

Review article

Contralateral Effects after Unilateral Strength Training: A Meta-Analysis Comparing Training Loads

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Abstract

There is solid evidence on the cross-training phenomenon, but the training load required to achieve it has yet to be established. The aim of this meta-analysis was to deduce which unilateral strength training load (duration, frequency, intensity, rest and type) would enable the biggest strength increases to be obtained in the inactive contralateral limb. The examined studies were limited to those written in the English language within the Web of Science, PubMed and SPORTDiscus databases. Ten of the 43 eligible studies were included, covering a total of 409 participants. The studies included in the meta-analysis showed a low risk of bias and had an estimated pooled effect size of 0.56 (95% CI from 0.34 to 0.78). Greater effect sizes were observed in lengthy protocols involving fast eccentric exercises using designs of 3 sets of 10 repetitions and a 2-minute rest time. Effect size did not relate to absolute volume, relative intensity, absolute duration and speed of execution. In conclusion, to optimize contralateral strength improvements, cross-training sessions should involve fast eccentric sets with moderate volumes and rest intervals.

Key words: Cross-education, cross transfer, effect size, immobilization.

Introduction

Previous studies have proved strength increases in the contralateral limb after performing unilateral strength exercises with the ipsilateral limb (Lee and Carroll, 2007). Several terms have been used to refer to this phenomenon: *cross-transfer*, *cross-over effect*, *cross-exercise*, *contralateral learning*, *contralateral training* or *inter-limb transfer*. However, since it was coined by Walter W. Davis (1899), the most commonly used term is *cross-education* (CE).

In recent years, CE has been proposed as a therapeutic strategy (Farthing et al., 2011; Hendy et al., 2012; Magnus et al., 2013) because it was found that, after strength training with the ipsilateral limb, there was an increase in strength levels in the contralateral, non-trained sides (Farthing et al., 2009; Lepley and Palmieri-Smith, 2014; Magnus et al., 2013) and less atrophy of inactive muscles in injured areas of the body (Hendy et al., 2012; Magnus et al., 2010). Unfortunately, despite the significance of the adaptations, most of the studies had been conducted with little control of the potential variables that might have influenced the strength increase. Consequently, several recent studies have proposed research designs and methodologies allowing the main effect-modifying

factors to be controlled for (Carroll et al., 2006; Lee and Carroll, 2007; Voet et al., 2013). Of note among them are test learning effects, control of inactivity in the non-trained hemisphere and sample diversity (Carroll et al., 2006).

Despite the abundance of previous studies, there is large variability between their findings. This fact hinders their applicability and seems to be related to a variety of factors such as: a) the trained half of the body, with the greatest effects being observed when the dominant side is trained (Farthing and Zehr, 2014); b) the level of the participants' daily physical activity, with the effect being lower in trained subjects; c) the level of prior knowledge of the training task used, with greater effects being found when the training tasks are unknown (Farthing et al., 2005); d) the type of contraction, it being observed that eccentric work seems to induce a greater effect than isometric and concentric work (Farthing and Chilibeck, 2003; Hortobagyi et al., 1996); and finally, e) the characteristics of the training protocol, with the existence of a proportional relationship between the load applied and the strength increase observed (Zhou, 2000).

Regarding the type of adaptation generated, evidence seems to suggest that neural adaptations are better candidates for the explanation of the results than muscular adaptations are (Dragert and Zehr, 2011; Farthing and Zehr, 2014; Ruddy and Carson, 2013). This is largely due to the fact that no significant vascular adaptations have been found (Zoeller et al., 2009), nor were any histological changes in hypertrophy levels, in enzyme concentration, in contractile protein composition alteration, in fiber type or in cross-sectional area (CSA) (Carroll et al., 2006). In trying to explain these adaptations, two theories are currently postulated that, although compatible with each other, try to explain how the neural adaptation mechanisms occur (Ruddy and Carson, 2013): a) the "cross-activation" model, which suggests that adaptations to unilateral exercise extend to the opposite half of the body, and b) the "bilateral access" model, which maintains that the motor schema of a unilateral task is accessible by trying to reproduce the same task in the opposite half of the body.

