Determining the corticospinal responses and cross-transfer of ballistic motor performance in young and older adults: a systematic review and meta-analysis

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Abstract

Ballistic motor training induces plasticity changes and imparts a cross-transfer effect. However, age-related differences in these changes remain unclear. Thus, the purpose of this study was to perform a meta-analysis to determine the corticospinal responses and cross-transfer of motor performance following ballistic motor training in young and older adults. Meta-analysis was performed using a random-effects model. A best evidence synthesis was performed for variables that had insufficient data for meta-analysis. There was strong evidence to suggest that young participants exhibited greater cross-transfer of ballistic motor performance than their older counterparts. This meta-analysis showed no significant age-related differences in motor-evoked potentials (MEPs), short-interval intracortical inhibition (SICI) and surface electromyography (sEMG) for both hands following ballistic motor training.

Keywords: aging, corticospinal excitability, motor performance, short-interval intracortical inhibition, transcranial magnetic stimulation

1 Introduction

1.1 Cross-transfer of motor performance

Several studies have shown that performing unilateral motor tasks can result in performance improvements in both the trained and untrained limbs (Carroll et al., 2008; Hinder et al., 2011, 2013b; Lauber et al., 2013; Manca et al., 2021). This effect is known as cross-education, cross-transfer, interlimb transfer, or cross-limb transfer, and it has been demonstrated for various motor tasks (Manca et al., 2021). However, the magnitude of cross-transfer is predicted to vary with the type of task and learning environment (Lauber et al., 2013; Lee et al., 2010, Teixeira, 2000). Evidence suggests that cross-transfer is predicated either by neural network adaptations that are accessible to the trained and untrained limbs (bilateral access hypothesis), or bilateral motor adaptations produced by unilateral motor training (as a result of the cross-activation hypothesis) (Carroll et al., 2008; Lauber et al., 2013; Lee et al., 2010). However, the precise mechanisms underlying cross-transfer remain unclear. As of the 19th century, the concept of cross-transfer has been known (Scripture et al., 1894) and several recent studies have extended this concept to ballistic motor training (Carroll et al., 2008; Hinder et al., 2011, 2013b; Lauber et al., 2013; Lee et al., 2010; Manca et al., 2021) which deserve systematic evaluation. In the present meta-analysis, ballistic motor training refers to a form of training where the participants perform a specific movement task (i.e., repeated abduction movements of the digits of the hand) as quickly as possible.

There are now several studies that have investigated whether cross-transfer is altered to a similar extent in young and older adults after ballistic motor training. In healthy participants, Hinder et al. (2013b) observed that both age groups demonstrated substantial and homogenous magnitude of cross-transfer (i.e., 70.3% for young adults and 64.5% for older adults) following ballistic motor training of the non-dominant hand. Similarly, Reissig et al. (2015) also reported a similar degree of cross-transfer across the two age groups following dominant-hand motor training. However, in contrast, Hinder et al. (2011) observed that older adults showed reduced capacity for cross-transfer compared to young adults (i.e., 11% in older adults versus 75% in young adults). The reduced cross-transfer observed in the older adults could be due to age-related changes in the neural control of movements (Fujiyama, et al., 2009; Hinder et al., 2011; Parikh & Cole, 2013; Reissig et al., 2015). Thus, neurophysiological changes supporting cross-transfer may manifest differently in young and older adults. For example, the lack of cross-transfer could be as a result of changes in the structural integrity of the corticospinal tract (Calvert and Carson, 2022). Further, this line of evidence is supported by imaging data that showed the structural integrity of connecting white matter pathways influences the level of cross-transfer (Ruddy et al., 2017).

1.2 Corticospinal excitability following ballistic training

Substantial evidence indicates that the human primary cortex (M1) is highly plastic and motor skill learning can alter M1 activation patterns (Sanes & Donoghue, 2000; Rogasch et al., 2009). Thus, the learning of new skilled motor actions is associated with neural plasticity (Classen et al., 1998). The potential for functional plasticity following physiological or pathological changes has been clearly demonstrated in M1 (Cirillo et al., 2010; Rogasch et al., 2009). The excitability of M1 can be studied using transcranial magnetic stimulation (TMS), which is a non-invasive method of inducing an electric field in a specific area of the brain to stimulate nerve cells (Bashir et al., 2010; Freitas et al., 2013; Kidgell et al., 2017a). Comparison of TMS measures before and after training provide an indicator of training-induced corticospinal plasticity (Cirillo et al., 2010).

Various TMS measures are used to examine the changes in corticospinal excitability. Motor-evoked potential (MEP) amplitude is one of the common measures that provide important information about the excitability of corticospinal and spinal motor neurons (Bestmann & Krakauer, 2015; Rogasch et al., 2009). It is elicited in the peripheral muscle following TMS of the M1 (Bestmann, 2012; Bestmann & Krakauer, 2015; Chen, 2004). Overall, the amplitude of the MEP is a measure of the excitability of the corticospinal pathway and, thus, a larger MEP following motor training indicates increased corticospinal excitability (Cirillo et al., 2010; Muellbacher et al., 2001; Siddique et al., 2020). Previous studies have shown that strength training and motor skill training, such as ballistic motor training and externally-paced strength training, may share similar corticospinal responses (Leung et al., 2015a, 2015b, 2017; Mason et al., 2019).

In line with the cross-activation hypothesis, previous TMS studies revealed that unilateral ballistic motor training facilitated MEP size in the trained (contralateral) and untrained (ipsilateral) M1 (Carroll et al., 2008; Perez et al., 2007). In contrast, other studies demonstrated decreased MEP amplitude in the untrained hand following rapid finger movements (Bonato et al.,1996; Duque et al., 2008). The magnitude of corticospinal excitability is predicted to vary with the type of motor task (Kidgell et al., 2017b; Leung et al., 2018; Perez et al., 2007; Poh et al., 2013), the availability of visual feedback and the timing of corticospinal excitability assessment (Perez et al., 2007; Poh et al., 2013). For instance, Teo et al. (2012) observed that a maximal finger flexion-extension movement resulted in a transient increase in first dorsal interosseus (FDI) MEP amplitude followed by a period of depressed corticospinal excitability for up to 6-8 minutes. Furthermore, Giesebrecht et al. (2011) showed an increase in corticospinal excitability immediately after a 10-second maximal voluntary contraction (MVC) of the FDI muscle. However, after 1 minute of MVC, the evoked potentials showed depression for approximately 10 minutes. A number of recent studies have examined the influence of age on corticospinal excitability following motor training (Cirillo et al., 2010; Berghuis et al., 2017; Dickins et al., 2015; Hinder et al., 2011, 2013b; Reissig et al., 2015; Rozand et al., 2019). It has been shown that ballistic motor training elicited bilateral increases in corticospinal excitability in young adults (Cirillo et al., 2010; Hinder et al., 2011; Lee et al., 2010; Reissig et al., 2015). However, corticospinal excitability responses to motor training were variable and less well established in older adults (Cirillo et al., 2010; Reissig et al., 2015; Rogasch et al., 2009).

In addition to assessment of M1 excitability and its descending pathways through single-pulse TMS, paired-pulse TMS can be used to study M1 intracortical modulatory mechanisms (Neva et al., 2017; Singh et al., 2014; Smith et al., 2014; Valero-Cabre et al., 2017). Paired-pulse TMS protocol consists of a conditioning stimulus followed by a test stimulus separated by an interstimulus interval (ISI) (Valero-Cabre et al., 2017). It can reveal different intracortical modulatory mechanisms depending on the ISI between the conditioning and the test TMS stimulus (Hallett, 2000; Oliveri et al., 2000). For instance, the MEP evoked by suprathreshold test stimulus at ISI of 1-6ms after subthreshold conditioning stimulus is suppressed compared with the MEP evoked by single-pulse stimuli at the same intensity. This phenomenon is referred to as short-interval intracortical inhibition (SICI) which is the ratio of paired-pulse MEP amplitude to single-pulse MEP amplitude (Kujirai et al., 1993). It has been assumed that the $GABA_A$-mediated intracortical inhibitory circuits are involved in the inhibition produced by a subthreshold cortical stimulation (Petersen et al., 2010).

Training-related SICI changes in young and older adults are inconsistent, with reports of reduced SICI in young adults following ballistic thumb movements (Rosenkranz et al., 2007), increased SICI ratio in both age groups following ballistic finger movements (Hinder et al., 2011), unchanged SICI after training across both age groups (Cirillo et al., 2010; Rogasch et al., 2009) or increased SICI in older adults following ballistic movements of both index fingers (Hinder et al., 2013a). In the absence of training, other studies have also reported discrepant findings, with reports of age-related decrease in SICI (Peinemann et al., 2001), no age-related changes in SICI (Oliviero et al., 2006; Smith et al., 2009) or age-related increase in SICI (Kossev et al., 2002; McGinley et al., 2010), suggesting that the effect of age on SICI is complex. Although SICI is a complex measure, a recent meta-analysis showed that following both acute and chronic unilateral motor practice, that SICI was reduced in the ipsilateral motor cortex (Manca et al., 2019). At a minimum, this suggests that unilateral motor training affects the syntactic efficacy of GABAAergic receptors of neurons that form cortico-cortical networks within the ipsilateral M1. The functional significance of this reduced SICI, is that it releases corticospinal neurons from inhibition, improving the activation off the motoneuron pool and likely modulates the change in motor function of the untrained limb (Frazer et al., 2018).

1.3 Possible contributions to changes in corticospinal excitability

Aging is associated with various functional changes in cortical motor networks including motor function (Seidler et al., 2010; Ward, 2006; Ward et al., 2008). Several lines of evidence have shown increasing motor task-related activity in a wider brain region in older adults compared to younger counterparts (Walker et al., 2020; Ward, 2006). It has been suggested that such greater activation in diffuse brain regions may indicate a reduced ability of the brain to modulate a specific neural activity (Bernard & Seidler, 2012; Inuggi et al., 2011; Langan, et al., 2010). It may also indicate a compensatory mechanism, whereby wider networks of brain regions are recruited in an attempt to maintain motor functions (Goble et al., 2010; Reissig et al., 2015; Ward, 2006). Although older adults exhibited exaggerated activity of motor cortices (i.e., greater degree of mirror activity), Hinder et al. (2011) showed no correlation between extent of mirror activity and degree of cross- transfer, suggesting that the increased motor overflow in older adults may not aid in the cross-transfer.

Furthermore, evidence from the previous studies suggests that aging is associated with reduced ability of M1 to reorganize following motor training that may limit motor performance improvements (Sawaki, et al., 2003; Rogasch et al., 2009). Although, there is limited information on the association between corticospinal excitability and motor performance improvements in older adults, previous studies have shown that training-induced-facilitated MEP amplitude is associated with improved motor performance in young adults (Garry et al., 2004; Muellbacher et al., 2001; Ziemann et al., 2001). However, other studies showed no significant association between MEP amplitude and improvements in motor performance in both age groups (Cirillo et al., 2010; Rogasch et al., 2009), suggesting that the corticospinal excitability changes could be mediated by factors other than the extent of motor training.

Substantial evidence indicates structural and functional asymmetries in cortical organization that might contribute to asymmetries in hand dominance (Guye et al., 2003; Hammond, 2002). Studies in right-handed young adults have shown greater practice-related MEP facilitation in the left than in the right M1, suggesting a greater ability of dominant M1 to reorganize with practice compared to the non-dominant M1 (Garry et al., 2004; Hammond & Vallence, 2006). Cirillo et al. (2010) showed no difference in use-dependent corticospinal plasticity between young and older subjects following ballistic abduction movements of the thumb. Hemispheric asymmetries are affected by various conditions including aging (Dolcos et al., 2002). In accordance with the model of hemispheric asymmetry reduction in older adults, recent studies have shown that asymmetries in motor lateralization are reduced during aging (Paizis et al., 2014; Przybyla et al., 2011).

There is now an emerging area of research that has used TMS to probe the corticospinal responses to ballistic motor training and the effect of motor training on the cross-transfer of motor skills in young and older adults. However, the body of evidence is largely equivocal and, therefore, a systematic review with meta-analysis will serve to clarify the present circumstances regarding the corticospinal responses to ballistic motor training in young and older adults. Specifically, conducting a meta-analysis on this topic enables the findings from related studies to be collated resulting in a pooled outcome that has a higher statistical power than any single one of the individual studies. Thus, a systematic review with meta-analysis is needed to determine how ballistic motor training affects TMS indicators of corticospinal plasticity in young and older adults. Furthermore, determining the corticospinal responses and cross-transfer of motor skills will have implications for rehabilitation programs, whereby older adults have pathology to a single limb. In addition, unilateral motor training provides a beneficial rehabilitation model for a number of unilateral injuries or disorders; including, but not limited to, limb immobilization, neurological disease, such as stroke and multiple sclerosis, and musculoskeletal pathology such as unilateral knee osteoarthritis (Green and Gabriel, 2018). In addition, there is a consensus that that the effects of unilateral motor practice are likely driven by neuroplasticity in the primary and supplementary motor brain regions (Manca et al., 2021). Therefore, the present systematic review examined the hypothesis that ballistic motor practice differentially modulates corticospinal excitability and inhibition (a marker for neuroplasticity of the motor cortex) in young and older adults. The specific aim of this systematic review and meta-analysis was to determine the corticospinal responses and the magnitude of cross- transfer of ballistic motor performance following ballistic motor training in young and older adults.

