakos et al., 2010; Laidlaw et al., 1999; Lixandrao et al., 2016; Lohne-Seiler et al., 2013; Marsh et al., 2009; Tracy et al., 2004; Unhjem et al., 2020; Walker and Häkkinen, 2014; Wolfson et al., 1996) that measured maximum strength post-strength-training in older adults (n = 312) compared to age-matched controls (n = 280). The pooled data indicated that, following strength-training, the older trained group exhibited a moderate increase in strength (25.49%; SMD 0.68; 95% CI

0.39, 0.97; n = 312; $P < 0.00001$), with heterogeneity of the results between studies being moderate ($Tau^2 = 0.26$; $I^2 = 62\%$; $P = 0.0002$; Figure 3).

Eleven out of 20 studies (Bellew, 2002; Beurskens et al., 2015; Caserotti et al., 2008; Earles et al., 2001; Gurjão et al., 2012; Hortobagyi et al., 2001; Judge et al., 1994; Lixandrao et al., 2016; Tracy et al., 2004; Unhjem et al., 2020; Wolfson et al., 1996) trained the lower-body to assess strength gains whereas only two studies trained the upper-body (Jiang et al., 2016; Laidlaw et al., 1999). The remaining seven studies (De Vos et al., 2005; Henwood and Taaffe, 2005; Hvid et al., 2016; Kalapotharakos et al., 2010; Lohne-Seiler et al., 2013; Marsh et al., 2009; Walker and Häkkinen, 2014) trained both the upper- and lower-body for examination but kept the focus on the lower-body.

Insert Figure 3 here.

3.5 Changes in RFD

Changes in RFD were extracted from four studies (Caserotti et al., 2008; Gurjão et al., 2012; Hortobagyi et al., 2001; Unhjem et al., 2020) in older adults (n = 48) compared to age-matched controls (n = 45) post-strength-training. The pooled data illustrated a moderate increase in RFD post-strength-training in the trained older adults (SMD 0.65; 95% CI 0.09, 1.22; n = 48; $P = 0.02$) with moderate heterogeneity between the studies ($Tau^2 = 0.14$; $I^2 = 41\%$; $P = 0.17$; Figure 4).

Insert Figure 4 here

3.6 Changes in Corticospinal Excitability and Inhibition

One study (Christie and Kamen, 2014) (n =15) examined the effects of strength-training on MEP amplitude compared to an age-matched control group (n =15). The results showed an increase in MEP amplitude following training in the older group (MD 2.87; 95% CI 1.73, 4.01; n = 15). In addition (n =15), the same study also assessed the duration of silent period post-strength-training compared to an age-matched control group (n =15); the results indicated that strength-training reduced the silent period in the older trained group (MD 12.92; 95% CI 2.95, 22.89; n = 15). There were no other studies that examined corticospinal excitability and inhibition.

3.7 Changes in H-Reflexes

Changes in H-reflexes were extracted from two studies (Christie and Kamen, 2014; Unhjem et al., 2020) that assessed older adults (*n* =26) post-strength-training compared to an age-matched control group (*n* = 27). Strength-training had no effect on H-reflexes (SMD 0.06; 95% CI-0.48, 0.60; *n* = 26; *P* = 0.84) with no heterogeneity ($Tau^2 = 0.00$; $I^2 = 0\%$; *P* = 0.45; Figure 5) between the studies.

Insert Figure 5 here.

3. 8 Changes in Voluntary Activation between Age Groups

Complete VA data were extracted from three studies (Hvid et al., 2016; Unhjem et al., 2020; Walker and Häkkinen, 2014) that assessed VA following strength-training between trained older adults (*n* = 53) and age-matched controls (*n* = 42). Pooled data indicated no significant increase in VA of trained older adults compared to the aged-matched control group following training (SMD 0.16; 95% CI-0.46, 0.78; *n* = 53; *P* = 0.62) with moderate heterogeneity ($Tau^2 = 0.15$; $I^2 = 51\%$; *P* = 0.13; Figure 6) between the studies.

Insert Figure 6 here.

3.9 Changes in M_{MAX}

Two studies (Christie and Kamen, 2014; Unhjem et al., 2020) examined the change in the amplitude of the M-wave of older adults (*n* =27) compared to an age-matched control group (*n* =16) following strength-training. The pooled data indicated that strength-training did not significantly increase M-wave amplitude in the older trained group (SMD 0.23; 95% CI -0.41, 0.88; *n* = 27; *P* = 0.48). No heterogeneity was observed between the two studies ($Tau^2 = 0.00$; $I^2 = 0\%$; *P* = 0.43; Figure 7).

Insert Figure 7 here.

3.10 Changes in V-wave

A single study (Unhjem et al., 2020) (*n* =11) examined the effects of strength-training on V-wave amplitude compared to an age-matched control group (*n* =12). The results showed no significant increase in the amplitude of the V/M ratio following training in the older group (MD 0.12; 95% CI -0.00, 0.24; *n* = 11).

3.11 Changes in sEMG

Changes in sEMG data from two studies (Gurjão et al., 2012; Jiang et al., 2016) were extracted which compared older adults (*n* =20) to age-matched controls (*n* = 14). The results showed there was no difference in sEMG between the trained older group and the aged-matched control group (SMD 0.28; 95% CI -0.41, 0.97; *n* = 20; *P* = 0.42). No heterogeneity was observed between the two studies (Tau^2=0.00; I^2 = 0%; *P* = 0.65; Figure 8).

Insert Figure 8

3.12 Changes in CSA

One study (Walker and Häkkinen, 2014) (*n* =26) examined the effects of strength-training on CSA compared to an age-matched control group (*n* =11). The results showed no increases in CSA following training in the older trained group (MD 1.49; 95% CI -0.65, 3.63; *n* = 26).

3.13 Best Evidence Synthesis

3.13.1 Pre-Post Changes in Strength for Older Adults

Thirty four studies (Berg et al., 2018; Cannon et al., 2007; Connelly and Vandervoort, 2000; Fielding et al., 2002; Frontera et al., 1988; Häkkinen et al., 2000; Hakkinen et al., 1998b; Häkkinen et al., 1998a; Häkkinen et al., 2001; Harridge et al., 1999; Hicks et al., 1991; Hunter et al., 1999; Ivey et al., 2000; Jozsi et al., 1999; Keen et al., 1994; Knight and Kamen, 2001; Kostek et al., 2005; Moritani and Devries, 1980; Newton et al., 2002; Radaelli et al., 2014B; Radaelli et al., 2014A; Rodriguez-Lopez et al., 2022; Schlicht et al., 2001; Slivka et al., 2008; Sousa et al., 2011; Tøien et al., 2018; Trappe et al., 2001; Trappe et al., 2000; Unhjem et al., 2015; Van Roie et al., 2013; Van Roie et al., 2020; Verdijk et al., 2009; Verdijk et al., 2016; Wang et al., 2017) measured changes in strength recorded from the trained limb pre- to post-strength-training. Twenty-nine studies trained the lower-body and two studies ((Keen et al., 1994; Moritani and Devries, 1980) trained the upper-body. Three studies (Häkkinen et al., 2001; Jozsi et al., 1999; Sousa et al., 2011) trained both the upper- and lower-body. There was strong evidence to suggest that 2-12 weeks of strength-training resulted in an increase in strength. All the studies, showed increased strength of the trained limb, with small to large effect sizes (Cohen's *d* range 0.26-5.82, Figure 9).