Regarding the changes observed in the nervous system, these can occur at peripheral, medullar, subcortical and cortical levels (Lee and Carroll, 2007). At peripheral and medullar levels, various studies suggest the existence of alterations in the synchronization of motor units and of neural conductivity similar to those observed in the trained side (Carroll et al., 2006). At sub-cortical

and cortical levels, there is some evidence confirming the existence of a neural interaction between the two hemispheres (Carroll et al., 2006; Farthing et al., 2011), thus supporting the cross-activation model suggested by Ruddy and Carson (2013). Recent studies on the mirror neuron system (MNS) have shown that simple visualization of a movement is enough to provoke adaptations (Howatson et al., 2013; Zult et al., 2014). In addition to all of the above, it seems that motor learning provokes cortical reorganizations (Carroll et al., 2006) and that unilateral training produces inter-hemispheric plasticity (Farthing and Zehr, 2014), thus supporting the bilateral access model.

Although the findings we have described, the contralateral strength improvements have been obtained through a wide variety of training protocols. Consequently, the outcomes of this research are disparate and may be difficult to extrapolate. This suggests that a meta-analysis of existing literature could provide us with new information about the type of training that needs to be applied in order to achieve an optimum CE between hemispheres. Thus, based on a meta-analysis of the existing literature, the aim of this study was to deduce which unilateral strength training load (duration, frequency, intensity, rest and type) would optimize the strength increases in the contralateral limb.

Methods

Search strategy

An electronic search was performed on Web of Science (articles from 1900 to 2016), SPORTDiscus (articles from 1978 to 2016) and PubMed (articles from 1809 to 2016) databases. We complemented the results with two alternative searches: one of non-indexed literature in Google Scholar and Research Gate, and a cluster search based on previously located meta-analyses. The literature search process was completed in August 2016. Then a search was performed within each of the indicated sources using the following additive search key with two terms, regarding phenomenon and intervention descriptors:

(cross-education OR cross-exercise
OR contralateral OR inter-limb)
AND
(training OR exercise OR strength)

Inclusion criteria

The inclusion criteria were applied in accordance with Population, Intervention, Comparison and Outcome (PICO) variables and we followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) from Moher et al. (2009). Only randomized controlled trials published in the English language were selected for inclusion.

POPULATION – no restrictions were applied to the sex or age of the sample, and healthy subjects who had not sustained any injuries in the year prior to the intervention were accepted. **INTERVENTION** – studies in which the independent variable was the application of unilateral strength training programs were included. Exercises that manifested strength statically (isometric) and

dynamically (concentric and eccentric) were accepted. Excluded studies were those on training techniques using electro-stimulation, transcranial magnetic stimulation or vibrating surfaces, as were those on treatments using acupuncture, drugs or dietary supplements. **COMPARISON** – the dependent variable in this meta-analysis was strength recorded for the non-trained counterpart muscle group, contralateral to the trained one. Values for absolute strength (kg, lb and N), joint moment strength (N·m), and increases in absolute strength (kg, lb and N) and in relative strength (%) were accepted. **OUTCOME** – included studies were required to report mean strength (and standard deviation thereof) in the pre-intervention and post-intervention moments for both the experimental and control groups.

Study inclusion

The process was divided into four stages: identification, screening, selection and inclusion. After identifying the documents by means of an electronic search, duplicates were discarded and the studies were screened by title and abstract. The full text was obtained for the screened units, and two of the authors, FCS and RCS, reviewed them independently, excluding any that deviated from the inclusion criteria. In this step, a third author, VBG, resolved any discrepancies between the two experts. The studies remaining after this process were included in the meta-analysis.