2 Methods

The present systematic review and meta-analysis were conducted in conformity with the latest Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021).

2.1 Eligibility criteria

Studies were eligible for inclusion if they met the following criteria: (I) studies of healthy humans that compare young adults with older adults or an untrained control group; (II) only studies involving ballistic motor training; (III) those that applied TMS to the M1 to quantify changes in ipsilateral and contralateral corticospinal responses; and (IV) a paper must have been published in a peer-reviewed journal (no restriction on the year of publication). The following exclusion criteria were established: (I) samples with diseased population groups; (II) those published in non-English language; and (III) conference proceedings, conference abstracts, review articles, books and unpublished studies.

2.2 Information sources

The following electronic databases were searched to identify relevant studies: PubMed, Science Direct, Cochrane Library and Google Scholar. Each database was searched from inception up to

20 November 2020. Additionally, all reference lists of studies included in the systematic review were examined for further relevant papers. Figure 1 summarizes the flow of records through the systematic review process.

2.3 Search strategy

Databases were searched using a combination of keywords or Medical Subject Headings (MeSH) and their synonyms. The following key search terms were used with the limits English language and humans: “ballistic movement”, “transcranial magnetic stimulation” and “motor cortex” (Table 1).

2.4 Selection process

All retrieved studies were exported to Endnote program (version X8.1; Thompson Reuters). One of the authors (GGW) screened all returned articles to remove duplicates and those that were clearly non-relevant papers to the present meta-analysis. Then, two authors (GGW and DJK) screened the abstracts and full text of the remaining articles. Any discrepancies were discussed and agreement reached among the assessors in all cases.

2.5 Data collection process and data items

Data from included studies were extracted by two review authors (GGW and DJK) using a standardized form in Microsoft Excel. In addition, data extraction was checked for accuracy. Data on the study design, sample size, participant characteristics (age, sex) and interventions were extracted from the available text. Moreover, information about the following outcome measures were extracted: motor performance, cross-transfer (motor performance gain in the untrained hand as a percentage of motor performance gain in the trained hand) (Green and Gabriel, 2018; Hinder et al., 2011), MEP amplitude (peak-to-peak waveform and reported either as a percentage of M-wave amplitude, arbitrary units from a recruitment curve, or raw amplitude) (Alibazi et al., 2021; Siddique et al., 2020), SICI (the ratio of the test stimulus and conditioning stimulus) (Kujirai et al., 1993), and surface electromyogram (sEMG) amplitude. Where available, the pre-training, mid-training and post-training data (mean and standard deviation [SD]) of the outcome measures for all groups were extracted. When the results were presented in figures, the data were extracted from the figures using WebPlot Digitizer software (Rohatgi, 2020).

2.6 Study risk of bias assessment

The quality of included studies was assessed by two authors (GGW and DJK) using a modified version of the Downs and Black checklist (Downs & Black, 1998) (Table 2). Sixteen items (1, 2, 3, 5, 6, 7, 10, 11, 12, 14, 16,18 ,20, 21, 25 & 26) of the Downs and Black checklist were used as not all 27 items were relevant to the present systematic review and meta-analysis. Modified versions of this checklist have been used in the work of others (Alibazi et al., 2021; Maniar et al., 2016). The Cochrane Collaboration Risk of Bias Tool (Higgins and Green, 2011) was used to assess the risk of bias in included studies (Figure 2). The risk of bias was categorized as ‘low risk’, ‘high risk’ or ‘unclear risk’ of bias across the seven domains namely: sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other sources of bias. Any discrepancies between review authors regarding the risk of bias assessment were resolved by discussion.

2.7 Statistical analysis

The mid-training (150 ballistic movements) and post-training (300 ballistic movements) data of the young, older and untrained control groups from included studies were used for the following outcome variables: motor performance, MEP amplitude, SICI and EMG amplitude. Where mean ± SD were not reported, these data were calculated from standard error (SE), 95% confidence intervals (CI), P values, or t values. Furthermore, when the percentage change in motor performance gains was not reported, it was calculated as the difference between the mean change in motor performance and expressed as a percentage of the initial motor performance before training (Green and Gabriel, 2018; Manca et al., 2017).

Meta-analysis was performed using a random-effects model as it was assumed that the included studies were not all estimating the same intervention effect. The effect size would vary from study to study due to differences in the study population, researchers, methods or interventions (Borenstein et al., 2010). When the included studies measured the same outcome in a variety of ways, the standardized mean difference (SMD) with 95% CI was used to estimate the intervention effect. The SMD values of $0.2 \leq 0.49$, $0.5 \leq 0.79$ and ≥ 0.8 indicated small, medium and large effects, respectively (Cohen, 1988). However, the mean difference (MD) with 95% CI was used when outcome measurements in all studies were made on the same scale. Inverse variance was used as a statistical method to calculate SMD and MD.

The effect size was calculated for both the trained and untrained hand. To ensure independence of observations, the sample size was divided in half for studies involving ballistic motor training in both the left and right hands. For studies that compared young adults (experimental group) to untrained control group, the right hand of the control group was included as a control for the right experimental hand, and the left hand of the control group was included as a control for the left experimental hand. If only one hand of the control group was measured, it was included as the control for both hands of the experimental group.

Statistical heterogeneity between studies was identified by the inconsistency (I^2) statistic, where <25%, 25 -75% and >75% indicates low, moderate and high risk of heterogeneity, respectively (Higgins et al. 2003; Siddique et al., 2020). In case of I^2 value greater than 50%, a leave-one-out sensitivity analysis was performed to find out whether our results were influenced by a single study (Manca et al., 2017).

Statistical analysis was conducted using RevMan 5.3 software. Pearson's correlation (Pearson's r) was carried out using SPSS version 21 software to examine the association between the performance gain of the trained hand and the performance gain of the untrained hand. The statistical significance level was set at $P < 0.05$, and the meta-analysis results were displayed using forest plots.

In a situation where the reported data were insufficient (i.e., SD for cross-transfer), it was not possible to conduct meta-analysis and thus data were synthesized using best evidence synthesis. The level of evidence was categorized in agreement with previous systematic reviews (Alibazi et al., 2021; Maniar et al., 2016) as defined below:

- No evidence: no supportive findings in the literature,
- Conflicting evidence: inconsistent findings (< 75% of studies showing consistent results),
- 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 high quality and generally consistent findings (≥ 75% of studies showing consistent results).

Studies with a risk of bias assessment score of ≥70% and < 70% were considered as high-quality and low- quality studies, respectively (Alibazi et al., 2021; Maniar et al., 2016).

3 Results

3.1 Study selection

The PRISMA flow chart (Figure 1) shows the flow of records through the systematic review process. The initial search returned 4970 records from all sources. After duplicates were removed, the titles and abstracts of the remaining 4224 records were screened. Out of these, 4149 records were excluded for not meeting the eligibility criteria. Seventy-five full-text articles were assessed for eligibility, of which 66 were excluded for the reasons outlined in Figure 1. Additional search yielded one record, whereupon 10 studies were included in the final analysis.

3.2 Study characteristics

A total of 320 subjects (130 males & 190 females; 210 young & 110 older adults) were examined across the 10 included studies. In all included studies, participants were healthy young and older adults, within the age range of 18 - 82 years. A total of seven studies compared young adults to older adults (Cirillo et al., 2010; Dickins et al., 2015; Hinder et al., 2011, 2013a, 2013b; Reissig et al., 2015; Rogasch et al., 2009), while three studies compared young adults to an untrained control group (Carroll et al., 2008; Lee et al., 2010; Stockel et al., 2016).

The motor training used in the included studies were ballistic abduction movements of the index finger (Carroll et al., 2008; Hinder et al., 2011, 2013a, 2013b; Reissig et al., 2015; Stockel et al., 2016) and ballistic abduction movements of the thumb (Cirillo et al., 2010; Dickins et al., 2015; Rogasch et al., 2009). In two studies, participants were asked to perform ballistic movements of both index fingers (Hinder et al., 2013a) and both thumbs (Cirillo et al., 2010). Overall, the motor training in the included studies consisted of 300 ballistic movements (Carroll et al., 2008; Cirillo et al., 2010; Dickins et al., 2015; Hinder et al., 2011, 2013a, 2013b; Lee et al., 2010; Reissig et al., 2015; Rogasch et al., 2009) and 150 ballistic movements (Stockel et al., 2016). Motor performance testing consisted of 10 ballistic movements (Carroll et al., 2008; Hinder et al., 2011, 2013a, 2013b; Reissig et al., 2015; Rogasch et al., 2009) and 15 ballistic movements (Dickins et al., 2015) performed in the absence of feedback or encouragement. A detailed description of study characteristics is provided in Table 2. The list of studies included in the present meta-analysis is presented in Table 3.

3.3 Quality Assessment

The quality of the included studies was assessed using a modified version of the Downs and Black checklist (Table 2). This checklist showed that the included studies ranged between 11 (65%) and 13 (76.5%) out of 17 points, with a mean (± SD) score of 12.2 ± 0.6. The scores of the six studies and three studies were 12 (70.6%) and 13 (76.5%) points, respectively. The remaining one study scored 11(65%) points. The Cochrane risk of bias tool showed that the majority of the included studies did not provide adequate details on random sequence generation, allocation concealment and blinding of outcome assessment. Thus, the studies were categorized as having “unclear risk of bias” for these domains (Figure 2). In addition, half of the included studies were found to be from the same laboratory group.

3.4 Motor performance

The mid-training and post-training motor performance data were extracted from the studies that compared motor performance of young adults with older adults following ballistic motor training. The pooled data indicated that, during mid-training, the young group exhibited a moderate increase in motor performance of the trained hand (SMD 0.62, 95% CI 0.29 to 0.95, $P < 0.001$, 6 studies, $n = 158$), and untrained hand (SMD 0.60, 95% CI 0.17 to 1.04, $P = 0.007$, 3 studies, $n = 86$), with low heterogeneity ($I^2 = 0\%$) across these studies. Upon completion of training (i.e., during post-training), the young group exhibited a large increase in motor performance compared to the older group for the trained hand (SMD 0.81, 95% CI 0.52 to 1.11, $P < 0.001$, 7 studies, $n = 198$, $I^2 = 0\%$), and for the untrained hand (SMD 0.96, 95% CI 0.54 to 1.38, $P < 0.001$, 4 studies, $n = 126$, $I^2 = 20\%$; Figure 3).

Furthermore, the mid-training and post-training motor performance data were extracted from the studies that compared motor performance of young adults with an untrained control group following ballistic motor training. The meta-analysis relating to the studies focused on the mid-training motor performance revealed a large increase in motor performance of the trained hand (MD 0.93, 95% CI 0.55 to 1.31, $P < 0.001$, 3 studies, $n = 95$), with a substantial level of heterogeneity ($I^2 = 84\%$). Thus, a study by Lee et al. (2010) was removed, which resulted in low heterogeneity ($I^2 = 38\%$) and a large increase in motor performance (MD 1.11, 95% CI 0.88 to 1.35, $P < 0.001$, 2 studies, $n = 66$). The details are presented in Figure 4.

3.4.1 Correlation between performance gains in the trained and untrained hands

Pearson's correlational analysis was performed to determine linear correlations between the performance gains in the trained and untrained hands following ballistic motor training (i.e., during post-training). For the young group, there was a significant correlation between the percentage of performance gain in the trained hand and the percentage of performance gain in the untrained hand (*r* = 0.981, p = 0.001; n = 6; Figure 5). For the older group, this relationship was not evaluated due to the small number of included studies within this analysis.

3.4.2 Cross-transfer of ballistic motor performance

As shown in Figure 3, the young group exhibited large performance gains compared to the older group in the untrained hand as a result of cross-transfer. With regard to magnitude of cross-transfer, the reported data were insufficient for statistical data pooling and thus we performed a best evidence synthesis. The magnitude of cross-transfer was assessed in seven studies (four studies compared young adults with older group and the remaining three studies compared young group with an untrained control group), and there was strong evidence to suggest that young participants exhibited greater levels of cross-transfer than observed for the older group. Moreover, three studies reported that cross-transfer was greater for the young group with no changes in the control group, demonstrating strong evidence (Table 4).

3.5 Motor-evoked potential (MEP)

The mid-training and post-training MEP amplitude data of the target muscle were extracted from the studies that compared MEP amplitude of young adults with older adults following ballistic motor training. The pooled data indicated that ballistic motor training, irrespective of the time points (mid-training or post-training) and the hands (trained hand or untrained hand), did not result in any significant difference in the MEP amplitude of the target muscle ($P > 0.05$; Figure 6).