Insert Figure 9 here.

3.13.2 Pre-Post Changes in RFD for Older Adults

Nine studies (Berg et al., 2018; Connelly and Vandervoort, 2000; Hakkinen et al., 1998b; Häkkinen et al., 1998a; Rodriguez-Lopez et al., 2022; Tøien et al., 2018; Unhjem et al., 2015; Van Roie et al., 2020; Wang et al., 2017) assessed the change in RFD post-strength-training with reports of small to large effect sizes (Cohen's *d* range -0.28-3.39) (Figure 10). The included studies provide strong evidence for strength-training to increase RFD in older adults (Table 1, Figure 10).

Insert Figure 10 here.

3.13.3 Pre-Post Changes in sEMG for Older Adults

Changes in sEMG was assessed by eleven studies (Cannon et al., 2007; Connelly and Vandervoort, 2000; Häkkinen et al., 2000; Hakkinen et al., 1998b; Häkkinen et al., 1998a; Häkkinen et al., 2001; Keen et al., 1994; Moritani and Devries, 1980; Newton et al., 2002; Radaelli et al., 2014B; Radaelli et al., 2014A) following chronic (2-12 weeks) strength-training, with all studies reporting no to large effect for increasing sEMG (Cohen's *d* range 0.00-2.31) (Figure 11). Best Evidence synthesis demonstrated strong evidence for strength-training to increase muscle activation of the trained muscle for older adults (Table 1, Figure 11).

Insert Figure 11 here.

3.13.4 Pre-Post Changes in CSA for Older Adults

Strength-training induced changes in CSA were assessed by eleven studies (Cannon et al., 2007; Frontera et al., 1988; Häkkinen et al., 1998a; Harridge et al., 1999; Keen et al., 1994; Lixandrao et al., 2016; Moritani and Devries, 1980; Slivka et al., 2008; Verdijk et al., 2009; Verdijk et al., 2016; Welle et al., 1996). All the studies reported an increase in CSA post-strength-training with small to moderate effect sizes (Cohen's *d* range 0.08-0.79), demonstrating strong evidence for strength-training to increase CSA in older adults (Table 1, Figure 12).

Insert Figure 12 here.

3.13.5 Pre-Post Changes in VA for Older Adults

Changes in VA was assessed by three studies (Cannon et al., 2007; Harridge et al., 1999; Knight and Kamen, 2001) following chronic (2-12 weeks) strength-training, with all studies demonstrating limited evidence (Cohen's *d* range 0.39-0.85) (Figure 13) for strength-training to increase VA in older adults (Table 1, Figure 13).

Insert Figure 13 here.

3.13.6 Pre-Post Changes in H-reflex for Older Adults

Two studies (Scaglioni et al., 2002; Unhjem et al., 2015) examined changes in H-reflex post-strength-training. The results (Cohen's *d* range -0.21-0.22), indicate limited evidence for changes in H-reflex post strength-training in older adults (Table 1, Figure 14).

Insert Figure 14 here.

3.13.7 Pre-Post Changes in M_{MAX} for Older Adults

Changes in M-wave amplitude were assessed by three studies (Keen et al., 1994; Scaglioni et al., 2002; Unhjem et al., 2015). The results (Cohen's *d* range -0.70-0.03), reported conflicting evidence for strength-training in older adults on peripheral muscle excitability (Table 1, Figure 15).

Insert Figure 15 here.

3.13.8 Pre-Post Changes in V-wave for Older Adults

A single study (Unhjem et al., 2015) assessed changes in V-wave amplitude following strength-training showing limited evidence and reporting a moderate effect (ES = 0.47) for increased V-wave in older adults (Table 1).

4. Discussion

The present systematic review with meta-analysis and best evidence synthesis aimed to identify the potential sites of neural adaption (cortical, spinal and muscular) to strength-training in older adults. Overall, both the meta-analysis and best evidence synthesis revealed that:

- Large comparative effects and strong evidence supports the notion that strength-training increases maximal force production and RFD in older adults.
- Strength-training in older adults' results is a modest increase in muscle activation.
- Strength-training does not alter VA or neural drive as assessed by the V-wave in older adults.
- There is conflicting evidence for strength-training to increase H-reflex and limited evidence for strength-training to modulate M_{MAX}.
- Best evidence synthesis showed strong evidence for strength-training to increase CSA in older adults.

It is well accepted that ageing is associated with a reduction in maximal force production (Moritani, 1979; Narici et al., 1989) that is due to reduced neuromuscular function as well as a loss of muscle mass (Doherty, 2003; Janssen et al., 2000). Previous studies have supported the notion that strength-training could be a suitable exercise intervention that may act as a 'countermeasure' to regain the age-related loss in maximal force production (Häkkinen et al., 1998a). Early studies have shown that systematic strength-training, in both older men and women, leads to substantial increases in maximal force production, that are likely due to both neural and muscular adaptations (Hakkinen et al., 1998b; Häkkinen et al., 1998a; Häkkinen et al., 2001; Walker, 2021). The current findings of this review suggest that 2-12 weeks of strength-training in older adults is an effective intervention to improve maximal force production (SMD 0.68). In addition, we examined the effectiveness of strength-training to increase maximal force production in older adults via best evidence synthesis which showed strong evidence with large effects (e.g., g = 5.82). As expected, the selected articles show that strength-training is an important countermeasure to the age-related loss in force production. However, the mechanisms underpinning increased maximal force production in older adults, is less clear, remains under studied and remains unresolved.

Notwithstanding the aforementioned, the increase in maximal force production is a positive adaptation to strength-training, whereby it is likely that strength-training leads to subtle adaptations along the entire neuroaxis (Siddique et al., 2020). There is evidence to show that strength-training in older adults results in increased muscle activation of the trained muscles (Moritani and Devries, 1980); increased recruitment and discharge rates of motor units (Hortobágyi et al., 2020; Kamen and Knight, 2004); increased motor output from the motor cortex, increased spinal motoneurone excitability and reduced inhibition in descending motor pathways (Aagaard and Thorstensson, 2003; Christie and Kamen, 2014). In the current study, the increase in maximal force production was accompanied by an increase in muscle activity and RFD, however, strength-training had no effect on VA, V-wave, M-wave or the H-reflex, but had a moderate effect on increasing CSA. The moderate and variable (wide confidence intervals) increases in CSA shown are unsurprisingly given the heterogeneity of the strength-training study design and duration. Though increases in muscle mass have been suggested to occur after only 2-4 weeks (Hughes et al., 2018), generally notable increases in CSA are considered to occur between 8-12 weeks in young (Hughes et al., 2018) and older adults (Mayer et al., 2011). The findings for CSA are likely heavily influenced by the duration of the study and need to be interpreted accordingly. Conversely, as little as 3-5 training sessions has been shown to elicit increases in strength (Hortobágyi et al., 2011; Mason et al., 2020), which are attributed to neurological adaptations. It is likely that the duration of the strength-training studies in our systematic review is less influential in determining neurological changes in older adults.

