

An updated systematic review and meta-analysis on the compatibility of concurrent aerobic and strength training for skeletal muscle size and function

Moritz Schumann^{1*}, Joshua F Feuerbacher¹, Marvin Sünkeler¹, Nils Freitag^{1,2}, Bent R Rønnestad³, Kenji Doma⁴ & Tommy R Lundberg^{5,6}

1: Department of Molecular and Cellular Sports Medicine, German Sport University, Cologne

2: Olympic Training Centre Berlin, Germany

3: Section for Health and Exercise Physiology, Department of Public Health and Sport Sciences, Inland Norway University of Applied Sciences, Elverum, Norway

4: Sport and Exercise Science, College of Healthcare Sciences, James Cook University, Townsville, Australia.

5: Division of Clinical Physiology, Department of Laboratory Medicine, Karolinska Institutet, Stockholm, Sweden

6: Unit of Clinical Physiology, Karolinska University Hospital, Stockholm, Sweden

***Correspondence to:**

Moritz Schumann, PhD

E-Mail: m.schumann@dshs-koeln.de

Twitter handles:

Moritz Schumann: @moritz_schumann

Nils Freitag: @NilsFreitag3

Kenji Doma: @kenji_doma

Tommy Lundberg: @TLexercise

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ABSTRACT

Objective

This systematic review assessed the compatibility of concurrent aerobic and strength training compared to sole strength training regarding adaptations in muscle function (maximal and explosive strength) and muscle mass. Subgroup analyses were conducted to examine the impact of training modality, exercise type, exercise order, training frequency, age, and training status.

Design

A systematic literature search was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). PROSPERO: CRD42020203777

Data sources

PubMed/MEDLINE, ISI Web of Science, Embase, CINAHL, SPORTDiscus and Scopus were systematically searched (12th of August 2020, updated on the 15th of March 2021).

Eligibility criteria

Population: Healthy adults of any sex and age; Intervention: Supervised, concurrent aerobic and strength training of at least 4 weeks; Comparison: Sole strength training with matched strength training volume; Outcome: maximal strength, explosive strength and muscle hypertrophy.

Results

A total of 43 studies were included. The estimated average standardised mean differences (SMD) based on the random-effects model were -0.06 (95% CI: -0.20, 0.09, $p=0.446$), -0.28 (95% CI: -0.48, -0.08, $p=0.007$) and -0.01 (95% CI: -0.16, 0.18, $p=0.919$) for maximal strength, explosive strength and muscle hypertrophy, respectively. The attenuation in explosive strength was more pronounced when concurrent training was performed within the same session ($p=0.043$) compared with separating the sessions by at least 3 h ($p>0.05$).

Summary/Conclusion

Concurrent aerobic and strength training does not compromise muscle hypertrophy and maximal strength development. However, explosive strength gains may be attenuated, especially when aerobic and strength training are performed within the same session.

KEY WORDS: body composition, muscle physiology, endurance, interference effect

KEY POINTS

- While concurrent aerobic and strength training is recommended to improve physical fitness and health, the compatibility of these two distinct exercise modes remains unclear.
- In this meta-analysis, we report that concurrent training does not interfere with adaptations in maximal strength and muscle hypertrophy, irrespective of the training modality, exercise type, exercise order, training frequency, age, and training status.
- However, concurrent training may attenuate gains in explosive strength, which is exacerbated when aerobic and strength training are performed within the same training session.

INTRODUCTION

The World Health Organization (WHO) published its updated guidelines on physical activity and sedentary behaviour in 2020 as part of their Global Action Plan on Physical Activity¹, highlighting the importance of regularly performing both aerobic and muscle-strengthening exercise². Specifically, the recommendations for adults include 150–300 minutes moderate- or 75–150 minutes vigorous-intensity aerobic exercise per week, and at least two weekly sessions of muscle-strengthening activities (i.e. strength exercise). The guidelines clearly emphasise additional health benefits if the aerobic training volume is further increased beyond 300 or 150 minutes, respectively².