Furthermore, the mid-training and post-training MEP amplitude data were extracted from the studies that compared FDI MEP amplitude of young adults with an untrained control group following ballistic motor training. The meta-analysis relating to the studies focused on the mid-training revealed a large increase in FDI MEP amplitude of the trained hand (MD 8.62, 95% CI 5.84 to 11.40, $P < 0.001$, 2 studies, n = 47, $I^2 = 0\%$) and the untrained hand (MD 5.84, 95% CI 3.16 to 8.52, $P < 0.001$, 2 studies, n = 47, $I^2 = 0\%$). Upon completion of training, the pooled data indicated a further increase in FDI MEP amplitude of the trained hand (MD 9.50, 95% CI 6.66 to 12.34, $P < 0.001$, 2 studies, n = 47, $I^2 = 0\%$) and the untrained hand (MD 6.20, 95% CI 2.34 to 10.06, P = 0.002, 2 studies, n = 47, $I^2 = 0\%$; Figure 7).

3.6 Short-interval intracortical inhibition (SICI)

The mid-training and post-training SICI data were extracted from the studies that compared SICI of young adults with older adults following ballistic motor training. The pooled data indicated that ballistic motor training, irrespective of the time points (mid-training or post-training) and the hands (trained hand or untrained hand), did not result in any significant difference in SICI between young and older subjects [mid-training (trained hand: MD -0.03, 95% CI -0.43 to 0.37, P = 0.89, 4 studies, n = 77, $I^2 = 53\%$; untrained hand: MD -0.10, 95% CI -0.27 to 0.08, P = 0.28, 2 studies, n = 60, $I^2 = 0\%$), post-training (trained hand: MD -0.10, 95% CI -0.39 to 0.20, P = 0.52, 4 studies, n = 77, $I^2 = 26\%$; untrained hand: MD -0.10, 95% CI -0.31 to 0.11, P = 0.33, 2 studies, n = 60, $I^2 = 0\%$)]. However, the mid-training result for the trained hand was highly influenced by Hinder et al. (2013a). Therefore, this study was removed which resulted in low heterogeneity (MD 0,15, 95% CI -0.15 to 0.44, P = 0.33, 3 studies, n = 68, $I^2 = 0\%$; $I^2 = 0\%$; Figure 8).

3.7 Electromyographic (EMG) recordings

The mid-training and post-training EMG data of the trained hand were extracted from the studies that compared EMG activity of the target muscles (i.e., the muscle that was primarily involved in the movement) between young and older adults following ballistic motor training. The pooled data indicated that ballistic motor training produced a moderate, but not significant, increase in EMG activity of the trained hand at mid-training (SMD 0.63, 95% CI -0.19 to 1.44, P = 0.13, 4 studies, n = 75, I^2 = 60%) and post-training (SMD 0.5, 95% CI -0.42 to 1.43, P = 0.29, 4 studies, n = 75, I^2 = 69%) in young adults compared to older adults. However, the result was highly influenced by Rogasch et al. (2009). Therefore, this study was removed which resulted in low heterogeneity and small effect size for the mid-training (SMD 0.18, 95% CI -0.4 to 0.75, P = 0.55, 3 studies, n = 48, I^2 = 0%) and post-training (SMD 0.02, 95% CI -0.56 to 0.6, P = 0.94, 3 studies, n = 48, I^2 = 0%; Figure 9).

The mid-training and post-training mirror activity data were extracted from the studies that compared the level of mirror activity between young and older adults following ballistic motor training. The pooled data indicated that the level of mirror activity was significantly greater for the older adults than for the young adults at the post-training (right FDI: MD 0.04, 95% CI 0.01 to 0.08, P = 0.007, 2 studies, n = 48, I^2 = 0%; left FDI: MD 0.07, 95% CI 0.03 to 0.11, P = 0.002, 2 studies, n = 48, I^2 = 0%; Figure 10).

4) Discussion

The present systematic review and meta-analysis aimed to determine the corticospinal responses and cross-transfer of ballistic motor performance following ballistic motor training in young and older adults. In this meta-analysis and best evidence synthesis, we investigated whether ballistic motor practice differentially modulates corticospinal excitability and inhibition in young and older adults. Overall, this meta-analysis revealed that: (i) young adults exhibited a large increase in motor performance of the trained and untrained hand; (ii) young adults exhibited greater cross-transfer than older adults; (iii) ballistic motor training did not result in any significant difference in MEP amplitude, SICI and sEMG activity between young and older adults; (iv) there was a large effect of increased MEP amplitude of the trained and untrained hand in young adults compared to an untrained control group.

4.1 Age-related differences in motor performance and cross-transfer

The present meta-analysis revealed that ballistic motor training leads to a large increase in motor performance of the trained and untrained hands in young adults compared to their older counterparts or untrained control group. The data showed a greater effect on motor performance at post-training than at mid-training for both the trained and the untrained hand. In a similar manner, previous studies have reported that several repetitive movements for less than 30 minutes can lead to large performance improvements (Carroll et al., 2008; Cirillo et al., 2010, Muellbacher et al., 2002; Rogasch et al., 2009). In fact, aging is known to be associated with various changes in the peripheral and central nervous system (CNS) as well as the neuromuscular system. These changes could influence motor performance improvements during ballistic motor training (Seidler et al., 2010; Vandervoort 2002).

The best evidence synthesis revealed strong evidence to suggest that young participants exhibited greater cross-transfer than the older group. Similarly, best evidence synthesis demonstrated strong evidence that ballistic motor training caused a strong cross-transfer of motor performance to the opposite (untrained) hand in young adults, with no changes for an untrained control group. Previous works have shown that performance improvement was accompanied by a bilateral increase in the excitability of the corticomotor pathways. This suggests that the ipsilateral motor cortex (untrained hemisphere) played a critical role in the performance improvement of the untrained hand (Hinder et al., 2011; Lee et al., 2010). Although this meta-analysis failed to identify a difference in corticospinal excitability between young and older adults following ballistic motor training, cross-transfer is not altered to a similar extent in young and older adults. In line with this finding, previous studies reported a poor cross-transfer of performance gains in older adults (Hinder et al., 2011; Parikh & Cole, 2013). This finding may suggest altered cross-transfer process between the two hemispheres in older adults as healthy older adults have a high capability to learn new motor skills (Cirillo et al., 2010; Hinder et al., 2011; Parikh & Cole, 2012, 2013; Voelcker-Rehage, 2008; Wu & Hallett, 2005). Overall, the transfer of information between the hemispheres could be impaired by age-related changes in the functional connectivity between the two motor cortices in older adults (Fling et al., 2012; Sale & Semmler, 2005; Seidler, 2007; Ward & Frackowiak, 2003).

Similar to a previous study (Hinder et al., 2013b), the present meta-analysis showed a strong positive correlation between the performance gains of the trained and untrained hand in young adults ($r^2 = 0.963$, $p = 0.001$). This finding confirms that the extent of the opposite (untrained) hand performance gains largely depends on those obtained ipsilaterally. Thus, the extent of performance improvements in the trained hand could predict the degree of transfer to the untrained hand in young adults (Hinder et al., 2013b).

The changes in muscle activation during ballistic motor training could be assessed by sEMG records (EMG timing and amplitudes) (Carroll et al., 2008). Previous studies have shown that greater sEMG activity was associated with increased task performance (Carroll et al., 2008; Hinder et al., 2013a; Rogasch et al., 2009). Furthermore, it has been suggested that various neuromuscular changes, including a decrease in type II muscle fiber area, could influence sEMG activity in older adults (Klein et al., 2003). However, there are inconsistences in the literature with regard to the age-related differences in sEMG amplitude during ballistic motor training. The present meta-analysis demonstrated no age-related differences in sEMG amplitude of the task-specific muscle in the trained hand between young and older adults following ballistic motor training. However, older adults exhibited a greater degree of mirror activity than young adults following ballistic motor training. This might be due to increased motor overflow in older adults (Bodwell et al., 2003; Hinder et al., 2011, 2013a; Hoy et al., 2004).

4.2 Age-related differences in MEP excitability

This meta-analysis found a large increase in target muscle (FDI) MEP amplitude of the trained and untrained hand in young adults compared to an untrained control group. The results showed a greater effect on MEP amplitude at post-training than at mid-training for both the trained and the untrained hand. However, our meta-analysis failed to identify a difference in training-induced MEP facilitation of the target muscle following ballistic motor training between young and older adults. Similarly, previous studies showed no age-related difference in corticospinal excitability following ballistic motor training (Cirillo et al., 2010; Reissig et al., 2015). Furthermore, it has been suggested that older adults have intact learning capabilities and ballistic skill acquisition is not affected by age (Voelcker-Rehage, 2008). However, these findings are not consistent as other TMS studies have shown decreasing use-dependent plasticity in older adults (Rogasch et al., 2009; Sawaki et al., 2003; Tecchio et al., 2008). This meta-analysis confirms that, although greater performance improvements occurred in young adults than in older adults, there was no significant difference in corticospinal excitability across the two age groups. It has recently been proposed that greater activation in diffuse brain regions of older adults may weaken the relationship between corticospinal excitability and motor skill acquisition (Berghuis et al., 2017). Furthermore, changes in corticospinal excitability could be mediated by various factors such as focus of attention (McNevin et al., 2000), difference in movement kinematic strategies (Rogasch et al., 2009), degree of hand use (Rosenkranz et al., 2007b), emotional status of the participants (Tormos et al., 1997), genetic variation (Ridding & Ziemann, 2010) and level of physical activity (Cirillo et al., 2010).

4.3 Age-related differences in short-interval intracortical inhibition

Practice-dependent plasticity of M1 could be regulated by GABA-mediated cortical inhibition (Ziemann et al., 2001) and modulation of SICI plays an important role during the performance of skilled hand movement (Stinear & Byblow, 2003; Zoghi et al., 2003). Thus, reductions in SICI increases use-dependent plasticity of the M1 (Ziemann et al., 2001). There are inconsistences in the literature with regard to the age-related SICI differences (Cirillo et al., 2010; Hinder et al., 2011, 2013a; McGinley et al., 2010; Peinemann et al., 2001; Rosenkranz et al., 2007; Smith et al., 2009). Although previous TMS studies demonstrated inconsistencies in training-related SICI changes, the findings of the present meta-analysis showed that ballistic motor training, irrespective of the time points (mid-training or post-training) and the hands (trained hand or untrained hand), did not result in any significant difference in SICI between young and older subjects. It has been suggested that selective target muscle activation may contribute to the modulation of SICI (Zoghi et al., 2003). The current finding of no age-related differences in SICI following ballistic motor training confirms that selective activation of the target muscle is needed for a more demanding task (Liepert et al., 1998; Zoghi et al., 2003).

4.4 Limitations and recommendations for further research

There are a number of limitations that should be considered when interpreting the findings of this systematic review and meta-analysis. The following are the limitations of this review: (i) only studies comparing young adults with older adults or an untrained control group were available to be included in the present meta-analysis. Thus, there is a need for further studies comparing older adults with an untrained control group; (ii) participants in one study (Hinder et al., 2013b) performed a bilateral ballistic motor training. The neural responses to bilateral ballistic motor training differ from the neural responses to unilateral ballistic tasks, and this may introduce bias to our findings. However, it is unlikely that there is a possibility of bias in the effect estimates as heterogeneity of results between the studies was low; (iii) although this meta-analysis provided new insight of the corticospinal responses and cross-transfer of ballistic motor performance following ballistic motor training, analysis results of young adults versus control group and mirror activity data must be considered with caution due to the low number of studies included within this analysis. However, the quality of the included studies is high, and most outcome variables displayed a low level of heterogeneity. Studies that have examined intracortical facilitation and long-interval intracortical inhibition were not available to be included in this meta-analysis. This indicates that there is a need for further research using more robust TMS techniques to comprehensively explore the corticospinal responses to ballistic motor training.

5) Conclusions

This systematic review and meta-analysis confirm the existence of cross-transfer of a ballistic motor skill following ballistic motor training in healthy young and older adults. The best evidence synthesis showed that the young participants exhibited greater cross-transfer than the older group. Furthermore, the findings demonstrated that ballistic motor training did not result in any significant age-related differences in corticospinal excitability, SICI and EMG activity. Overall, there is a need for future research to examine other components of corticospinal excitability, not only in healthy subjects but also in diseased populations.

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Tables

Table 1: Search strategy used in each database.

Source	**Search strategy**

PubMed	1. exercise OR "ballistic movement*" OR "ballistic exercise" OR "ballistic training" OR "motor training" OR "motor learning" OR "motor skills"[Mesh] AND ((humans [Filter]) AND (english[Filter])) 2. "Motor cortex" OR M1 OR "ipsilateral cortex" OR "primary motor cortex" OR "Motor Cortex"[Mesh] AND ((humans [Filter]) AND (english[Filter])) 3. "Transcranial magnetic stimulation" OR TMS OR "Transcranial stimulation" OR "motor evoked potential*" OR "corticospinal excitability" OR "intracortical inhibition" OR "intracortical facilitation" OR "Transcranial Magnetic Stimulation"[Mesh] AND ((humans [Filter]) AND (english[Filter])) 4. #1 AND #2 AND #3
Science Direct	(Exercise OR "Ballistic movement" OR "Ballistic exercise" OR "Ballistic motor training") AND (“Motor cortex") AND ("Transcranial magnetic stimulation" OR "motor evoked potential" OR “intracortical inhibition” OR "intracortical facilitation")
Cochrane Library	1. (Exercise OR “Ballistic movement*” OR “Ballistic exercise” OR “Ballistic training” OR “Motor training” OR “Motor learning”):ti,ab,kw 2. MeSH descriptor: [Motor Skills] explode all trees 3. #1 OR #2 4. (“Motor cortex” OR M1 OR “ipsilateral cortex” OR “primary motor cortex”):ti,ab,kw 5. MeSH descriptor: [Motor Cortex] explode all trees 6. #4 OR #5 7. (“Transcranial magnetic stimulation” OR TMS OR “Transcranial stimulation” OR “motor evoked potential*” OR “corticospinal excitability” OR “intracortical inhibition” OR “intracortical facilitation”):ti,ab,kw 8. MeSH descriptor: [Transcranial Magnetic Stimulation] explode all trees 9. #7 OR #8 10. #3 AND #6 AND #9
Google scholar	Articles with all of the following words were searched using the advanced search option: ballistic motor training, motor cortex, transcranial magnetic stimulation.