Bias control

Two authors, VBG and FCS, analyzed the methodological quality of the selected studies using the Cochrane Collaboration bias assessment tool (Higgins and Green, 2011). They analyzed six internal validity criteria: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting and other bias. Each item's risk level was assessed and given one of three possible scores: low risk of bias (+), high risk of bias (-) or unclear risk of bias (?). Finally, the inter-author reliability index was calculated using Cohen's kappa coefficient, the discrepancies between assessors were resolved and any studies in which high risk of bias scores prevailed were excluded. The publication bias probability was statistically checked using two tests based on funnel plot asymmetry: the tolerance for null results index (N_{fs}) by Rosenthal (1979), and the Egger's test (Egger et al., 1997).

Content coding

Each comparison found between the control group and the experimental group based on the results recorded in the contralateral limb (non-trained) was considered as a unit for statistical (meta-)analysis. For that purpose, any studies with more than one experimental group were subdivided into different units (considering each experimental group as a different unit), as were those reporting more than one includable dependent variable (assigning a different unit for each result). The studies were independently coded by two authors, RCS and FCS. Before performing the quantitative analysis, Cohen's kappa coefficients

in the qualitative variables were checked, as were Pearson's coefficients in the quantitative variables, and any discrepancies between the coders were resolved. The content was coded according to the following variables: Size (n) of the sample, of the control group and of the experimental groups, sex as proportion of men and age of the sample, level of participants' activity, duration of the training period in weeks, weekly training frequency, session workload (sets, repetitions, intensity and rest), manifestation of trained strength, trained side, mean and standard deviation of the results in the non-trained half of the body, for both groups (control and experimental) and for both moments (pre and post).

Data analysis

For each unit, the effect size and its confidence interval limits at 95% were calculated using the standardized mean change difference (Δ) between the pre- and post-intervention measurements in the experimental and control groups (Morris, 2008). The potential influence of effect-moderating variables was then checked using the Q-test of homogeneity (Lipsey and Wilson, 2001). All of the analyses were performed in R (R Core Team, 2016), and the "rmeta" analysis package (Lumley, 2012) was used, following the random effects model for all calculations and considering a statistical significance of $p < 0.05$.

After that, variance analysis and meta-regression were used to calculate the potential interaction between the coded training characteristics and the observed contralateral adaptation. For that purpose, we used the relative intensity required in each study. The total number of days trained in each training program and the total number of repetitions per session held in each of the studies were also calculated.

Results

Study characteristics

A total of 337 studies were identified (Web of Science = 144, PubMed = 108, SPORTDiscus = 77 and other sources = 8). These were screened for duplicates and by title and abstract. From a subtotal of 53 selected units, 43 were excluded for methodological reasons, detailed below, thus leaving a final sample of 10 studies for this work. These were used to perform the systematic review (Figure 1), and they included a total of 409 participants (187 women, 222 men).

Twenty-four units of analysis from the 10 included studies were then coded, with statistically significant inter-expert reliability. Twelve units came from 4 studies with several experimental groups (Farthing et al., 2005; Munn et al., 2005; Shaver, 1975; Shields et al., 1999), and 8 units came from 2 studies with various dependent variables (Lepley and Palmieri-Smith, 2014; Magnus et al., 2014). Table 1 summarizes the units for this analysis.

The two authors who analyzed the quality of the studies agreed in 89% of cases, and the discrepancies between them were resolved. According to the instrument used (Table 2), 8 studies (Komi et al., 1978; Lagerquist et al., 2006; Lepley and Palmieri-Smith, 2014; Magnus et al., 2014; Munn et al., 2005; Shaver, 1970; Shaver, 1975;

Shields et al., 1999) were considered to have a high risk of bias owing to the lack of blinding of participants and personnel. Nine studies (Fimland et al., 2009; Komi et al., 1978; Lagerquist et al., 2006; Lepley and Palmieri-Smith, 2014; Magnus et al., 2014; Munn et al., 2005; Shaver, 1970; Shaver, 1975; Shields et al., 1999) were considered to have a high risk of other potential bias owing to the methodologies used to determine the samples' laterality. A tolerance for null results index (Nfs) of 75.372 was calculated, suggesting a low publication bias probability among the units analyzed. However, Egger's test was significant, suggesting a publication bias probability ($\beta = 0.916$; $p < 0.01$).