Recommending both aerobic and strength training is important since these activities to some extent induce distinct adaptations and health benefits^{3,4}. For example, aerobic training promotes increased aerobic capacity (i.e. central adaptations) and metabolic changes of skeletal muscle, such as increased mitochondrial density and capillarisation⁵. Conversely, regular strength training results in muscle hypertrophy and increased strength and power⁶, but may also improve bone mineral density⁷. The role of skeletal muscle in health maintenance has received increased attention in the past decade, where muscle tissue is understood as a secretory organ, releasing several hundreds of myokines that are linked with the function of other organs, such as the brain, adipose tissue, bone, liver, gut, pancreas, vascular bed and skin⁸. In addition, the role of muscle power has recently been emphasised for its strong association with reduced risk of fall-related injuries in older adults⁹, which further underlines the importance of both muscle mass and function as an indicator of physical health and independency in daily life.

Aside from the health perspective, many sports require the athlete to simultaneously incorporate divergent training modalities, including aerobic and strength training, into their training regimen. Thus, considering that both athletes and recreational exercisers often perform relatively high volumes of aerobic exercise alongside resistance-type exercise, it is pertinent to revisit the compatibility of aerobic and strength training. Aerobic exercise has been shown to interfere with the development of maximal strength when the overall training volume is high¹⁰. In contrast, no interference on maximal strength was observed when the training volume was reduced to two weekly aerobic and strength training sessions, respectively^{11–13}. Importantly, however, even low volumes of concurrent aerobic training have been shown to diminish gains in rapid force production^{11,14}, which could translate into reduced muscle-power related benefits. Identifying additional moderators that influence neuromuscular adaptations to concurrent aerobic and strength training could further aid in fine-tuning exercise guidelines for health and/or fitness performance.

To date, scarce attempts have been made to quantitatively synthesise the literature concerning concurrent aerobic and strength training. The first meta-analysis conducted a decade ago by Wilson and colleagues showed that peak power was attenuated with concurrent training compared with strength training alone, while the development of muscle hypertrophy and maximal strength were not compromised¹⁵. A more recent meta-analysis aimed to compare the effect of concurrent aerobic and strength training with strength training alone on the development of maximal strength in untrained, moderately trained and trained individuals¹⁶. The results suggested that concurrent training may have a negative impact on lower body strength development in trained, but not in moderately trained or untrained individuals. While this study updated the information on the effect of training status on maximal strength development, it remains that several other key outcome variables related to muscle mass and function have not been collectively re-examined in a meta-analysis since 2012. Therefore, the aim of the current study was to systematically assess the compatibility of concurrent aerobic and strength training on adaptations in maximal strength, explosive strength, and muscle hypertrophy by means of pooled analyses. We also conducted subgroup analyses to examine

the impact of aerobic exercise type, training modality, exercise order, training frequency, age, and training status. An updated literature synthesis on this topic is relevant for physicians, physiotherapists, exercise scientists and sports practitioners when designing programmes aimed at developing both aerobic and strength qualities for health purposes, rehabilitation, and/or fitness performance.

METHODS

Systematic literature search

A systematic literature search was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and was registered with the international database of prospectively registered systematic reviews in health and social care (PROSPERO: CRD42020203777). The databases PubMed/MEDLINE, ISI Web of Science, Embase, CINAHL, SPORTDiscus and Scopus were systematically searched using a search string that was specifically adapted to the search-requirements for each database (Online supplemental table 2).

The search was conducted on the 12th of August 2020 and updated on the 15th of March 2021. The literature-search process was performed independently by two researchers and included saving the online search, removing duplicates and screening titles, abstracts and full texts. Possible conflicts were solved by consulting a third author. In addition, a grey literature search was performed by screening Google Scholar and the reference lists of previously identified eligible full texts. A flow-chart of the search process and the study selection is displayed in Figure 1.