Table 2: Study characteristics

Study	**Training**	**Participant characteristics**	**Sampling**	**Key DV**	**Key measures**	**Results**	**D & B score /17**

Carroll et al. (2008)	Ballistic abduction movements of the right index finger,300 contractions	-18 healthy young (18–39 years, 7 M & 11F) -Trained (n = 9[6RH, 2LH & 1amb]); Control (n = 9RH)	Random	Corticospinal excitability, motor performance	Task performance, MEP amplitude	↑Performance 111%, ↑MEP amplitude 13.5%,	12
Cirillo et al. (2010)	Ballistic thumb abduction movement of the hands (each hand was tested separately by at least 2 weeks gap), 300 contractions	- 26 healthy young and old - Young (n = 12RH, 7F & 5M, 18-27 years); Older (n =14RH, 7F &7M, 63-75years)	Not stated	Corticospinal excitability, motor performance	Task performance, MEP amplitude, M wave, EMG activity	↑Performance 142% in older & 208% in young, ↑MEP amplitude 13.3% in older & 37.3% in young, No change in M wave and EMG	13
Dickins et al. (2015)	Ballistic abduction movement of the right thumb, 300 contractions	- 40 healthy young and old - Young (n = 20 [19RH & 1amb.], 10F & 10M, 18-33 years); Older (n = 20RH, 10F &10M, 65-77 years)	Not stated	Corticospinal excitability, motor performance	Task performance, MEP amplitude,	↑Performance 28.2% in older & 63.3% in young, ↑ MEP amplitude 24.2% in older & 8.9% in young	12

Table 2 (continued)

Study	**Training**	**Participant characteristics**	**Sampling**	**Key DV**	**Key measures**	**Results**	**D & B score /17**

Hinder et al. (2011)	Ballistic abduction movements of the right index finger, 300 contractions	-30 healthy young and old - Young (n = 18RH, 13F & 5M, 18-32 years); Older (n =12RH, 8F &4M, 63-74 years)	Not stated	Corticospinal excitability, motor performance	Task performance, MEP amplitude, SICI, EMG	↑Performance 38% in older & 69% in young, ↑MEP amplitude 43.5% in older &3.5% in young, ↓SICI 19% in older & 25% in young, ↑EMG 19% in older & 19.5% in young	13
Hinder et al. 201(3a)	Bilateral ballistic abduction movements of the index fingers, 300 contractions	-18 healthy young and old - Young (n = 9RH, 19.4± 1.17 years, 6F & 3M); Older (n = 9RH, 66.3 ± 5.2years, 7F & 2M)	Not stated	Corticospinal excitability, motor performance	Task performance, MEP amplitude, SICI, EMG activity	↑Performance 21% in older & 66% in young), ↑EMG 13%, No change in MEP amplitude, ↓SICI in older group 39%	13

Table 2 (continued)

Study	**Training**	**Participant characteristics**	**Sampling**	**Key DV**	**Key measures**	**Results**	**D & B score/17**

Hinder et al. (2013b)	Ballistic abduction movements of the left index finger, 300 contractions	-30 healthy young and old - Young (n = 15RH, 18-27 years, 8F & 7M); Older (n = 15RH, 60-78years, 10F & 5M)	Not stated	Corticospinal excitability, motor performance	Task performance, MEP amplitude, SICI	↑Performance 22% in older & 50% in young, ↑MEP amplitude 38% in older & 23.5% in young, No change in SICI	12
Lee et al. (2010)	Ballistic abduction movements of the left index finger, 300 contractions	-29 healthy RH people (18–50 years, 25.8 ± 7.6 years, 19M & 10F) -Trained (n = 21); Control (n = 8)	Random	Corticospinal excitability, motor performance	Task performance, MEP amplitude	↑Performance 77.5%, ↑MEP amplitude 49%	12
Reissig et al. (2015)	Ballistic abduction movements of the right index finger, 300 contractions	-53 healthy people (51RH & 2LH) -Young (n = 27, 26.1 ± 5.3 years, 9M & 18F); Old (n = 26, 69.6 ± 5.6 years, 12M & 14F)	Not stated	Corticospinal excitability, motor performance	Task performance, MEP amplitude	↑Performance 30% in older & 59% in young, ↑MEP amplitude 27% in older & 64.5% in young	11

Table 2 (continued)

Study	**Training**	**Participant characteristics**	**Sampling**	**Key DV**	**Key measures**	**Results**	**D & B score/17**

Rogasch et al. (2009)	Ballistic abduction movement of the right thumb, 300 contractions	-28 healthy RH people -Young (n = 14, 18-24 years, 8M & 6F); Old (n = 14, 61-82 years, 8M & 6F)	Not stated	Corticospinal excitability, motor performance	Task performance, MEP amplitude, M wave amplitude,	↑Performance 124% in old & 177% in young, ↑MEP amplitude in young group 38%, No change in M wave amplitude	12
Stockel et al. (2016)	Ballistic abduction movements of the right index finger, 150 contractions	-48 healthy RH people -Trained (n = 36, 16M & 20F); - Control (n = 12, 25.9 ±7.3 years, 3M & 9F)	Random	Corticospinal excitability, motor performance	Task performance, MEP amplitude, SICI	↑Performance 68.6%, ↑MEP amplitude 19.5%, No change in SICI	12

amb ambidextrous, *D & B* Downs and Black Quality Assessment, *DV* dependent variable, *EMG* electromyography, *F* female, *LH* left handers, *M* male, *MEP* motor-evoked potential, *SICI* short-interval intracorical inhibition, *RH* right handers, ↑increase, ↓decrease

Table 3: Studies included in the meta-analysis

Author (year)	Title
Carroll et al. (2008)	Unilateral practice of a ballistic movement causes bilateral increases in performance and corticospinal excitability
Cirillo et al. (2010)	Hemispheric differences in use-dependent corticomotor plasticity in young and old adults
Dickins et al. (2015)	Intermanual transfer and bilateral cortical plasticity is maintained in older adults after skilled motor training with simple and complex tasks
Hinder et al. (2011)	Absence of cross-limb transfer of performance gains following ballistic motor practice in older adults
Hinder et al. (2013a)	Transfer of ballistic motor skill between bilateral and unilateral contexts in young and older adults: neural adaptations and behavioral implications
Hinder et al. (2013b)	Inter-limb transfer of ballistic motor skill following non-dominant limb training in young and older adults
Lee et al. (2010)	The ipsilateral motor cortex contributes to cross-limb transfer of performance gains after ballistic motor practice
Reissig et al. (2015)	Age-specific effects of mirror-muscle activity on cross-limb adaptations under mirror and non-mirror visual feedback conditions
Rogasch et al. (2009)	Corticomotor plasticity and learning of a ballistic thumb training task are diminished in older adults
Stockel et al. (2016)	Motor learning and cross-limb transfer rely upon distinct neural adaptation processes

Table 4: Best evidence synthesis data for cross-transfer assessed in young and old adults

Study	**Magnitude of cross-transfer assessment**	**Study quality (%)**
Dickins et al. 2015	61.7% for young adults, 43.6% for older adults	70.6
Hinder et al. 2011	75% for young adults, 11% for older adults	76.5
Hinder et al. 2013b	70.3% for young adults, 64.5% for older adults	70.6
Reissig et al. 2015	59.4% for young adults, 46.3% for older adults	64.7
Lee et al. 2010	66.7% for young adults*	70.6
Carroll et al. 2008	58.6% for young adults*	70.6
Stockel et al. 2016	59.3% for young adults*	70.6

*The studies compared young adults with an untrained control group

Figures

Figure 1: Flow chart of each stage of the study selection using the PRISMA 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: The mid-training (A) and post- training (B) motor performance following ballistic motor training in young adults compared to older participants. CI: confidence interval, IV: inverse variance, SD: standard deviation.

Figure 4: The mid-training (A) and post-training (B) motor performance following ballistic motor training in young adults (experimental group) compared to untrained control group. CI: confidence interval, IV: inverse variance, SD: standard deviation.

Figure 5: Performance gains for the trained and untrained hand following ballistic motor training, expressed as a percentage of pre-training motor performance in young (r = 0.981; p = 0.001, n = 6)

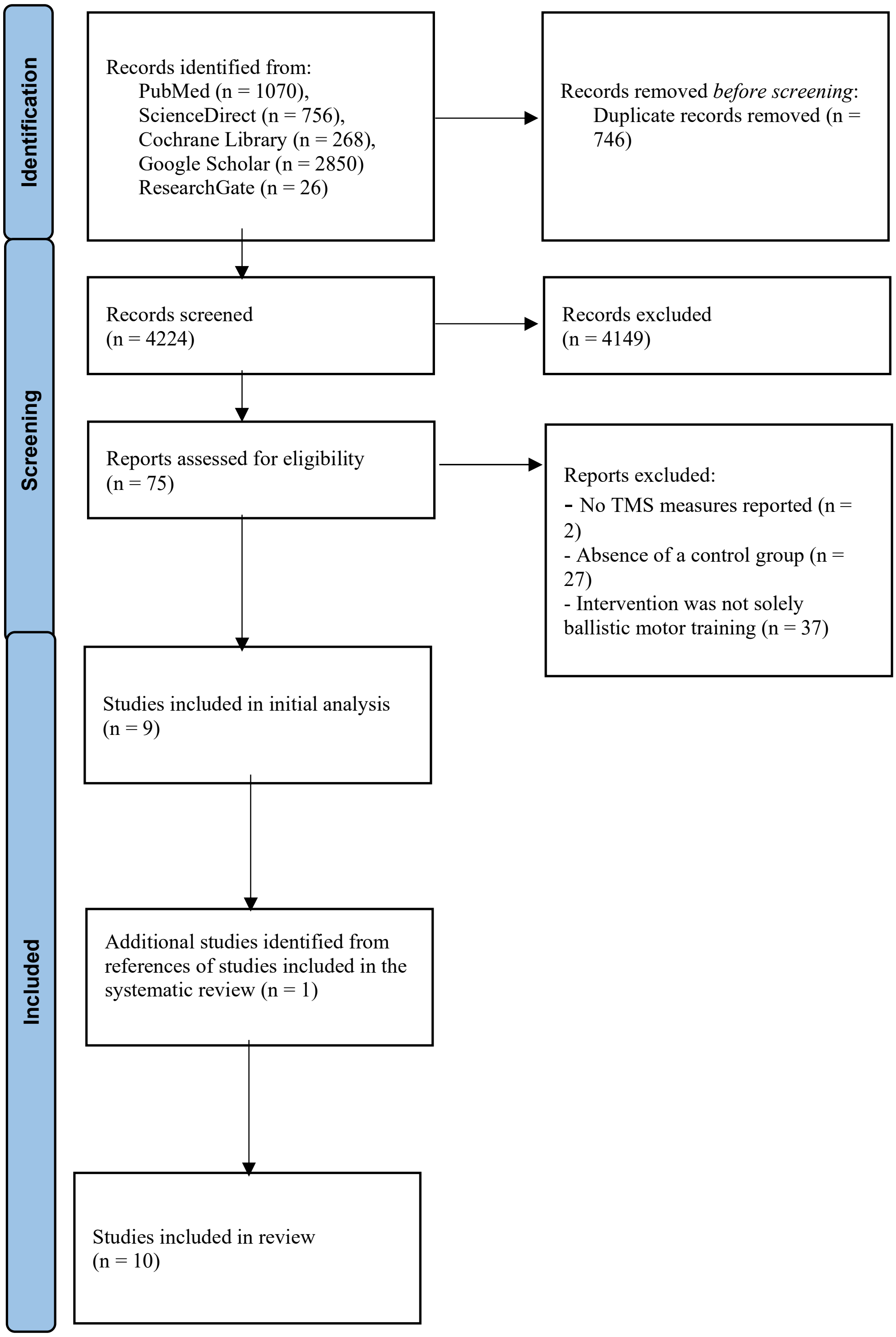
Figure 6: The mid-training (A) and post- training (B) target muscle MEP amplitude following ballistic motor training in young adults compared to older adults. CI: confidence interval, IV: inverse variance, SD: standard deviation.