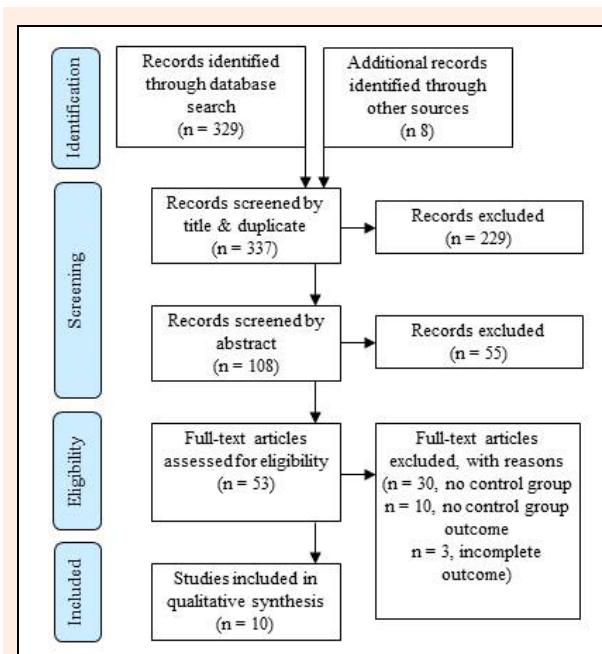


Figure 1. PRISMA flow diagram of the systematic review process.

Training

The interventions performed in the analyzed studies had a mean duration of 6.3 ± 2.31 weeks and a frequency of 3.5 ± 0.7 weekly sessions. In two studies (Munn et al., 2005; Shields et al., 1999), subjects exercised in different sets performing the maximum number of repetitions to failure, which were considered fatigue protocols. The remaining 8 (Farthing et al., 2005; Fimland et al., 2009; Komi et al., 1978; Lagerquist et al., 2006; Lepley and Palmieri-Smith, 2014; Magnus et al., 2014; Shaver, 1970; Shaver, 1975), organized the training protocol in sets and repetitions, involving a mean volume of 4.4 ± 1.7 sets and 10 ± 3.5 repetitions.

Outcome measures

The meta-analysis showed a statistically significant pooled effect size. (Pooled ES = 0.56; $p < 0.0$; 95% CI from 0.34 to 0.78), which we considered moderate according to Cohen's scale (Cohen, 1988) (Figure 2). The homogeneity test was statistically significant ($Q = 42.70$; $p < 0.01$), and that is why the corresponding tests were done to identify moderating variables. There were not statistically significant differences in effect size related to

Table 1. Summary of units of analysis.