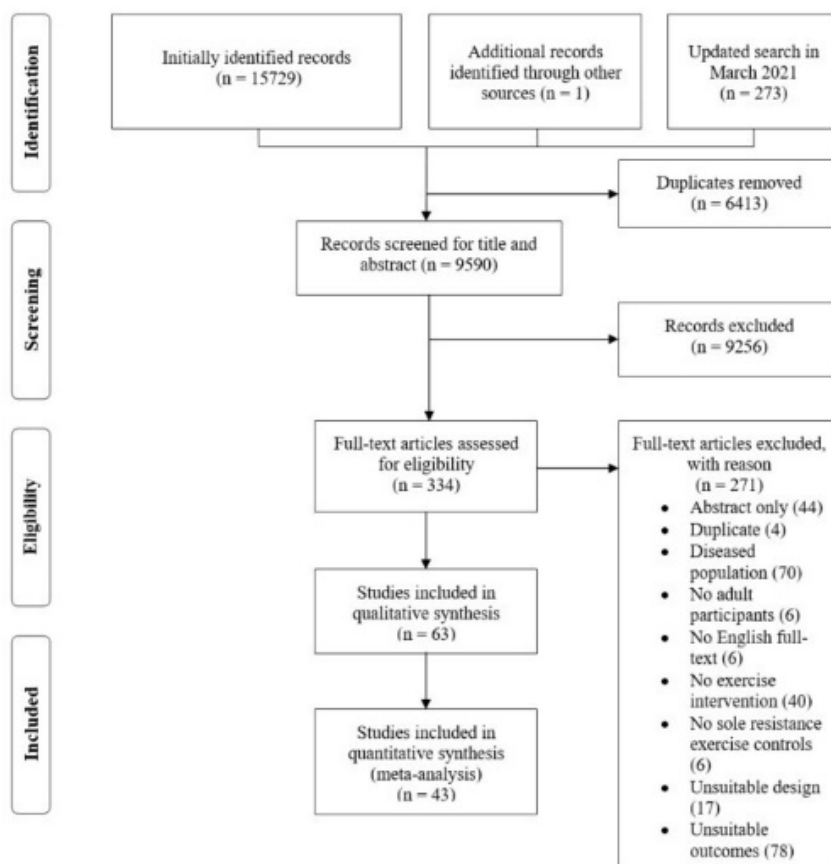


Figure 1. Flow-chart of the search process and the study selection.

Eligibility criteria

Inclusion criteria were defined based on the PICO criteria¹⁷. The population included healthy adults with no restrictions in terms of sex and age. The intervention had to be comprised of supervised, combined aerobic and strength training of at least 4 weeks. As a comparator, eligible studies needed to include a sole strength training group with matched strength training volume. The outcomes of interest were generally defined as maximal strength, explosive strength, and muscle hypertrophy. The included exercise tests had to be specific to the training performed. For maximal strength, both isometric and isoinertial measurements were accepted. As measures of explosive strength we accepted any form of jumping test, a measure of isometric rate of force development (RFD), or dynamic power assessments. For muscle hypertrophy we required objective measures of whole muscle cross-sectional area or muscle thickness (e.g. ultrasound, computed tomography (CT) or magnetic resonance imaging (MRI)). In addition, segmental lean mass assessed by dual-energy X-ray absorptiometry (DXA) was accepted if values were provided separately for the segments that were engaged in training. Exclusion criteria included language other than English or German, abstracts and theses, cross-sectional studies assessing only acute exercise responses and observational studies.

Data extraction

Data extraction was performed independently by two authors. The following data were extracted from each included study: (1) the general characteristics (e.g. author(s), year of publication and aim of the study); (2) participant information (e.g. sample size, training status and age); (3) intervention data for all groups (e.g. intervention duration, type of intervention); (4) specific outcomes (e.g. measures of maximal and explosive strength and hypertrophy). If the mean and standard deviation of the respective groups were not specified, authors of primary studies were contacted to request baseline and post-intervention data. In case data were presented within a graphic and no additional data were provided upon request, mean and standard deviation were extracted using WebPlotDigitizer (Pacifica, California, USA, Version: 4.4)¹⁸.

Data synthesis and analyses

Standardised mean differences (SMD) were calculated and an inverse variance-weighted random-effects model was fitted to the effect sizes (ES). Meta-analysis was performed using R (3.6.2), RStudio (1.2.5033) and the metafor package (version 2.4.0)¹⁹. Effect sizes were calculated for *pre-test post-test control group designs* using raw score standardisation recommended previously^{20,21}. Furthermore, exact sampling variance of the effect sizes was computed according to recommendations²⁰.