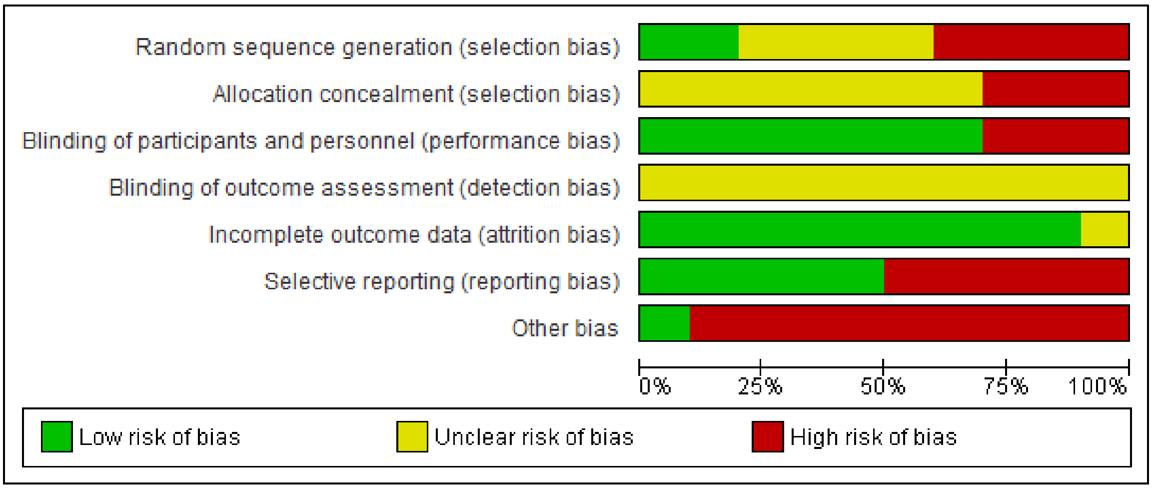
Figure 7: The mid-training (A) and post- training (B) first dorsal interosseus (FDI) MEP amplitude following ballistic motor training in young adults (experimental group) compared to untrained control group. CI: confidence interval, IV: inverse variance, SD: standard deviation

Figure 8: The mid-training (A) and post-training (B) SICI data following ballistic motor training in young adults compared to older participants. CI: confidence interval, IV: inverse variance, SD: standard deviation.

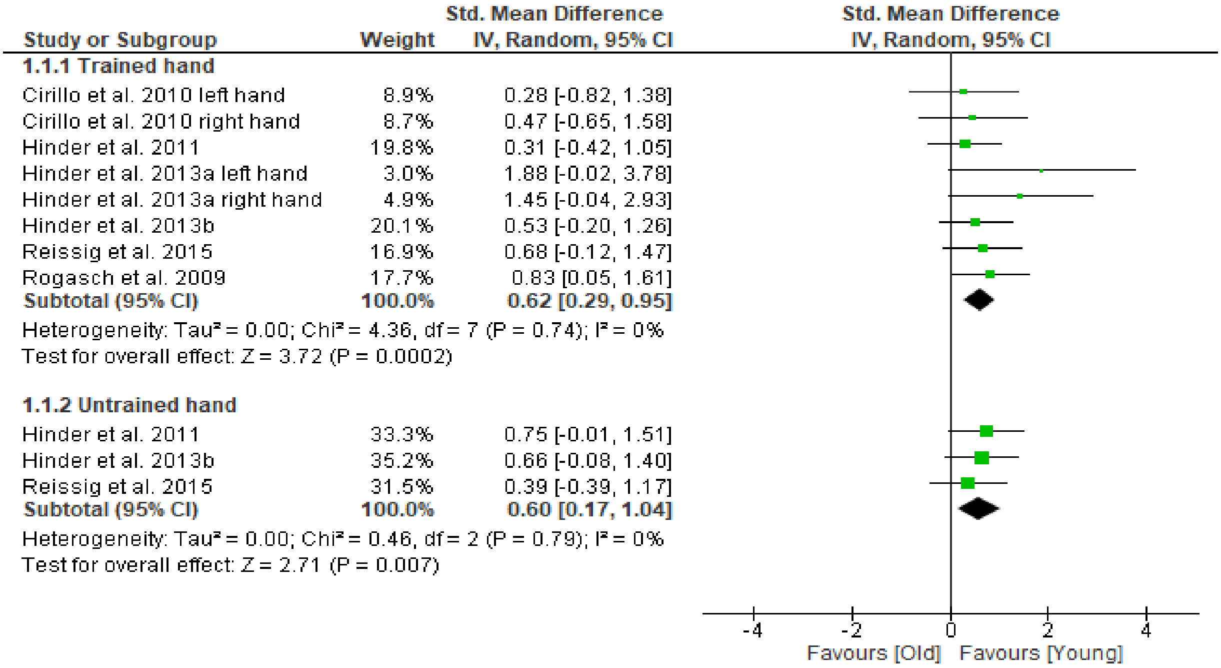
Figure 9: The mid-training (A) and post- training (B) EMG data following ballistic motor training in young adults compared to older participants. CI: confidence interval, IV: inverse variance, SD: standard deviation.

Figure 10: The mid-training (A) and post- training (B) mirror activity data following ballistic motor training in young adults compared to older participants. CI: confidence interval, IV: inverse variance, SD: standard deviation.


Identification
Screening
Included
Records identified from:
PubMed (n = 1070),
ScienceDirect (n = 756),
Cochrane Library (n = 268),
Google Scholar (n = 2850)
ResearchGate (n = 26)
Records removed before screening:
Duplicate records removed (n = 746)
Records screened (n = 4224)
Records excluded (n = 4149)
Reports assessed for eligibility (n = 75)
Reports excluded:
- No TMS measures reported (n = 2)
- Absence of a control group (n = 27)
- Intervention was not solely ballistic motor training (n = 37)
Studies included in initial analysis (n = 9)
Additional studies identified from references of studies included in the systematic review (n = 1)
Studies included in review (n = 10)

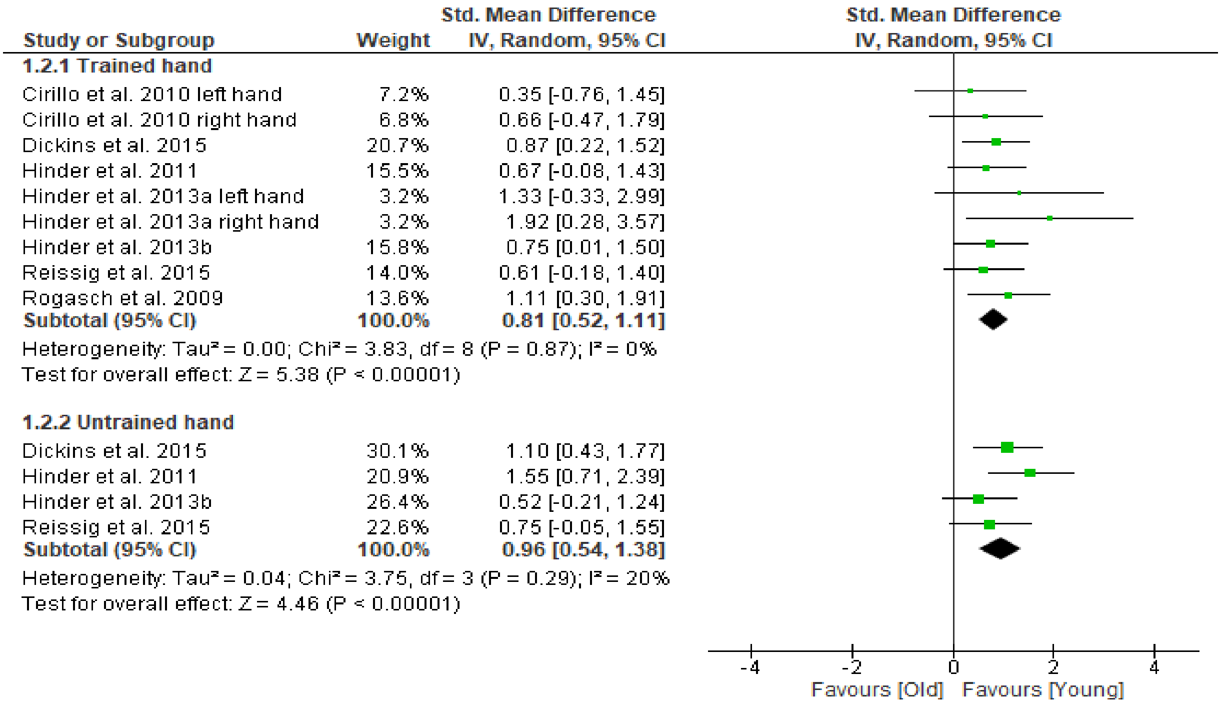

Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias)
Blinding of outcome assessment (detection bias)
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Other bias
0%
25%
50%
75%
100%
Low risk of bias
Unclear risk of bias
High risk of bias

A)



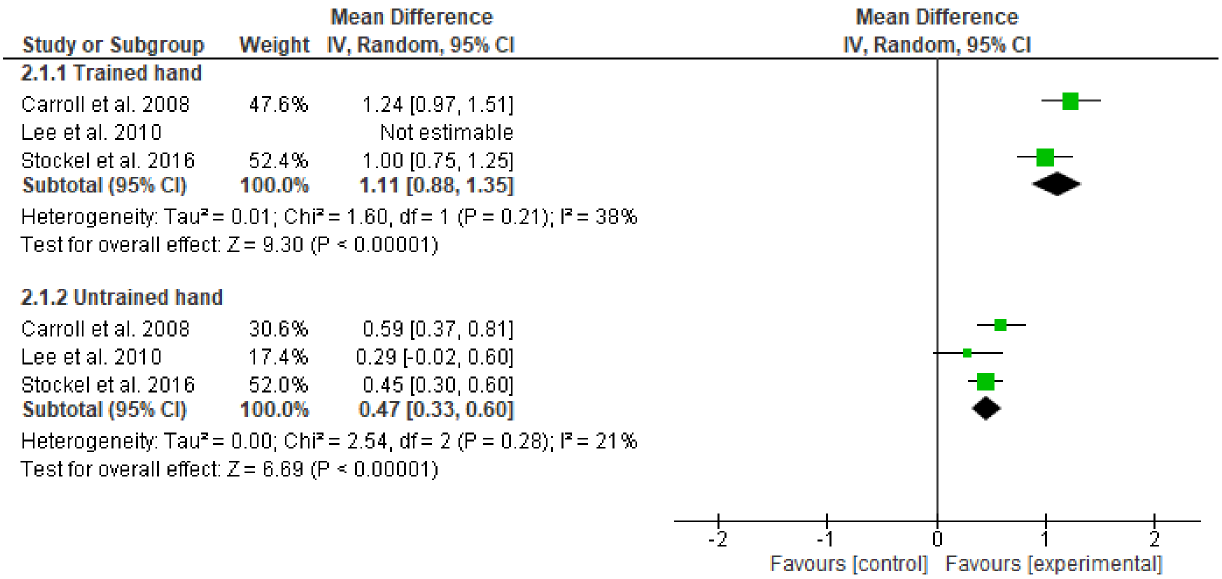
Study or Subgroup	Weight	Std. Mean Difference IV, Random, 95% CI
1.1.1 Trained hand		
Cirillo et al. 2010 left hand	8.9%	0.28 [-0.82, 1.38]
Cirillo et al. 2010 right hand	8.7%	0.47 [-0.65, 1.58]
Hinder et al. 2011	19.8%	0.31 [-0.42, 1.05]
Hinder et al. 2013a left hand	3.0%	1.88 [-0.02, 3.78]
Hinder et al. 2013a right hand	4.9%	1.45 [-0.04, 2.93]
Hinder et al. 2013b	20.1%	0.53 [-0.20, 1.26]
Reissig et al. 2015	16.9%	0.68 [-0.12, 1.47]
Rogasch et al. 2009	17.7%	0.83 [0.05, 1.61]
Subtotal (95% CI)	**100.0%**	**0.62 [0.29, 0.95]**
Heterogeneity: Tau² = 0.00; Chi² = 4.36, df = 7 (P = 0.74); I² = 0%		
Test for overall effect: Z = 3.72 (P = 0.0002)		
1.1.2 Untrained hand		
Hinder et al. 2011	33.3%	0.75 [-0.01, 1.51]
Hinder et al. 2013b	35.2%	0.66 [-0.08, 1.40]
Reissig et al. 2015	31.5%	0.39 [-0.39, 1.17]
Subtotal (95% CI)	**100.0%**	**0.60 [0.17, 1.04]**
Heterogeneity: Tau² = 0.00; Chi² = 0.46, df = 2 (P = 0.79); I² = 0%		
Test for overall effect: Z = 2.71 (P = 0.007)		

B)