At a minimum, during the early phases of strength-training, the mechanism driving the increase in force production in older adults, is likely to emanate from changes in motor unit behaviour (Duchateau et al., 2006). This line of enquiry is consistent with the reported mechanisms that underlie improvements in RFD which this review also found. The pooled data showed moderate evidence that strength-training results in increases in RFD (SMD 0.65) and best evidence synthesis showed strong effects. Given that we have shown increased muscle activity of the trained muscles, it is likely that strength-training in older adults improved both the recruitment of higher threshold motor units, increased rate coding and reduced recruitment thresholds (Blazevich et al., 2009; Kamen and Knight, 2004). Further, there appears to be an association between motor unit discharge rate and RFD (Van Cutsem and Duchateau, 2005). However, because all the included studies used sEMG during RFD testing, the technical limitations of sEMG should be considered when interpreting our findings of increased muscle activity and RFD (Farina et al., 2010).

Interestingly, only three studies determined VA and only one study used TMS to examine the corticospinal-motoneuronal responses to strength-training in older adults. Although the increase in muscle activity is likely reflective of improved recruitment and discharge rates of higher threshold MUs, which is an important mechanism of increased VA, it seems that methods employed to determine VA in the included studies may have been insensitive to detect small changes. In addition, there may have been a change a spinal sensitivity, such as reduced presynaptic inhibition (Aagaard et al., 2002) or reduced agonist-antagonist muscle activity that contributed to the increase in maximal force production in older adults. Previous strength-training studies have shown that spinal sensitivity (change in H-reflexes) remain unchanged when measured at rest, but increases when measured during an MVC (Aagaard et al., 2002). Irrespective of this, it is possible that the increase observed in maximal force production could have been due to increased motoneurone firing frequency. Firstly, evidence derived from TMS in both younger (Siddique et al., 2020) and older adults (Christie and Kamen, 2014) showed that consistent reductions in neural inhibition, determined by the cortical silent period, occur following strength-training. The cortical silent period is characterized by a pause in the ongoing sEMG signal that proceeds the motor-evoked potential (Kidgell and Pearce, 2010), which is mediated by gamma-aminobutyric acid-$_B$ (GABA-$_B$) and represents an interruption to volitional drive to the motoneurone pool (Yacyshyn et al., 2016). The reported reduction in silent period duration following strength-training in older adults, in the only study included in this meta-analysis that used TMS, suggests that strength-training targets intracortical inhibitory neurons within the motor cortex that act to reduce the synaptic efficacy of intracortical inhibitory neurons that synapse onto corticospinal-motoneuronal cells. The net effect would improve descending drive to the motoneurone pool. Indeed, there are now several lines of evidence showing reductions in silent duration are accompanied by increases in strength (Kidgell and Pearce, 2010; Mason et al., 2017; Mason et al., 2020) and increases in silent period durations are associated with strength loss (Clark et al., 2014a). Thus, the change in maximal force production might in part be due to increased motoneurone firing frequency via the removal of local inhibition at the motor cortex and spinal cord via reduced silent period durations. Lastly, the increase in maximal force production and RFD seems to be supported by the increase in muscle activation of the trained muscle. This is in general alignment with a large number of strength-training studies (Aagaard et al., 2007; Aagaard et al., 1999; Duchateau and Hainaut, 1984; Kamen and Knight, 2004; Leong et al., 1999; Pearson et al., 2002; Schmidtbleicher and Haralambie, 1981) that have also reported increased sEMG amplitudes, suggesting that strength-training in younger and older adults improves efferent drive (Aagaard et al., 2002).

One feature of muscle weakness is reduced efferent drive which can be quantified by VA and such deficits can be determined by the interpolated twitch technique (Gandevia et al., 1998). The measurement of VA typically involves applying supramaximal electrical stimulation to a motor nerve whilst performing a maximal voluntary contraction. If the supramaximal electrical stimulus produces additional force during the MVC, then VA is considered incomplete (Folland and Williams, 2007). Thus, an important question to ask is whether, in populations where VA may be reduced, can it be improved by strength-training? Only three studies examined the effect of strength-training on VA and showed a trivial effect (SMD 0.16). In addition, the included studies quantified VA by the use of the interpolated twitch technique, which has shown to lack sensitivity in detecting changes (Allen et al., 1995), which could help to explain the lack of significant comparative effects within this study. In addition to determining VA, neural drive to a muscle can be determined by the amplitude of the V-wave. Interestingly, only two studies were included that quantified neural drive, with both studies reporting a small effect size with a wide confidence interval. Further, the BES noted that there was only limited evidence for strength-training to increase V/M ratio. In addition, this limited evidence is likely driven by the few studies that have assessed neural drive with the V/M ratio in older adults following strength training, thus our data should be interpreted with caution. Moving forward, there is a need to use additional experimental techniques, such TMS voluntary activation and corticomedullary-evoked potentials, to provide greater insight into the effect of strength-training on motoneurone activation. This would enable the elements within the nervous system to be systematically examined to determine the potential sites of adaptations to strength-training in older adults.

In light of the above, the present study did examine the effect of strength-training on motoneurone excitability by pooling data that used the H-reflex. The H-reflex is often used to quantify motoneurone excitability and the efficacy of the 1a afferent synapse. Increases in the H-reflexes are thought to represent increased motoneurone excitability and /or reduced presynaptic inhibition. The current review showed that strength-training has no effect on the sensitivity of the H-reflex (even when measured during background muscle activity), a finding that is consistent with younger adults (Siddique et al., 2020). In addition, there are several limitations to the H-reflex technique that may underscore the effectiveness of strength-training on increasing motoneurone excitability. For example, the amplitude of the H-reflex is influenced by the level of presynaptic inhibition, which limits the interpretation of this technique as a quantifiable measure of motoneurone excitability (Carroll et al., 2011). Further, there is a degree of variability in the H-reflex, and more often than not, there are limited normalization procedures that are used which makes it difficult to compare changes following an intervention. Despite this, the increase in maximal force production observed in the current review does not discount a change in motoneurone excitability because the change in sEMG, increased RFD, and the potential reduction in silent period duration do implicate a change in motoneurone behaviour. Further, because the H-reflex itself cannot directly quantify the extent of presynaptic inhibition (a major mechanism that influences motoneurone excitability), the mechanism increasing the amplitude of the H-reflex remains unresolved. Therefore, additional measures are required, such as cervico-medullary evoked potentials, V-waves and, potentially, measures of the excitability of the reticular formation which are known to innervate motoneurones (Škarabot et al., 2022).