Heterogeneity (i.e. τ^2) was estimated using the restricted maximum-likelihood estimator (REML)²². In order to complete heterogeneity analyses, the Q-test for heterogeneity²³ and the I^2 statistic²⁴ were calculated in addition. Studentized residuals and Cook's distances were examined to assess whether studies may be outliers and/or influential²⁵. Studies with a studentized residual larger than the $100 \times (1 - 0.05 / (2 \times k))^{\text{th}}$ percentile of a standard normal distribution were declared potential outliers (i.e. using a Bonferroni correction with two-sided $\alpha = 0.05$ for k studies included in the meta-analysis). Studies with a Cook's distance larger than the median plus six times the interquartile range of the Cook's distances were considered influential. In case a study was identified as a potential outlier or overly influential, a sensitivity analysis was performed. A trim-and-fill-contour funnel plot was provided to estimate the number of studies potentially missing from the meta-analysis (Online Supplemental Figure 1). The rank correlation test²⁶ and the regression test²⁷, using the standard error of the observed outcomes as predictor, were used to check for funnel plot asymmetry.

Effect sizes from studies with more than two intervention or control groups were combined in accordance with the recommendations of the Cochrane handbook ²⁸, except for subgroup analysis when different interventions of single studies were included in separate subgroups. In the case of multiple measurements for the same outcome, only one measure was included in the analysis based on the following hierarchy. For maximal strength, 1) dynamic bilateral leg press, 2) squat, 3) unilateral isometric torque (knee extension) and 4) bilateral dynamic knee extensions. For explosive strength, 1) jump height and 2) other measurements of rapid force production as well as squat jump power and leg press power at 50% of maximal strength. For muscle hypertrophy, 1) whole muscle cross-sectional area of the quadriceps femoris muscles (i.e. panoramic ultrasound, CT, MRI), 2) muscle thickness of the *M. vastus lateralis*, 3) segmental DXA of the lower extremities. Thus, each study was included in the final analyses with only one parameter in order to avoid inflation of the weighting of individual studies.

Subgroup analyses were conducted for aerobic exercise type (i.e. cycling vs. running), concurrent training volume (i.e. low volume of 4.1 ± 0.3 vs. high volume of 6.1 ± 1.6 weekly sessions, relating to 2.0 ± 0.3 vs. 3.1 ± 0.6 weekly sessions in the sole strength training group), training status (i.e. untrained vs. active), mean age of the study population (18–40 years vs. >40 years) and training modality (i.e. different day concurrent training vs. same day concurrent training vs. same session concurrent training). For studies comparing same session concurrent training, if a sufficient number of studies was available we also compared the training order (i.e. aerobic before strength training vs. strength before aerobic training). Studies were placed into subgroups based on the description provided in the manuscript. This was especially true for training status, where studies were classified as “untrained” whenever participants were clearly described as “sedentary”, “previously untrained” or “inactive”. Conversely, all other studies were classified as “active” (i.e. “recreationally active”, “trained”, “well-trained” etc.). For specific justification of exclusion of individual studies, please refer to the Online Supplemental Table 2.

Assessment of methodological quality

The risk of bias assessment for the included studies was carried out using the PEDro scale independently by two reviewers. The PEDro scale has previously been rated as a valid measure of the methodological quality of randomised trials ²⁹. Studies with scores >6 were considered to be of “high-quality”, studies with scores 4–5 were considered to be of “medium-quality” and studies that scored <4 were considered to be of “low-quality”. The following sources of bias were considered: selection (sequence generation and allocation concealment), performance (blinding of participants/personnel), detection (blinding outcome assessors), attrition (incomplete outcome data), reporting (selective reporting), and other potential bias (e.g. recall bias). The risk of bias assessments for the included studies are shown in Online Supplemental Table 3. The mean score for the PEDro-scale criteria 2 – 11 was 4.3/10, i.e., medium quality.

RESULTS

Study characteristics

The database search identified 15,729 potentially eligible articles. After further screening and eligibility assessment, a total of 43 studies were included into the final analysis (Figure 1). The characteristics of studies, participants and training interventions are summarised in Supplemental Table 4. The meta-analysis included a total of 1,090 participants, of whom 590 participants performed supervised combined aerobic and strength training and 500 participants performed sole strength training. Of the included studies, cycling was the most common mode of aerobic exercise (24 studies), followed by running (16 studies). Additionally, the combination of running and cycling, rowing and continuous repeated leg extensions were assessed by one study, respectively.