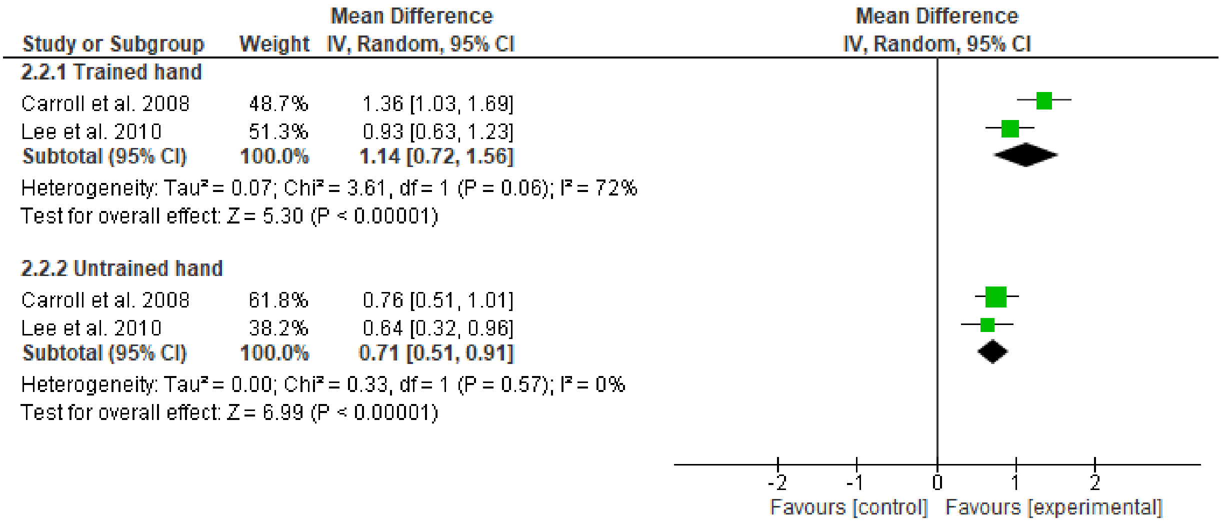
Study or Subgroup	Weight	Std. Mean Difference IV, Random, 95% CI
1.2.1 Trained hand		
Cirillo et al. 2010 left hand	7.2%	0.35 [-0.76, 1.45]
Cirillo et al. 2010 right hand	6.8%	0.66 [-0.47, 1.79]
Dickins et al. 2015	20.7%	0.87 [0.22, 1.52]
Hinder et al. 2011	15.5%	0.67 [-0.08, 1.43]
Hinder et al. 2013a left hand	3.2%	1.33 [-0.33, 2.99]
Hinder et al. 2013a right hand	3.2%	1.92 [0.28, 3.57]
Hinder et al. 2013b	15.8%	0.75 [0.01, 1.50]
Reissig et al. 2015	14.0%	0.61 [-0.18, 1.40]
Rogasch et al. 2009	13.6%	1.11 [0.30, 1.91]
Subtotal (95% CI)	**100.0%**	**0.81 [0.52, 1.11]**
Heterogeneity: Tau² = 0.00; Chi² = 3.83, df = 8 (P = 0.87); I² = 0%		
Test for overall effect: Z = 5.38 (P < 0.00001)		
1.2.2 Untrained hand		
Dickins et al. 2015	30.1%	1.10 [0.43, 1.77]
Hinder et al. 2011	20.9%	1.55 [0.71, 2.39]
Hinder et al. 2013b	26.4%	0.52 [-0.21, 1.24]
Reissig et al. 2015	22.6%	0.75 [-0.05, 1.55]
Subtotal (95% CI)	**100.0%**	**0.96 [0.54, 1.38]**
Heterogeneity: Tau² = 0.04; Chi² = 3.75, df = 3 (P = 0.29); I² = 20%		
Test for overall effect: Z = 4.46 (P < 0.00001)		

A)

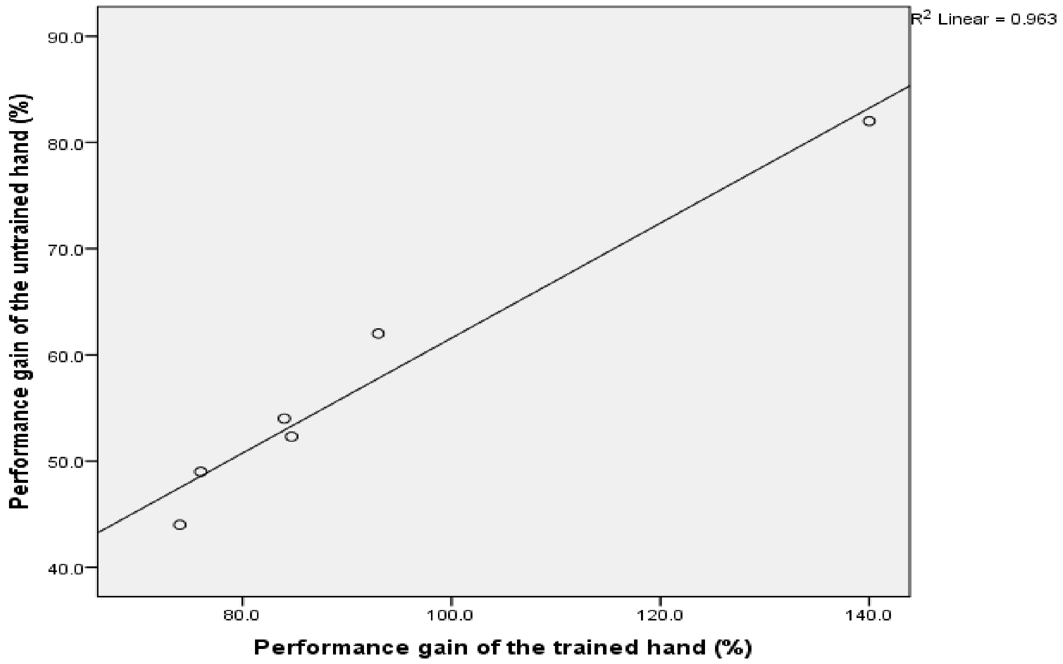


Study or Subgroup	Weight	Mean Difference IV, Random, 95% CI
2.1.1 Trained hand		
Carroll et al. 2008	47.6%	1.24 [0.97, 1.51]
Lee et al. 2010		Not estimable
Stockel et al. 2016	52.4%	1.00 [0.75, 1.25]
Subtotal (95% CI)	**100.0%**	**1.11 [0.88, 1.35]**
Heterogeneity: Tau² = 0.01; Chi² = 1.60, df = 1 (P = 0.21); I² = 38%		
Test for overall effect: Z = 9.30 (P < 0.00001)		
2.1.2 Untrained hand		
Carroll et al. 2008	30.6%	0.59 [0.37, 0.81]
Lee et al. 2010	17.4%	0.29 [-0.02, 0.60]
Stockel et al. 2016	52.0%	0.45 [0.30, 0.60]
Subtotal (95% CI)	**100.0%**	**0.47 [0.33, 0.60]**
Heterogeneity: Tau² = 0.00; Chi² = 2.54, df = 2 (P = 0.28); I² = 21%		
Test for overall effect: Z = 6.69 (P < 0.00001)		

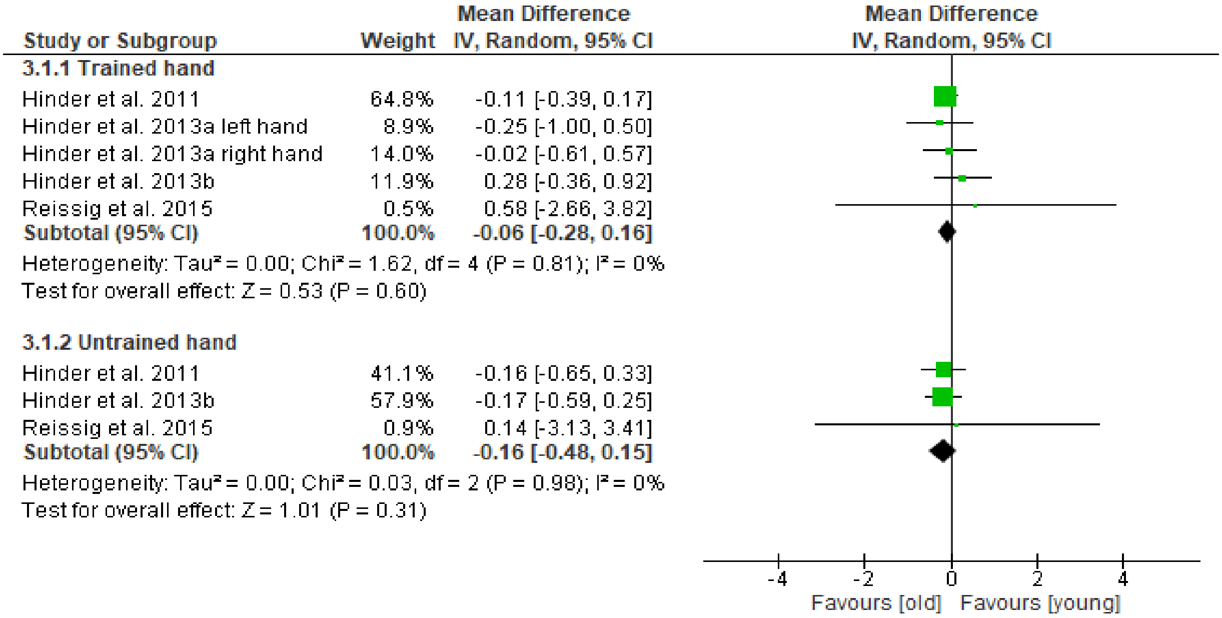
B)



Study or Subgroup	Weight	Mean Difference IV, Random, 95% CI
2.2.1 Trained hand		
Carroll et al. 2008	48.7%	1.36 [1.03, 1.69]
Lee et al. 2010	51.3%	0.93 [0.63, 1.23]
Subtotal (95% CI)	**100.0%**	**1.14 [0.72, 1.56]**
Heterogeneity: Tau² = 0.07; Chi² = 3.61, df = 1 (P = 0.06); I² = 72%		
Test for overall effect: Z = 5.30 (P < 0.00001)		
2.2.2 Untrained hand		
Carroll et al. 2008	61.8%	0.76 [0.51, 1.01]
Lee et al. 2010	38.2%	0.64 [0.32, 0.96]
Subtotal (95% CI)	**100.0%**	**0.71 [0.51, 0.91]**
Heterogeneity: Tau² = 0.00; Chi² = 0.33, df = 1 (P = 0.57); I² = 0%		
Test for overall effect: Z = 6.99 (P < 0.00001)		

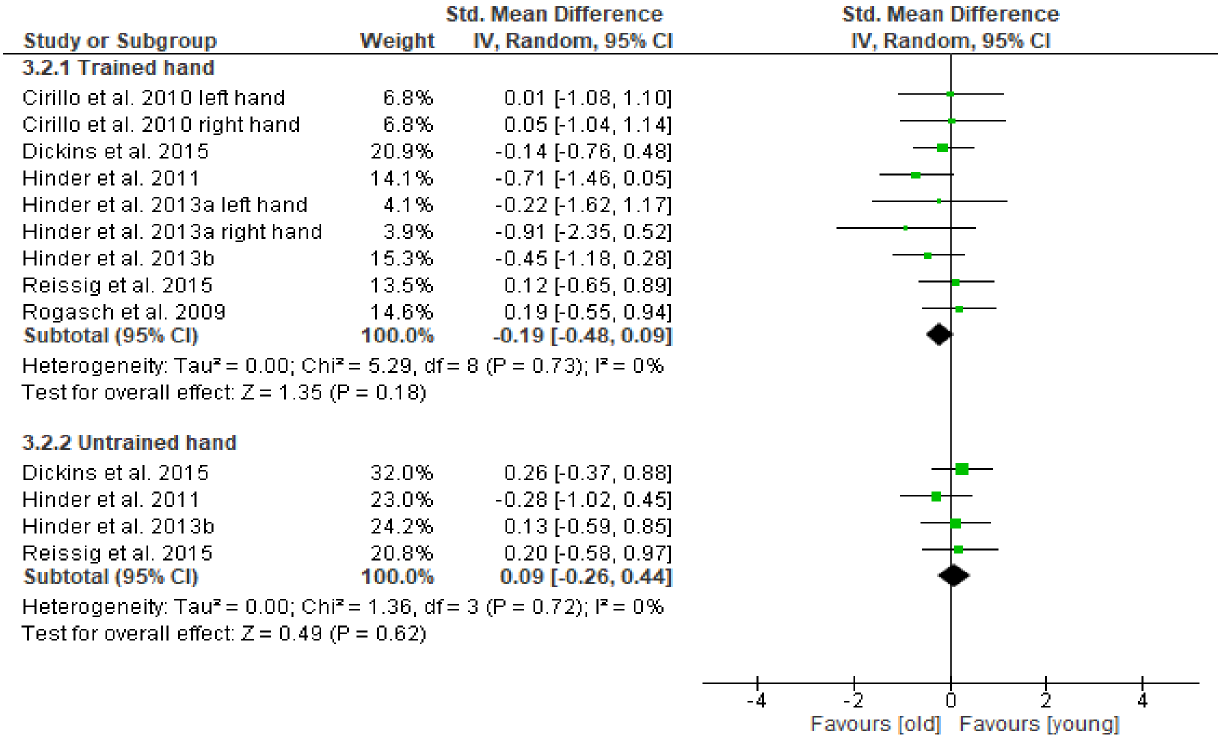

R^2 Linear = 0.963
Performance gain of the untrained hand (%)
90.0
80.0
70.0
60.0
50.0
40.0
80.0
100.0
120.0
140.0
Performance gain of the trained hand (%)