Reference	Unit	Sample size (control group size) Participants description Mean age (SD)	Training load (Duration, Frequency, Volume, Rest, Intensity, Exercise)	Outcome measure, Experimental group size	Calculated Effect Size [CI at 95%]
Komi et al., 1978	1	n = 12 (6) Twin pairs (2w, 4m) 14 (0.9) years old	D: 14 w, F: 4 days/w, V: 10 · 1, R: 30 sec, I: 5 sec at MVC E: ISO knee extension	ISO MVC n=6	0.36 [0.03 to 0.69]
Lagerquist et al., 2006	2	n = 16 (6) Unknown (10w, 6m) 21 - 42 years old	D: 5 w, F: 3 days/w, V: 5 · 8, R: 60 sec, I: 6 sec at MVC E: ISO ankle dorsal flexion	ISO MVC n=10	0.72 [0.46 to 0.98]
Lepley & Palmieri-Smith, 2014	3	n = 18 (9), Moderately active adults (10w, 8m), 22.95 (3.6) years old	D: 8 w, F: 3 days/w V: 8 · 10, R: 120 sec I: PT at -60°·s E: ECC knee extension	CON 30°·s⁻¹ CON 60°·s⁻¹ ECC 30°·s⁻¹ ECC 60°·s⁻¹ n=9	0.84 [0.61 to 1.06] 0.81 [0.58 to 1.04] 1.35 [1.1 to 1.59] 1.28 [1.04 to 1.52]
Munn et al., 2005	7		V: 1 · max, I: 8-RM load at ±140°·s⁻¹		n=22 0.08 [0.01 to 0.17]
	8	n = 111 (22), Not trained adults (94w, 21m), 20.6 (6.1) years old	D: 8 w F: 3 days/w R: 120 sec E: Elbow flexion	CON 1RM n=23	0 [-0.09 to 0.09]
	9		V: 1 · max, I: 8-RM load at ±50°·s⁻¹		n=23 0.13 [0.04 to 0.22]
	10		V: 3 · max, I: 8-RM load at ±140°·s⁻¹		n=22 -0.04 [-0.13 to 0.05]
Shaver, 1970	11	n = 40 (20) Recreationally active men, 18-20 years old	D: 6 w, F: 3 days/w, V: 3 · 10, R: 120 sec, I: 10-RM load E: Elbow flexion	ISO MVC n=20	0.42 [0.32 to 0.62]
Shaver, 1975	12	n = 100 (20)	D: 6 w, F: 3 days/w, V: 3 · 10, R:		n=20 0.95 [0.84 to 1.05]
	13	Unknown (all men)	120 sec, I: 10-RM load		n=20 0.96 [0.86 to 1.06]
	14	18-22 years old	E: Elbow flexion		n=20 1.02 [0.92 to 1.13]
	15				n=20 0.92 [0.82 to 1.02]
Shields et al., 1999	16	n = 24 (8), Not trained men, 26.07 (5.68) years old	D: 6 w, F: 5 days/w V: 2 · max, R: 300 sec, E: Isometric handgrip	I: 30% MVC	n=8 0.05 [-0.2 to 0.29]
	17			I: 0% MVC	ISO MVC n=8 0.6 [0.35 to 0.85]
Farthing et al., 2005	18	n = 39 (14), Slightly trained women, 20.8 (0.4)	D: 6 w, F: 4 days/w V: 6 · 8, R: 30 sec I: 2 sec at MVC		n=12 2.09 [1.9 to 2.28]
	19		E: Isometric ulnar deviation		ISO MVC n=13 -0.22 [-0.36 to -0.07]
Fimland et al., 2009	20	n = 26 (11), Recreationally active adults (17w, 9m), 24 (1.66) years old	D: 4 w, F: 4 days/w V: 6 · 6, R: 120 sec I: 4 sec at MVC	E: Isometric ankle dorsal flexion	ISO MVC n=15 1.19 [1.02 to 1.35]
	21		D: 4 w	E: Shoulder external rotation	0.54 [0.37 to 0.72]
Magnus et al., 2014	22	n = 23 (10), Trained adults (12w, 11m), 50 (9.0) years old	F: 3 days/w V: 4 · 15 R: 60 sec I: 15-RM	E: Shoulder internal rotation	ISO MVC n=13 0.24 [0.06 to 0.41]
	23			E: Shoulder adduction	0.26 [0.08 to 0.43]
	24			E: Handgrip	0.02 [-0.15 to 0.2]

CON: Concentric Strength; ECC: Eccentric strength; ISO MVC: Isometric Maximal Voluntary Contraction

sample sex or age (proportion of men: $\beta = 0.16$; $\alpha = 0.73$ and age: $\beta = -0.005$; $p = 0.62$).