Excluding the proposed neural responses to strength-training, many studies support the role for strength-training to increase muscle mass in older individuals (Frontera et al., 1988; Hakkinen et al., 1998b; Häkkinen et al., 1998a; Suetta et al., 2004). Indeed, seminal studies by Ikai and Fukunaga (1970) and Moritani and DeVries (1979) reported that the changes in maximal force production, at least after ~6 weeks of training, were largely due to increases in muscle mass. Interestingly, our meta-analysis reported strong evidence for strength-training to increase muscle mass in older adults. Although this finding for increased CSA is consistent within the literature, given the width of the confidence interval for the observed effect size, caution should be used when considering the effect of strength-training on increasing muscle mass and underpinning strength gain. Although muscle mass is important in producing force, there is evidence to show that the magnitude of force production loss during ageing is greater than the proportion of muscle mass loss (Delmonico et al., 2009). Given the larger effect size and the smaller with of the confidence interval for increased maximal force production and RFD in the current review, it seems that the overall change in CSA is only having a modest contribution to the increase in maximal force production and RFD (Clark and Taylor, 2011). Therefore, it seems that the increase in maximal force production observed in this study is likely predominantly influenced by changes within the nervous system that act to increase motoneurone firing frequency, with a smaller contribution from increased CSA. Never the less, the strong evidence for increased muscle mass is consistent with previous studies whereby strength training increases muscle mass in older adults (Cannon et al., 2007; Frontera et al., 1988; Häkkinen et al., 1998a; Harridge et al., 1999; Keen et al., 1994; Lixandrao et al., 2016; Moritani and Devries, 1980; Slivka et al., 2008; Verdijk et al., 2009; Verdijk et al., 2016; Welle et al., 1996).

There are several limitations to the current study that should be considered when interpreting the main findings. First, the included studies had a high risk of bias for several domains (e.g., allocation bias), which might lead to an overestimation of the pooled effect for the changes in strength and RFD. Moreover, methodological limitations, such as heterogeneity of the training schedules and body region studied/ type of muscle trained need to be considered for accurate quantification of both force production and the underlying neuromuscular mechanisms. Determining the potential sites (cortical, spinal and muscular) of neuromuscular adaptation of neural adaptation to strength-training in older adults is important as it will add clarity to the mechanisms that contribute to strength gain. However, many of the included studies did not assess specific neurological variables, which limits our understanding into the potential sites of neural adaptation to strength-training in older adults. Although this may seem like a limitation, it is also an important finding that highlights, compared to young adults, there is a paucity of studies that have probed the neural adaptations to strength training in older adults. Therefore, future studies should adopt a range of TMS-based measurements such as single- and paired-pulse measures, TMS voluntary activation, cervico-medullary and reticulospinal responses coupled with measures of spinal excitability such as the V-wave. By addressing these gaps, studies will be able to provide a comprehensive chain of events detailing the corticospinal-motoneuronal, reticulospinal and spinal responses to strength-training in older adults. Investigating changes from cortical to subcortical to the muscular level will help in understanding the mechanism or factors contributing towards strength gain or loss in older adults and could be used to guide targeted and effective guidelines for exercise prescription aim at strength gain. Finally, whilst we classified older adults as above 60 years old, further research should understand the differing responses in older vs very old adults as these are likely to differ.

5. Conclusions

This systematic review and meta-analysis provide a detailed quantitative analysis of the cortical, spinal and muscular adaptations to strength-training in older adults. In accordance with our hypothesis, strength-training increased maximal force production and RFD in untrained older adults. Based upon previous evidence and the primary hypothesis of this study, it is likely that strength-training increases motoneurone firing frequency (via increased motor unit recruitment and rate coding), which collectively improved muscle activation. Due to methodological issues, improved VA and neural drive, do not seem to be an adaptation induced by strength-training in older adults, a finding that is in contrast to our primary aim and hypothesis. There is a need for a better understanding of the subtle changes or modifications that occur from the cortical, spinal and muscular level that may contribute to the increase in force production following strength-training in older adults.

6. Author Contributions

Dawson Kidgell, Ash Frazer, Jamie Tallent and Ummatul Siddique: Conceptualization, Methodology, Data curation, formal analysis, writing-original preparation, Writing- review and editing. **Glyn Howatson, Janne Avela, Simon Walker and Juha P. Ahtiainen:** Writing – review & editing.

7. Statement of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Table Legends:

Table 1: Study characteristics for included studies within the meta-analysis and Best evidence Synthesis

Table 2: Itemised scoring of quality assessment using a modified Downs and Black checklist

Figure legends:

Figure 1: Flow chart of each stage of the study selection using the PRISMA 2020 guidelines.

Figure 2: Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Figure 3: Forest plot showing the effect of strength-training on maximal force production. Std, Standardised mean difference; IV, inverse variance; Random, random effect model; CI, confidence interval; df, degrees of freedom; I^2, inconsistency statistic. Statistical significance set at $P < 0.05$.

Figure 4: Forest plot showing the effect of strength-training on the rate of force development (RFD). Std, Standardised mean difference; IV, inverse variance; Random, random effect model; CI, confidence interval; df, degrees of freedom; I^2, inconsistency statistic. Statistical significance set at $P < 0.05$.

Figure 5: Forest plot showing the effect of strength-training on H-reflex. Std, Standardised mean difference; IV, inverse variance; Random, random effect model; CI, confidence interval; df, degrees of freedom; I^2, inconsistency statistic. Statistical significance set at $P < 0.05$.

Figure 6: Forest plot showing the effect of strength-training on voluntary activation (VA). Std, Standardised mean difference; IV, inverse variance; Random, random effect model; CI, confidence interval; df, degrees of freedom; I^2, inconsistency statistic. Statistical significance set at $P < 0.05$.

Figure 7: Forest plot showing the effect of strength-training on M_{MAX}. Std, Standardised mean difference; IV, inverse variance; Random, random effect model; CI, confidence interval; df, degrees of freedom; I^2, inconsistency statistic. Statistical significance set at $P < 0.05$.

Figure 8: Forest plot showing the effect of strength-training on surface electromyography (sEMG). Std, Standardised mean difference; IV, inverse variance; Random, random effect model; CI, confidence interval; df, degrees of freedom; I^2, inconsistency statistic. Statistical significance set at $P < 0.05$.

Figure 9. Forest plot showing effect sizes for strength following strength-training.

Figure 10. Forest plot showing effect sizes for rate of force development (RFD) following strength-training.

Figure 11. Forest plot showing effect sizes for sEMG following strength-training.

Figure 12. Forest plot showing effect sizes for cross-sectional area (CSA) following strength-training.

Figure 13. Forest plot showing effect sizes for voluntary activation (VA) following strength-training.

Figure 14. Forest plot showing effect sizes for H-reflex following strength-training.

Figure 15. Forest plot showing effect sizes for M_{MAX} following strength-training.