A)



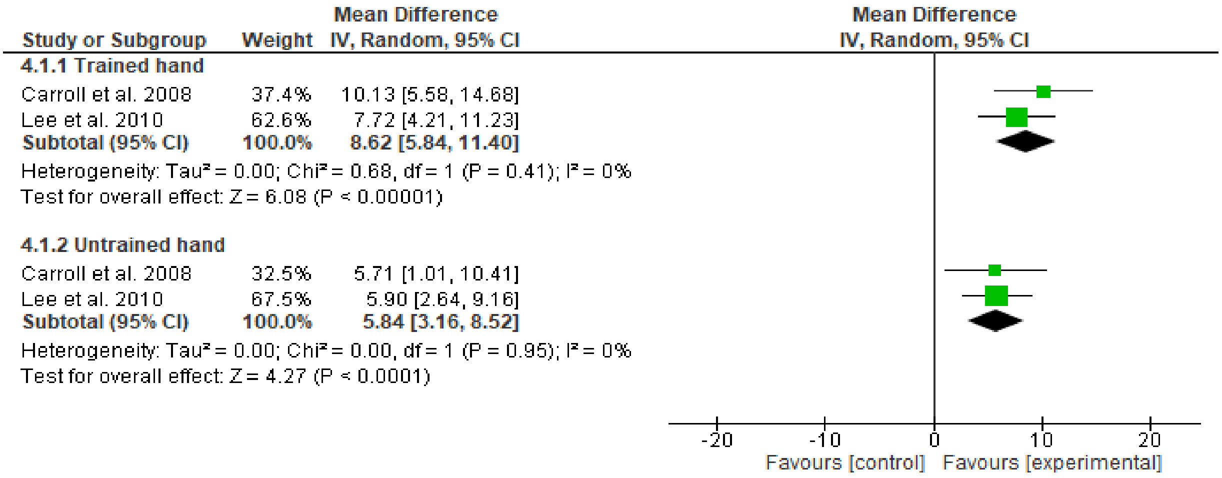
Study or Subgroup	Weight	Mean Difference IV, Random, 95% CI
3.1.1 Trained hand		
Hinder et al. 2011	64.8%	-0.11 [-0.39, 0.17]
Hinder et al. 2013a left hand	8.9%	-0.25 [-1.00, 0.50]
Hinder et al. 2013a right hand	14.0%	-0.02 [-0.61, 0.57]
Hinder et al. 2013b	11.9%	0.28 [-0.36, 0.92]
Reissig et al. 2015	0.5%	0.58 [-2.66, 3.82]
Subtotal (95% CI)	**100.0%**	**-0.06 [-0.28, 0.16]**
Heterogeneity: Tau² = 0.00; Chi² = 1.62, df = 4 (P = 0.81); I² = 0%		
Test for overall effect: Z = 0.53 (P = 0.60)		
3.1.2 Untrained hand		
Hinder et al. 2011	41.1%	-0.16 [-0.65, 0.33]
Hinder et al. 2013b	57.9%	-0.17 [-0.59, 0.25]
Reissig et al. 2015	0.9%	0.14 [-3.13, 3.41]
Subtotal (95% CI)	**100.0%**	**-0.16 [-0.48, 0.15]**
Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 2 (P = 0.98); I² = 0%		
Test for overall effect: Z = 1.01 (P = 0.31)		

B)



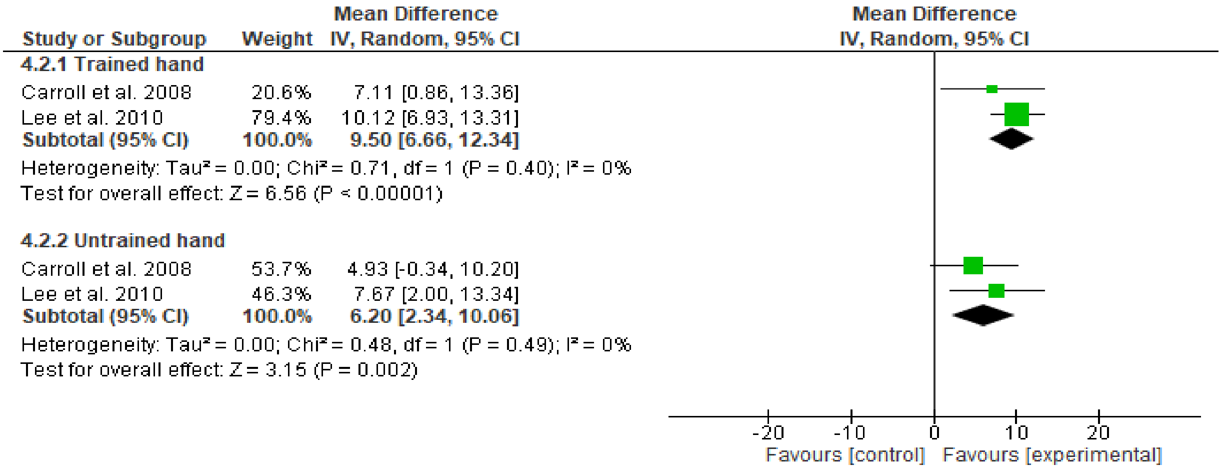
Study or Subgroup	Weight	Std. Mean Difference IV, Random, 95% CI
3.2.1 Trained hand		
Cirillo et al. 2010 left hand	6.8%	0.01 [-1.08, 1.10]
Cirillo et al. 2010 right hand	6.8%	0.05 [-1.04, 1.14]
Dickins et al. 2015	20.9%	-0.14 [-0.76, 0.48]
Hinder et al. 2011	14.1%	-0.71 [-1.46, 0.05]
Hinder et al. 2013a left hand	4.1%	-0.22 [-1.62, 1.17]
Hinder et al. 2013a right hand	3.9%	-0.91 [-2.35, 0.52]
Hinder et al. 2013b	15.3%	-0.45 [-1.18, 0.28]
Reissig et al. 2015	13.5%	0.12 [-0.65, 0.89]
Rogasch et al. 2009	14.6%	0.19 [-0.55, 0.94]
Subtotal (95% CI)	**100.0%**	**-0.19 [-0.48, 0.09]**
Heterogeneity: Tau² = 0.00; Chi² = 5.29, df = 8 (P = 0.73); I² = 0%		
Test for overall effect: Z = 1.35 (P = 0.18)		
3.2.2 Untrained hand		
Dickins et al. 2015	32.0%	0.26 [-0.37, 0.88]
Hinder et al. 2011	23.0%	-0.28 [-1.02, 0.45]
Hinder et al. 2013b	24.2%	0.13 [-0.59, 0.85]
Reissig et al. 2015	20.8%	0.20 [-0.58, 0.97]
Subtotal (95% CI)	**100.0%**	**0.09 [-0.26, 0.44]**
Heterogeneity: Tau² = 0.00; Chi² = 1.36, df = 3 (P = 0.72); I² = 0%		
Test for overall effect: Z = 0.49 (P = 0.62)		

A)



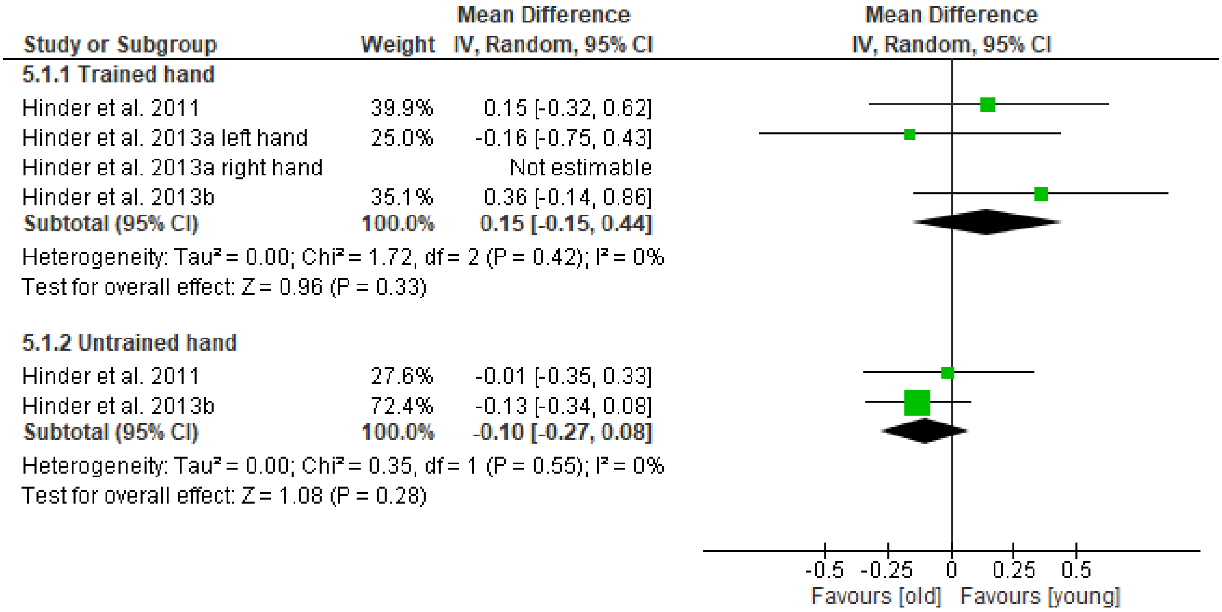
Study or Subgroup	Weight	Mean Difference IV, Random, 95% CI
4.1.1 Trained hand		
Carroll et al. 2008	37.4%	10.13 [5.58, 14.68]
Lee et al. 2010	62.6%	7.72 [4.21, 11.23]
Subtotal (95% CI)	**100.0%**	**8.62 [5.84, 11.40]**
Heterogeneity: Tau² = 0.00; Chi² = 0.68, df = 1 (P = 0.41); I² = 0%		
Test for overall effect: Z = 6.08 (P < 0.00001)		
4.1.2 Untrained hand		
Carroll et al. 2008	32.5%	5.71 [1.01, 10.41]
Lee et al. 2010	67.5%	5.90 [2.64, 9.16]
Subtotal (95% CI)	**100.0%**	**5.84 [3.16, 8.52]**
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.95); I² = 0%		
Test for overall effect: Z = 4.27 (P < 0.0001)		

B)



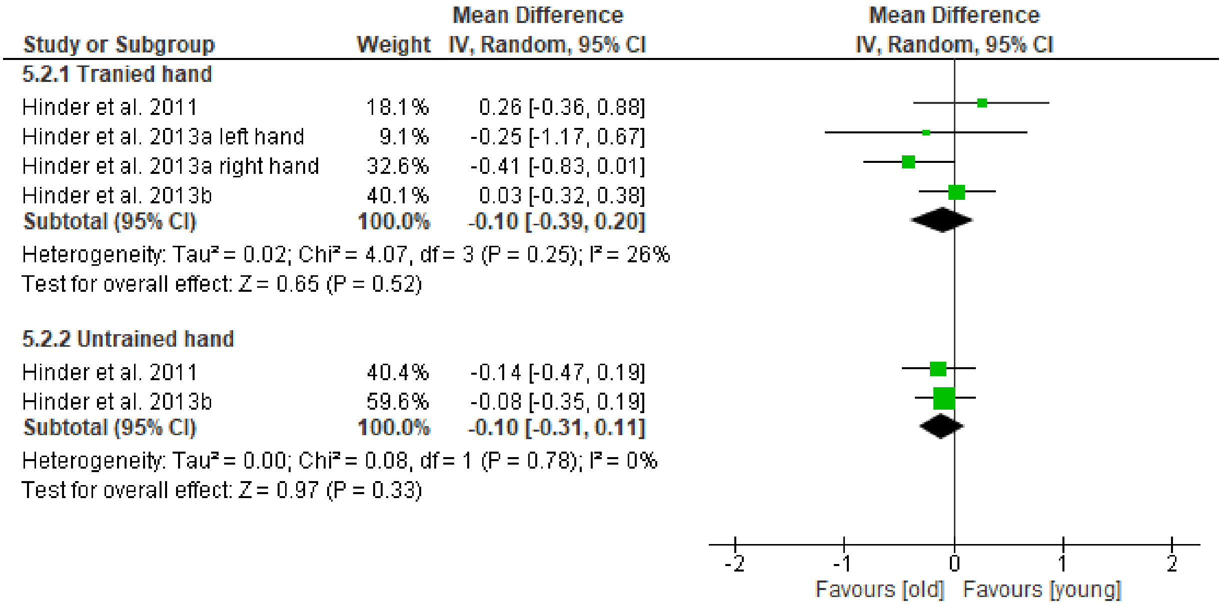
Study or Subgroup	Weight	Mean Difference IV, Random, 95% CI
4.2.1 Trained hand		
Carroll et al. 2008	20.6%	7.11 [0.86, 13.36]
Lee et al. 2010	79.4%	10.12 [6.93, 13.31]
Subtotal (95% CI)	**100.0%**	**9.50 [6.66, 12.34]**
Heterogeneity: Tau² = 0.00; Chi² = 0.71, df = 1 (P = 0.40); I² = 0%		
Test for overall effect: Z = 6.56 (P < 0.00001)		
4.2.2 Untrained hand		
Carroll et al. 2008	53.7%	4.93 [-0.34, 10.20]
Lee et al. 2010	46.3%	7.67 [2.00, 13.34]
Subtotal (95% CI)	**100.0%**	**6.20 [2.34, 10.06]**
Heterogeneity: Tau² = 0.00; Chi² = 0.48, df = 1 (P = 0.49); I² = 0%		
Test for overall effect: Z = 3.15 (P = 0.002)		