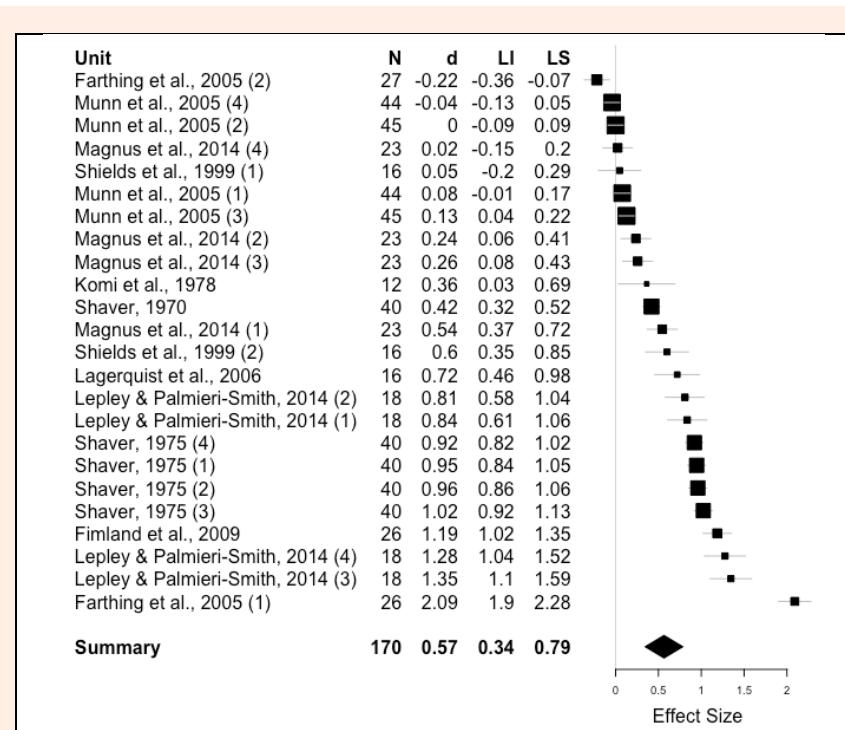
The results obtained showed interaction between the characteristics of the training programs carried out and the increase in recorded contralateral strength. The manifestation of trained strength (isometric, concentric, eccentric or mixed) proved to have an influence on the contralateral effect ($Q = 6.266$; $p < 0.05$), with a higher, statistically significant effect size ($ES = 1.05$; $p < 0.01$) being observed in eccentric protocols (95% CI from 0.56 to 1.52). The type of training (sets of repetitions or repetitions to failure) also influenced the observed adaptation ($Q = 14.96$; $p < 0.01$), with a higher, statistically significant effect size ($ES = 0.74$; $p < 0.01$) found in protocols with sets of repetitions (95% CI from 0.55 to 0.93). No statistically significant correlations with the volume of work done in each session ($\beta = 0.16$; $p = 0.69$) were found. Regarding the exercise characteristics, no statistically significant correlations with the speed of execution ($\beta = 0.004$; $p = 0.36$) or with the relative work intensity ($\beta = 0.71$; $p = 0.17$) were found.

Interaction with the trained side could not be analyzed owing to the lack of degrees of freedom in the non-dominant (ND) level. Nor was interaction with the participants' level analyzed owing to the diversity of criteria in the studies' sample descriptions.

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Table 2. Assessment of risk of bias according to Cochrane Collaboration bias assessment tool.

References	Random sequence generation (Selection bias)	Allocation concealment (Selection bias)	Blinding of participants and personnel (Performance bias)	Blinding of outcome assessment (Detection bias): Self-reported outcomes	Blinding of outcome assessment (Detection bias): Objective measures	Incomplete outcome data (Attrition bias)	Selective reporting (Reporting bias)	Other bias
Shaver, 1970	+	+	-	+	+	+	+	-
Shaver, 1975	+	+	-	+	+	+	+	-
Komi et al., 1978	+	?	-	+	+	-	+	-
Shields et al., 1999	+	+	-	+	+	+	+	-
Munn et al., 2005	+	+	-	+	+	+	+	-
Farthing et al., 2005	+	+	+	+	+	?	+	+
Lagerquist et al., 2006	+	?	-	+	+	+	+	-
Fimland et al., 2009	+	?	+	+	+	+	+	-
Magnus et al., 2014	+	+	-	+	+	-	+	-
Lepley & Palmieri-Smith, 2014	+	+	-	+	+	+	+	-

**Figure 2.** Forest plot of Cohen's d in each unit of analysis. * Sample size, N; effect size, d; limits of confidence interval inferior, LI, and superior, LS.