Sl. no	Study	Training	Participant characteristics	Sampling	Key measure (s)	Results	D & B Score	Meta-analysis	Best Evidence Synthesis (BES)
(1)	Bellew et al. [9]	24 training sessions over 12 weeks-2x/wk, high intensity strength training of quadriceps femoris muscle	27 untrained healthy old Control [(n=5, 67.4±7.3yrs, 3M & 2F); Trained [(n=22, 67.7±5.5yrs, 11M & 11F)]	Matched for age.	Strength	↑Strength [isometric (+12.6%)]	13	✓	
(2)	Berg et al. [10]	24 training sessions over 8 weeks-3x/wk, supervised maximal strength training of the quadriceps muscle	10 untrained healthy old (75±9yrs, 7M &3F)	Matched for age, pre-train strength	Strength, RFD	↑ Strength [concentric (30.4%)]; ↑ RFD 15.9%	14		✓
(3)	Beurskens et al. [12]	36 training sessions over 12 weeks-3x/wk, heavy strength training of lower limb	39 untrained healthy old Control [(n=20, 66.7±4.0yrs, 20M); Trained [(n=19, 66.4±4.9yrs, 19M)]	Random	Strength	↑Strength [isometric (+8.7%)]	11	✓	
(4)	Cannon et al. [15]	30 training sessions over 10 weeks-3x/wk, isometric strength training of the knee extensor muscle	8 untrained healthy old women (69.8±6.6yrs)	Matched for age	Strength, Voluntary activation, EMG, CSA	↑Strength [isometric (+18.1%)]; ↑CSA 9.9%; ↑EMG 20.6%; ↑ VA 2.1%	10		✓
(5)	Caserotti et al. [18]	24 training sessions over 12 weeks-2x/wk, Explosive-type heavy-strength training of the lower limbs	40 untrained healthy women Control [(n=20, 62.7±2.2yrs); Trained [(n=20, 62.2±2.2yrs)]	Matched for age	Strength, RFD	↑Strength 21.5%; ↑ RFD 18.1%	11	✓	

(6)	Christie & Kamen et al. [20]	6 training sessions over 2 weeks-3x/wk, isometric strength training of the dorsiflexors	30 untrained healthy old (15M & 15F) Control [(n=15, 72.9±4.6yrs); Trained [(n=15, 72.9±4.6yrs)]	Random	Strength, EMG, MEP_{max}, cSP duration, M_{max}, H_{max}	↓ MEP_{max} 10.5%; ↓ cSP duration 8.3ms; ↓ M_{max} 3.8mV; ↑ H_{max} 7.38%	14	✓	
(7)	Connelly et al. [25]	6 training sessions over 2 weeks -3x/wk, Isokinetic strength training of the dorsiflexors	28 untrained healthy old [(76.3±4.6yrs, 13M & 15F)]	Matched for age	Strength, EMG, RTD	↑Strength 27.5%; ↑ EMG [eccentric (+55.3%) and concentric (+62.5%)]; ↑ RTD 18.1%	15		✓
(8)	De Vos et al. [27] *	16-24 training sessions over 8-12weeks-2x/wk. explosive strength training of knee extensors.	56 untrained healthy old adults Trained[(69.0±6.4yrs), n=28)] Control [(67.6±6yrs), n=28)]	Random	Strength	↑Strength 27%	14	✓	
(9)	Earles et al. [32] *	36 training sessions over 12 weeks-3x/wk, High intensity power training of the knee extensors	40 untrained healthy old Walking Group [(78±5yrs), n=22]; Training Group [(77±5yrs), n=18]	Random	Strength	↑Strength 22%	12	✓	
(10)	Fielding et al. [36]	36 training sessions over 12 weeks-3x/wk high-velocity strength training of the knee extensors	15 untrained healthy old (73.2±4.6yrs, 15F)	Random	Strength	↑Strength 1.4%	14		✓
(11)	Frontera et al. [39]	34 training sessions over 12 weeks-3x/wk, Isokinetic strength training of knee extensors and flexors	12 untrained healthy old men (60-72yrs)	Matched for age	Strength, CSA	↑ Strength 125%; ↑CSA 11.04%	8		✓
(12)	Gurjao et al. [43]	24 training sessions over 8 weeks-3x/wk, isometric strength	17 untrained healthy old women	Random	Strength, RFD, EMG	↑ Strength 18.6%; ↑ RFD 41.4%; ↑EMG 38.6%	11	✓	

		training of the knee extensors	Control [(n=7, 65.0±5.1yrs); Trained [(n=10, 61.7±4.8yrs)]						
(13)	Hakkinen et al. [44]	16 training sessions over 8 weeks-2x/wk, Strength training of the knee extensors	10 untrained healthy old [(70±4yrs, 5M & 5F)]	Matched for age	Strength, EMG	↑ Strength 16.67%, ↑IEMG 5.73%	13		✓
(14)	Hakkinen et al. [46]	30 training sessions over 10 weeks-3x/wk, Isometric strength training of the knee extensors (bilateral)	18 untrained healthy old [(60.8±4.0yrs), 10M]	Matched for age	Strength, EMG, RFD	↑ Strength 16.1%; ↑IEMG 38.3%; no change in RFD; ↑CSA (Quadriceps femoris) 8.5%	10		✓
(15)	Hakkinen et al. [45]	16 training sessions over 8 weeks-2x/wk, Isometric strength training of the leg extensors	21 untrained healthy old [(69.5±3yrs, 11M & 10F)]	Matched for age	Strength, RFD, iEMG	↑ Strength (isometric) 10.93%; ↑RFD 5.39%; ↑iEMG 19.63%	13		✓
(16)	Hakkinen et al. [47]	14 training sessions over 7 weeks-2x/wk, isometric strength training of leg extensors	10 untrained healthy old women (64±3yrs)	Matched for age	Strength, EMG	↑ Strength 10.49%; ↑ EMG 27.93%	10		✓
(17)	Harridge et al. [48]	12 weeks of strength training of the knee extensor muscles	11 untrained healthy old [(85-97yrs) 8F, (85-92yrs) 3M]	Matched for age	Strength, CSA, VA	↑ Strength 101.29%, ↑CSA 9.82; ↑ VA 4.94	9		✓
(18)	Henwood et al. [49]	16 training sessions over 8 weeks -2x/wk, isotonic strength training of the knee extensors	25 untrained healthy old Trained [(n=15, 69.9±6.5yrs, 5M & 10F); Control [(n=10, 71.3±5.6yrs, 3M & 7F)]	Matched for age	Strength	↑ Strength 36%	14	✓	
(19)	Hicks et al. [51]	24 training sessions over 12 weeks-2x/wk,	11 untrained healthy old [(66.3±3.7yrs, 4M & 7F)]	Matched for age	Strength	↑ Strength 14.75%	11		