A)



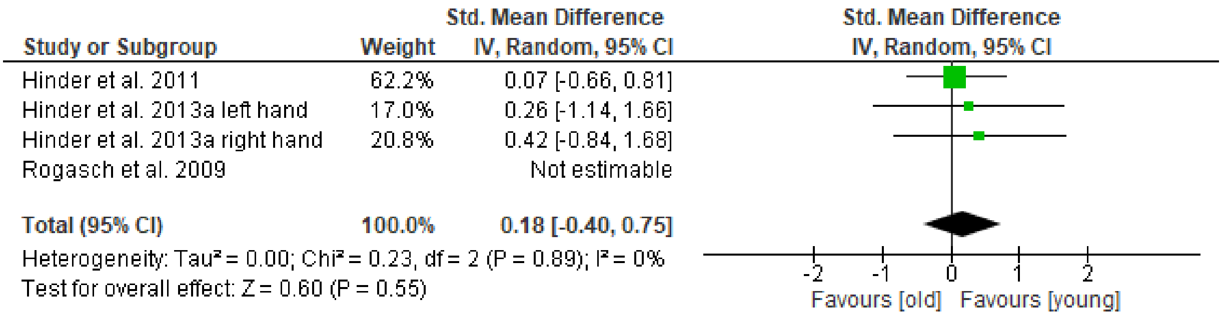
Study or Subgroup	Weight	Mean Difference IV, Random, 95% CI
5.1.1 Trained hand		
Hinder et al. 2011	39.9%	0.15 [-0.32, 0.62]
Hinder et al. 2013a left hand	25.0%	-0.16 [-0.75, 0.43]
Hinder et al. 2013a right hand		Not estimable
Hinder et al. 2013b	35.1%	0.36 [-0.14, 0.86]
Subtotal (95% CI)	**100.0%**	**0.15 [-0.15, 0.44]**
Heterogeneity: Tau² = 0.00; Chi² = 1.72, df = 2 (P = 0.42); I² = 0%		
Test for overall effect: Z = 0.96 (P = 0.33)		
5.1.2 Untrained hand		
Hinder et al. 2011	27.6%	-0.01 [-0.35, 0.33]
Hinder et al. 2013b	72.4%	-0.13 [-0.34, 0.08]
Subtotal (95% CI)	**100.0%**	**-0.10 [-0.27, 0.08]**
Heterogeneity: Tau² = 0.00; Chi² = 0.35, df = 1 (P = 0.55); I² = 0%		
Test for overall effect: Z = 1.08 (P = 0.28)		

B)



Study or Subgroup	Weight	Mean Difference IV, Random, 95% CI
5.2.1 Tranied hand		
Hinder et al. 2011	18.1%	0.26 [-0.36, 0.88]
Hinder et al. 2013a left hand	9.1%	-0.25 [-1.17, 0.67]
Hinder et al. 2013a right hand	32.6%	-0.41 [-0.83, 0.01]
Hinder et al. 2013b	40.1%	0.03 [-0.32, 0.38]
Subtotal (95% CI)	**100.0%**	**-0.10 [-0.39, 0.20]**
Heterogeneity: Tau² = 0.02; Chi² = 4.07, df = 3 (P = 0.25); I² = 26%		
Test for overall effect: Z = 0.65 (P = 0.52)		
5.2.2 Untrained hand		
Hinder et al. 2011	40.4%	-0.14 [-0.47, 0.19]
Hinder et al. 2013b	59.6%	-0.08 [-0.35, 0.19]
Subtotal (95% CI)	**100.0%**	**-0.10 [-0.31, 0.11]**
Heterogeneity: Tau² = 0.00; Chi² = 0.08, df = 1 (P = 0.78); I² = 0%		
Test for overall effect: Z = 0.97 (P = 0.33)		

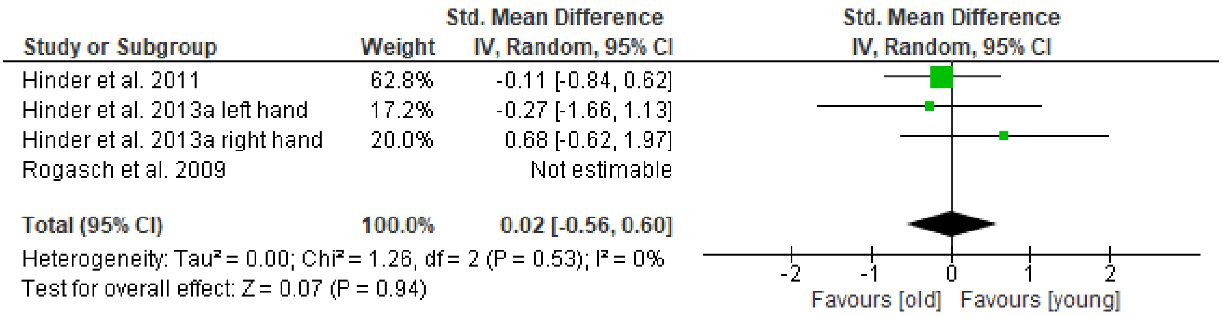
A)



Study or Subgroup	Weight	Std. Mean Difference IV, Random, 95% CI
Hinder et al. 2011	62.2%	0.07 [-0.66, 0.81]
Hinder et al. 2013a left hand	17.0%	0.26 [-1.14, 1.66]
Hinder et al. 2013a right hand	20.8%	0.42 [-0.84, 1.68]
Rogasch et al. 2009		Not estimable
Total (95% CI)	**100.0%**	**0.18 [-0.40, 0.75]**

Heterogeneity: Tau² = 0.00; Chi² = 0.23, df = 2 (P = 0.89); I² = 0%
Test for overall effect: Z = 0.60 (P = 0.55)

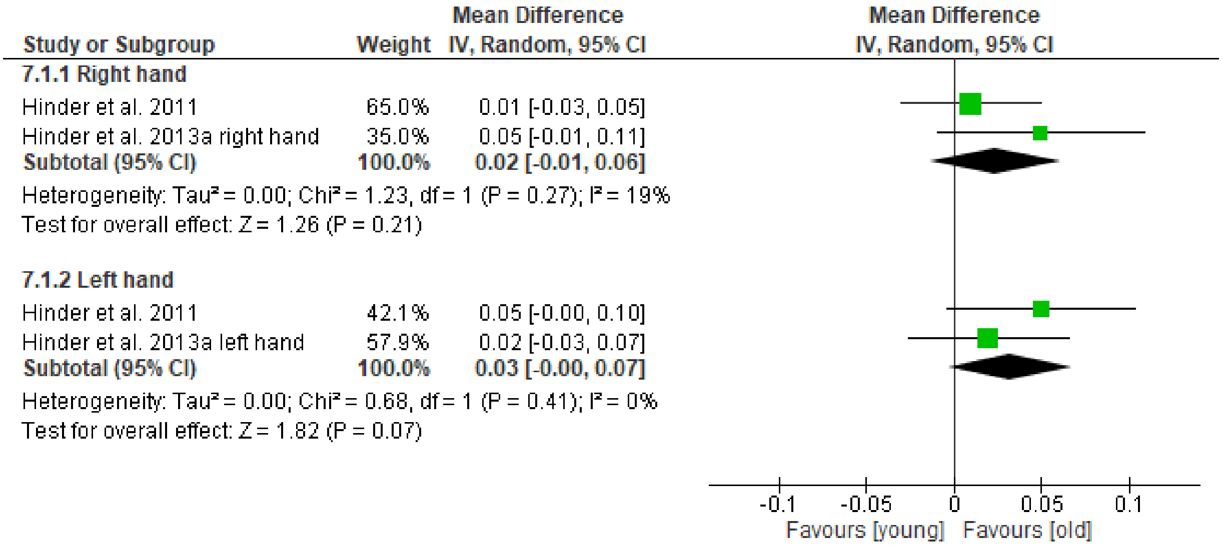
B)



Study or Subgroup	Weight	Std. Mean Difference IV, Random, 95% CI
Hinder et al. 2011	62.8%	-0.11 [-0.84, 0.62]
Hinder et al. 2013a left hand	17.2%	-0.27 [-1.66, 1.13]
Hinder et al. 2013a right hand	20.0%	0.68 [-0.62, 1.97]
Rogasch et al. 2009		Not estimable
Total (95% CI)	**100.0%**	**0.02 [-0.56, 0.60]**

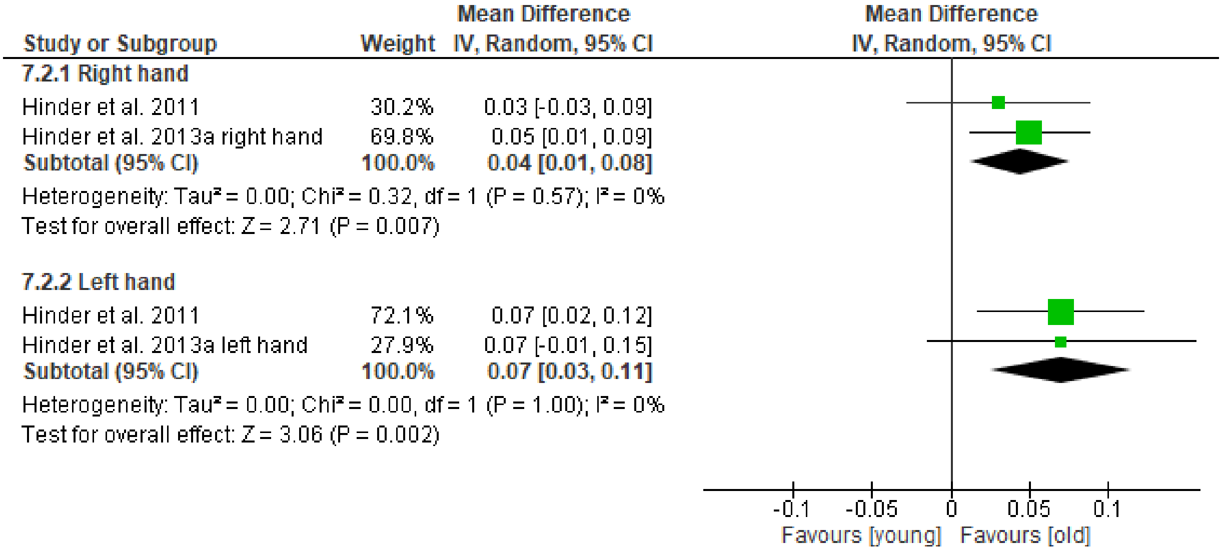
Heterogeneity: Tau² = 0.00; Chi² = 1.26, df = 2 (P = 0.53); I² = 0%
Test for overall effect: Z = 0.07 (P = 0.94)

A)



Study or Subgroup	Weight	Mean Difference IV, Random, 95% CI
7.1.1 Right hand		
Hinder et al. 2011	65.0%	0.01 [-0.03, 0.05]
Hinder et al. 2013a right hand	35.0%	0.05 [-0.01, 0.11]
Subtotal (95% CI)	**100.0%**	**0.02 [-0.01, 0.06]**
Heterogeneity: Tau^2 = 0.00; Chi^2 = 1.23, df = 1 (P = 0.27); I^2 = 19%		
Test for overall effect: Z = 1.26 (P = 0.21)		
7.1.2 Left hand		
Hinder et al. 2011	42.1%	0.05 [-0.00, 0.10]
Hinder et al. 2013a left hand	57.9%	0.02 [-0.03, 0.07]
Subtotal (95% CI)	**100.0%**	**0.03 [-0.00, 0.07]**
Heterogeneity: Tau^2 = 0.00; Chi^2 = 0.68, df = 1 (P = 0.41); I^2 = 0%		
Test for overall effect: Z = 1.82 (P = 0.07)		

B)



Study or Subgroup	Weight	Mean Difference IV, Random, 95% CI
7.2.1 Right hand		
Hinder et al. 2011	30.2%	0.03 [-0.03, 0.09]
Hinder et al. 2013a right hand	69.8%	0.05 [0.01, 0.09]
Subtotal (95% CI)	**100.0%**	**0.04 [0.01, 0.08]**
Heterogeneity: Tau^2 = 0.00; Chi^2 = 0.32, df = 1 (P = 0.57); I^2 = 0%		
Test for overall effect: Z = 2.71 (P = 0.007)		
7.2.2 Left hand		
Hinder et al. 2011	72.1%	0.07 [0.02, 0.12]
Hinder et al. 2013a left hand	27.9%	0.07 [-0.01, 0.15]
Subtotal (95% CI)	**100.0%**	**0.07 [0.03, 0.11]**
Heterogeneity: Tau^2 = 0.00; Chi^2 = 0.00, df = 1 (P = 1.00); I^2 = 0%		
Test for overall effect: Z = 3.06 (P = 0.002)		