Discussion

The aim of this meta-analysis was to deduce which unilateral strength training load (duration, frequency, intensity, rest and type) would optimize the strength increases in the contralateral limb. Our results suggest that the organization of training content interacts with the strength increases observed in the non-trained side. In this respect,

studies conducted on programs involving the most strenuous training (RF) – organized into single sets to fatigue or muscle failure – were those that produced the lowest contralateral strength increases. Conversely, training programs organized into multiple sets (3-5 sets of 8-15 repetitions with rest times of 1-2 minutes) obtained strength improvements in the opposite limb up to $39.2 \pm 7.8\%$ of those achieved in the trained hemisphere. All of

this suggests that, in programs aimed at improving strength in the opposite side, training loads similar to those found in the sets and repetitions (SR) level of this meta-analysis should be used.

None of the studies described which manifestation of the strength (speed strength, power, etc.) aimed to stimulate further than maximum strength. According to its training protocols as well as the pooled results in this analysis, we appreciate a predominance of power and strength-speed training loads. The analysis of variance between units in function of the type of contraction showed stronger interaction in solely eccentric (EC) exercises, compared with concentric (CO) and mixed (M) exercises. This finding had been noted previously by Lepley and Palmieri-Smith (2014), and it might be related to the neuromuscular adaptations that eccentric exercise produces (Hortobagyi et al., 1997).

Correlations between quantitative variables related to training load (absolute volume, relative intensity, absolute duration and speed of execution) and effect size were not statistically significant. Data in all the comparisons made were too dispersed to enable any statistical assertion. This might bear some relation to the high number of variables interacting with each other when producing an increase in contralateral strength.

Although earlier studies (Farthing et al., 2009) suggested greater adaptations in the ND limb when training the dominant (D) limb, we were unable to study the effect that the trained side produces because of the absence of degrees of freedom, that is to say, units for comparison in which training with the ND limb had taken place. On the other hand, in the analysis of potential bias, several studies (Farthing et al., 2005; Lagerquist et al., 2006; Lepley and Palmieri-Smith, 2014; Magnus et al., 2014; Shields et al., 1999) showed a high risk in relation to the procedures used to determine the participants' laterality. Several studies suggest that individual laterality may be different (both in terms of direction and magnitude) depending on the region of the body or the organ assessed and the type of task (strength or precision) analyzed (Voyer and Voyer, 2015). This argument suggests the need for future research to establish and relate the complete profile of a subject's laterality.

Owing to the diversity of criteria, the effect size in relation to the participants' fitness level could not be analyzed because some authors understood this to be the level of usual physical activity (Fimland et al., 2009; Lepley and Palmieri-Smith, 2014) while others considered it the degree of training prior to the intervention (Farthing et al., 2005; Magnus et al., 2014; Munn et al., 2005; Shaver, 1970; Shields et al., 1999). The remaining studies (Komi et al., 1978; Lagerquist et al., 2006; Shaver, 1975) did not provide any information on this aspect. Only five studies (Farthing et al., 2005; Lepley and Palmieri-Smith, 2014; Magnus et al., 2014; Munn et al., 2005; Shields et al., 1999) reported the technique used to determine the level. Four used descriptive techniques, while only one (Lepley and Palmieri-Smith, 2014) used comparable instruments (Tegner Scale and Marx Scale). It would be interesting to focus future works on distinguishing the CE effect according to standardized scales for the

participant's level of physical activity and degrees of prior training.

Conclusion

This meta-analysis suggests that unilateral strength training produces adaptations in the opposite limb, depending on the characteristics of the intervention performed. The training parameters that might determine a greater effect after a CE program are the execution of 3-5 sets of 8-15 repetitions of eccentric contractions with rest times of 1-2 minutes between sets. In addition, there seems to be a direct relationship between the training load applied and the effect achieved, albeit statistical not significant.

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Key points

- Inter-limb transfer of the strength is more effective in high speed eccentric exercises.
- Muscular endurance training is not advisable to induce contralateral adaptations.
- Cross-education effect may depend more on volume of training than on load.

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