		Isometric strength training of the tibialis anterior muscle.							✓
(20)	Hortobagyi et al. [57] *	30 training sessions over a period of 10 weeks-3x/wk strength training of the knee extensors	18 untrained healthy Old trained [(n= 9, 72±4.7yrs)]; Control (n=9)	Random	Strength, RTD_{max}	↑ Strength 35.41%, ↑, RTD_{max} 20.09%	15	✓	
(21)	Hunter et al. [59]	36 training session over a period of 12 weeks-3x/wk, high-strength training of the knee extensors	10 untrained healthy old women (70.7±1.6yrs)	Matched for age	Strength	↑ Strength 39.02%	9		✓
(22)	Hvid et al. [60]	24 training sessions over 12 weeks-2x/wk, progressive high-strength power training of the knee extensor	37 untrained healthy Trained [(n= 16, 82.3±1.3yrs, 7M & 9F)]; Control [(n=21, 81.6±1.1yrs, 7M & 14F)]	Random	Strength	↑ Strength 14.36%, ↑ VA 7.60%	13	✓	
(23)	Ivey et al. [61]	27 training sessions over 9 weeks-3x/wk, Strength training of knee extensors	22 untrained healthy old [11M (65-75yrs) & 11F (65-75yrs)]	Matched for age and pre-train strength	Strength	↑ Strength 27.32%	13		✓
(24)	Jozsi et al. [65]	24 training sessions over 12 weeks-2x/wk, Progressive strength training of knee extensor	17 untrained healthy old [9M (60.2±3.3yrs) & 8F (60.4±3.7yrs)]	Matched for age & pre-train strength	Strength	↑ Strength 31.71%	13		✓
(25)	Jiang et al. [64]	60 training sessions over 12 weeks-5x/wk, conventional strength training of the elbow flexors	12 untrained healthy Trained [n= 10, 7M & 3F (75±7.9yrs)]; Control [n=7, 5M & 2F (75±7.9yrs)]	Random	Strength, EMG	↑ Strength 17.32%; ↑ EMG 9.47	7	✓	

(26)	Judge et al. [66] *	36 training sessions over 12 weeks-3x/wk, Strength training of the knee extensors	55 untrained healthy Trained [(n=28, 80.3±4.0yrs)]; Control [(n=27, 80.6±4.5yrs)]	Random	Strength	↑ Strength 17.81%	13	✓	
(27)	Kalapotharakos et al. [67]	16 training sessions over 8 weeks-2x/wk, strength training of the knee extensors	14 untrained healthy old men Trained [(n=7, 83.4±2.8yrs)]; Control [(n=7, 82.5±3yrs)]	Random	Strength	↑ Strength 41.67%	10	✓	
(28)	Keen et al. [70]	36 training sessions over 12 weeks-3x/wk, Strength training of the first dorsal interosseus muscle	11 untrained healthy old [(59-74yrs), 5M & 6F]	Matched for age	Strength, EMG, M-wave, CSA	↑ Strength 43.33%; no change in EMG; ↓Mwave 20.60%; ↑ CSA 2.8%	13		✓
(29)	Knight et al. [73]	18 training sessions over 8 weeks-3x/wk, strength training of knee extensors	7 untrained healthy old [(77.0±5.3yrs, 6M & 1F)]	Matched for age	Strength, VA	↑ Strength (isometric) 30.95%; ↓VA 33.25%	12		✓
(30)	Kostek et al. [74]	30 training sessions over 10 weeks-3x/wk, Strength training of the knee extensors	65 untrained healthy old [(70.0±6yrs, 32M & 67.0±8yrs, 35F)]	Matched for age	Strength	↑ Strength 25%	15		✓
(31)	Laidlaw et al. [76]	12 training sessions over 4 weeks-3x/wk, Strength training of the first dorsal interosseus muscle	24 untrained healthy older adults Control [(n= 16, 72.4±6.8yrs, 5M & 11F)]; Trained [(n=8, 68.3±6.2yrs, 4M & 4F)]	Random	Strength	↑ Strength (isometric) 36.63%	10	✓	

(32)	Lixandrao et al. [79] #	20 training sessions over 10 weeks-2x/wk, Strength training of the lower limb	14 untrained healthy old Trained [n=6, 60.3±2.7yrs, 4M & 2F)] Control [(n=8, 65.7±4.6, 4M & 4F)]	Random	Strength, CSA	↑ Strength 42.38%; ↑CSA 7.84	6	✓	✓
(33)	Lohne-Seiler et al. [80] *	22 training sessions over 11 weeks-2x/wk, Strength training of the knee extensors.	33 untrained healthy Control [(n= 10, 69.3±4.2yrs)]; Trained [(n=23, 69.4±4.0yrs)]	Random	Strength	↑ Strength (isometric) 20.59%	14	✓	
(34)	Marsh et al. [83]	36 training sessions over 12 weeks-3x/wk, strength training of the knee extensors	24 untrained healthy Control [(n= 13, 74.4±5.2yrs, 9F & 4M)]; Trained [(n=11, 74.6±5.4yrs), 9F & 2M]	Matched for age	Strength	↑ Strength 24.15%	15	✓	
(35)	Moritani et al. [92]	24 training sessions over 8 weeks-3x/wk, isometric strength training of the elbow flexors	5 untrained healthy old males (67-72yrs)	Matched for age	Strength, CSA, EMG	↑ Strength 22.62%; ↑CSA 1.48%; ↑EMG 22.97%	8		✓
(36)	Newton et al. [94]	30 training sessions over 10 weeks-3x/wk, strength training of the knee and hip extensors	10 untrained healthy old males (61±4yrs)	Matched for age	Strength, iEMG	↑ Strength (isometric) 24.05%; ↑EMG 24.26%	9		✓
(37)	Radaelli et al. [100]	12 training sessions over 6 weeks-2x/wk, isometric strength training of the knee extensors	13 untrained healthy females (60-74yrs)	Random	Strength, EMG	↑ Strength 18.7%, ↑EMG 2.83%	12		✓
(38)	Radaelli et al. [99]	12 training sessions over 6 weeks-2x/wk, isometric strength	9 untrained healthy old females (62.9±2.3yrs)	Random	Strength, EMG	↑ Strength 21.89%, ↑EMG 9.09%	12		✓

		training of the knee extensors							
(39)	Rodriquez Lopez et al. [101]	24 training sessions over 12 weeks-2x/wk, heavy load power training of the knee extensors	10 untrained healthy old (5M & 5F, 64-83yrs)	Random	Strength, RFD,	↑ Strength 23.76, ↑RFD 6.18%	14		✓
(40)	Scaglioni et al. [105]	30 training sessions over 10 weeks-3x/wk, strength training of the plantar flexors	14 untrained healthy old males (65-80yrs)	Matched for age	H_{max}, M_{max}	↓ **H_{max} 11.54%;** ↓ M_{max} 1.51%;	11		✓
(41)	Schlicht et al. [106] #	18 training sessions over 6 weeks-3x/wk, intense strength training	22 untrained healthy (10M & 14F) Control [(n=11, 72±6.3yrs)] Trained [(n=11, 72±6.3yrs)]	Random	Strength	↑ Strength 28.90%	13		✓
(42)	Slivka et al. [112]	36 training sessions over 12 weeks-3x/wk, progressive strength training of the knee extensors	6 untrained healthy old males (82±1yrs)	Matched for age	Strength, CSA	↑ Strength (isotonic)41.07% ↑CSA (Quadriceps femoris) 2.5%	9		✓
(43)	Sousa et al. [113]	36 training sessions over 12 weeks-3x/wk, strength training of upper and lower limb	10 untrained healthy old males (73±6yrs)	Random	Strength	↑ Strength 65.09%	10		✓
(44)	Toein et al. [118] #	9 training sessions over 3 weeks-3x/wk, maximal strength training of the plantar flexors	23 untrained healthy males Control [(n=12, 72±3yrs)] Trained [(n=11, 75±5yrs)]	Random	Strength, RFD,	↑ Strength 18.41%;↑ RFD 32.79%	14		✓

(45)	Tracy et al. [119] *	24 training sessions over 8 weeks-3x/wk, strength training of the knee extensors	20 untrained healthy Control [(n=9, 74.2±4.9)] Trained [(n=11, 73.1±4.9)	Random	Strength	↑ Strength 22.11%	12	✓	
(46)	Trappe et al. [121]	36 training sessions over 12 weeks-3x/wk, progressive strength training of the knee extensors	7 untrained healthy old males (74±1.8yrs)	Matched for age	Strength	↑ Strength 49.53%	10		✓
(47)	Trappe et al. [120]	36 training sessions over 12 weeks-3x/wk, progressive strength training of the knee extensors	7 untrained healthy old females (74±2yrs)	Matched for age	Strength	↑ Strength 56.25%	10		✓
(48)	Unhjem et al. [122]	24 training sessions over 8 weeks-3x/wk, Isometric strength training of the plantar flexors	9 untrained healthy old males (74±6yrs)	Matched for age	Strength, RFD, M_{max}, H_{max}, V_{max}	↑ Strength 20.52%; ↑ RFD 36.39%; ↑ M_{max} 0.88%; **↑ H_{max} 2.64%; ↑ V_{max} 38.18%**	14		✓
(49)	Unhjem et al. [123]	9 training sessions over 3x/wk, isometric maximal strength training of the plantar flexors	23 untrained healthy males Control [(n=12, 73±2yrs)] Trained [(n=11, 74±5yrs)]	Random	Strength, RFD, M_{max}, H_{max}, VA, V_{max}	↑ Strength 17.14%; ↑ RFD 35.09%; ↑ M_{max} 1.86%; **↓ H_{max} 4.00 %;** ↑ VA 6.33%; **↑ V_{max} 71.42%**	10	✓	
(50)	Vanroie et al. [125]	36 training sessions over12 weeks-3x/wk, High-strength training of the knee extensors	18 untrained healthy old [(8M & 10F, 68±4yrs)]	Random	Strength	↑ Strength (isometric) 35.59%	14		✓
(51)	Vanroie et al. [126]	36 training sessions over12 weeks-3x/wk, Resistance training of the lower limb	11 untrained healthy old males (68.2±2.7yrs)	Random	Strength, RFD	↑ Strength 25.79%; ↓RFD -8.89%	14		✓

(52)	Verdijk et al. [127]	36 training sessions over 12 weeks-3x/wk, strength training of the knee extensors	13 untrained healthy old males (72±2yrs)	Matched for age	Strength, CSA	↑ Strength 24.42%; ↑ CSA 8.56%	14		✓
(53)	Verdijk et al. [128]	36 training sessions over 12 weeks-3x/wk, progressive type strength training of the lower body	16 untrained healthy old males (72±1yrs)	Matched for age	Strength, CSA	↑ Strength 25.47%; ↑ CSA 7.84%	12		✓
(54)	Walker et al. [130]	20 training sessions over 10 weeks-2x/wk, dynamic strength training of the knee extensors	37 untrained healthy old males Control [(n=11, 65±3yrs)] Trained [(n= 26, 63±8yrs)]	Matched for age	Strength, CSA, Voluntary activation (VA)	↑ Strength 14.47%; ↑CSA 13.49%; ↑ VA 13.75%	12	✓	
(55)	Wang et al. [131]	24 training sessions over 8 weeks-3x/wk, Maximal strength training of legs	11 untrained healthy old males (72±3yrs)	Matched for age	Strength, RFD	↑ Strength 66.97%; ↑ RFD 41.08%	11		✓
(56)	Welle et al. [133]	36 training sessions over 12 weeks-3x/wk, Progressive strength training of the knee extensors	8 untrained healthy old [(62-72yrs, 4M & 4F)]	Matched for age	CSA	↑ CSA 4.88%	12		✓
(57)	Wolfson et al. [134]	36 training sessions over 12 weeks-3x/wk, Isokinetic strength training of knee extensors and ankle dorsiflexors	55 untrained healthy Control [(n=27, 80.6±4.5yrs, 16M & 11F)] Trained [(n=28, 80.0±4.1, 18M &10F)]	Matched for age	Strength	↑ Strength 23.07%	12	✓	

KEY:

CSA: Cross sectional area; cSP: Cortical silent period; D & B: Downs and Black Quality Assessment; DV: Dependent variable; EMG: Electromyography; F: Female; H_{MAX}: Maximum H reflex; IEMG: Integrated Electromyography; M: Male; MEP: Motor-evoked potential; MEP_{MAX}: maximum motor evoked potential; RFD: Rate of force development; RTD_{MAX}: Maximum rate of torque development; SICI: Short-interval intracortical inhibition; VA: Voluntary Activation; ↑ increase; ↓ decrease.

* Sex for the participants not reported for these studies

For Schlicht et al. [106] there were two dropouts from the experiment, but sex was not reported for the dropout participants. No data reported for the control group.

For Toein et al. [118], no data reported for control group for trained limb.

For Lixandrao et al. [79], note that the strength data extracted entered the meta-analysis whilst the data extracted for CSA entered the best evidence

Table 2. Itemised scoring of quality assessment using a modified Downs and Black checklist

Study	**1**	**2**	**3**	**5**	**6**	**7**	**10**	**11**	**12**	**14**	**16**	**18**	**20**	**21**	**25**	**26**	**27**	**Total**	**%**	**Quality**
Bellew et al. [9]	1	1	1	2	1	1	0	1	1	0	0	1	1	1	0	1	0	13	76.47	HIGH
Beurskens et al. [12]	1	1	1	2	1	1	0	0	0	0	0	1	1	0	0	1	1	11	64.70	LOW
Berg et al. [10]	1	1	1	2	1	1	1	1	1	0	0	1	1	1	0	1	0	14	82.35	HIGH
Cannon et al. [15]	1	1	1	2	1	1	0	0	0	0	0	1	1	0	1	0	0	10	58.82	LOW
Caserotti et al. [18]	1	1	1	2	1	1	1	0	0	0	0	1	1	0	0	1	0	11	64.71	LOW
Christie & Kamen et al. [20]	1	1	1	2	1	1	1	1	1	0	0	1	1	1	1	0	0	14	82.35	HIGH
Connelly et al. [25]	1	1	1	2	1	1	1	1	1	0	0	1	1	1	1	1	0	15	88.24	HIGH
De Vos et al. [27]	1	1	1	2	1	1	1	1	1	0	0	1	1	1	0	1	0	14	82.35	HIGH
Earles et al. [32]	1	1	1	2	1	1	0	1	1	0	0	1	1	1	0	0	0	12	70.59	HIGH
Fielding et al. [36]	1	1	1	2	1	1	1	1	1	0	0	1	1	1	0	1	0	14	82.35	HIGH
Frontera et al. [39]	1	1	0	2	1	1	0	0	0	0	0	1	1	0	0	0	0	8	47.06	LOW
Gurjao et al. [43]	1	1	1	2	1	1	1	0	0	0	0	1	1	0	0	1	0	11	64.71	LOW
Hakkinen et al. [46]	1	1	1	2	1	1	0	0	0	0	0	1	1	0	1	0	0	10	58.82	LOW
Hakkinen et al. [45]	1	1	1	2	1	1	0	1	1	0	0	1	1	1	1	0	0	13	76.47	HIGH
Hakkinen et al. [44]	1	1	1	2	1	1	0	1	1	0	0	1	1	1	1	0	0	13	76.47	HIGH
Hakkinen et al. [47]	1	1	1	2	1	1	0	0	0	0	0	1	1	0	1	0	0	10	58.82	LOW
Harridge et al. [48]	1	1	1	2	1	1	0	0	0	0	0	1	0	1	0	0	0	9	52.94	LOW
Henwood et al. [49]	1	1	1	2	1	1	1	1	1	0	0	1	1	1	0	1	0	14	82.35	HIGH
Hicks et al [51]	1	1	1	0	1	1	0	1	1	0	0	1	1	1	1	0	0	11	64.71	LOW
Hortobagyi et al. [57]	1	1	1	2	1	1	1	1	1	0	0	1	1	1	1	1	0	15	88.24	HIGH
Hunter et al. [59]	1	1	1	2	1	1	0	0	0	0	0	1	0	1	0	0	0	9	52.94	LOW
Hvid et al. [60]	1	1	1	2	1	1	0	1	1	0	0	1	1	1	0	1	0	13	76.47	HIGH
Ivey et al. [61]	1	1	1	2	1	1	1	1	1	0	0	1	1	1	0	0	0	13	76.47	HIGH
Jiang et al. [64]	1	1	0	1	1	1	0	0	0	0	0	1	1	0	0	0	0	7	41.18	LOW
Jozsi et al. [65]	1	0	1	2	1	1	0	1	1	0	0	1	1	1	1	1	0	13	76.47	HIGH
Judge et al. [66]	1	1	1	0	1	1	1	1	1	0	0	1	1	1	1	1	0	13	76.47	HIGH
Kalapotharakos et al. [67]	1	1	1	1	1	1	0	0	0	0	0	1	1	0	1	1	0	10	58.82	LOW
Keen et al. [70]	1	1	1	1	1	1	1	1	1	0	0	1	1	1	1	0	0	13	76.47	HIGH
Knight et al. [73]	1	1	0	2	1	1	1	1	1	0	0	1	1	1	0	0	0	12	70.59	HIGH
Kostek et al [74]	**1**	**1**	**1**	**2**	**1**	**1**	**0**	**1**	**1**	**0**	**0**	**1**	**1**	**1**	**1**	**1**	**1**	**15**	**88.23**	**HIGH**
Laidlaw et al. [76]	1	1	1	1	1	1	0	0	0	0	0	1	1	0	1	1	0	10	58.82	LOW
Lixandrao et al [79]	**1**	**1**	**1**	**2**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**0**	**0**	**0**	**0**	**0**	**6**	**35.29**	**LOW**
Lohne Seiler et al. [80]	1	1	1	2	1	1	1	1	1	0	0	1	1	1	0	1	1	15	88.23	HIGH
Marsh et al. [83]	1	1	1	2	1	1	1	1	1	0	0	1	1	1	1	1	1	16	94.12	HIGH
Moritani et al. [92]	1	1	0	1	1	1	1	0	0	0	0	1	1	0	0	0	0	8	47.06	LOW
Newton et al. [94]	1	1	1	2	1	1	0	0	0	0	0	1	1	0	0	0	0	9	52.94	LOW
Radaelli et al. [100]	1	1	1	2	1	1	0	0	0	0	0	1	1	0	1	1	1	12	70.59	HIGH
Radaelli et al. [99]	1	1	1	2	1	1	0	0	0	0	0	1	1	0	1	1	1	12	70.59	HIGH
Rodriquez Lopez et al. [101]	1	1	1	2	1	1	1	1	1	0	0	1	1	1	0	1	0	14	82.35	HIGH
Scaglioni et al. [105]	1	1	1	2	1	1	1	0	0	0	0	1	1	0	0	1	0	11	64.71	LOW
Schlicht et al. [106]	1	1	1	1	1	1	0	1	1	0	0	1	1	1	1	1	0	13	76.47	HIGH
Slivka et al. [112]	1	1	1	2	1	1	0	0	0	0	0	1	1	0	0	0	0	9	52.94	LOW
Sousa et al. [113]	1	0	1	2	1	1	1	0	0	0	0	1	1	1	0	0	0	10	58.82	LOW
Toien et al. [118]	1	1	1	2	1	1	1	1	1	0	0	1	1	1	0	1	0	14	82.35	HIGH
Tracy et al. [119]	1	1	1	2	1	1	0	1	1	0	0	1	1	1	0	0	0	12	70.59	HIGH

Trappe et al. [121]	1	0	0	2	1	1	0	1	1	0	0	1	1	1	0	0	0	10	58.82	LOW
Trappe et al. [120]	1	1	0	1	1	1	0	1	1	0	0	1	1	1	0	0	0	10	58.82	LOW
Unhjem et al. [122]	1	1	1	2	1	1	1	1	1	0	0	1	1	1	0	1	0	14	82.35	HIGH
Unhjem et al. [123]	1	1	1	1	1	1	1	0	0	0	0	1	1	0	0	1	0	10	58.82	LOW
Vanroie et al. [125]	1	1	1	2	1	1	1	1	1	0	0	1	1	1	0	1	0	14	82.35	HIGH
Vanroie et al. [126]	1	1	1	2	1	1	1	1	1	0	0	1	1	1	0	1	0	14	82.35	HIGH
Verdijk et al. [127]	1	1	1	2	1	1	1	1	1	0	0	1	1	1	0	1	0	14	82.35	HIGH
Verdijk et al. [128]	**1**	**1**	**1**	**2**	**1**	**1**	**1**	**0**	**0**	**0**	**0**	**1**	**1**	**0**	**1**	**1**	**0**	**12**	**70.59**	**HIGH**
Walker et al. [130]	1	1	0	2	1	1	1	1	1	0	0	1	1	1	0	0	0	12	70.59	HIGH
Wang et al. [131]	1	1	1	2	1	1	1	0	0	0	0	1	1	0	0	1	0	11	64.71	LOW
Welle et al. [133]	1	1	0	1	1	1	1	1	1	0	0	1	1	1	0	1	0	12	70.59	HIGH
Wolfson et al. [134]	1	1	1	1	1	1	0	1	1	0	0	1	1	1	0	1	1	13	76.47	HIGH

Low-quality studies were defined as having a risk-of-bias assessment score of <70%, whereas high-quality studies had a score of ≥70%