Maximal strength

The final analysis included 37 studies^{10–12,30–63}, including 525 participants performing combined aerobic and strength training and 442 participants performing sole strength training. The observed SMD ranged from -1.37 to 1.99. The estimated average SMD based on the random-effects model was -0.06 (95% CI: -0.20, 0.09, $p = 0.446$) (Figure 2). According to the Q-test, there was no significant heterogeneity in the true outcomes ($Q(36) = 32.591$, $p = 0.632$, $\hat{\tau}^2 = 0.000$, $I^2 = 0.00\%$). An examination of the studentized residuals showed that there was no indication of outliers in the context of this model, and none of the studies were overly influential. The subgroup analyses revealed no statistical differences ($p > 0.05$) (Online Supplemental Figures 2-7).

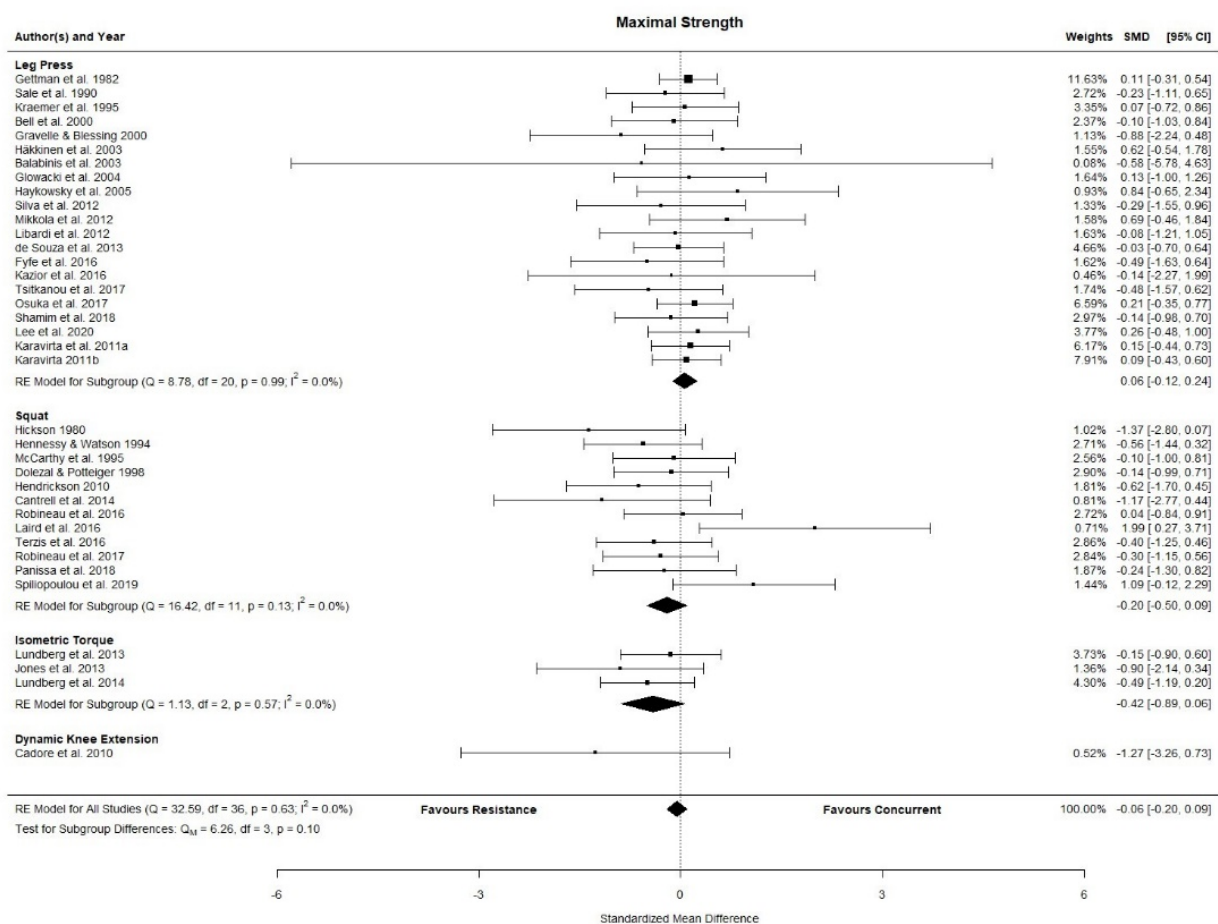


Figure 2. Forest plot of studies comparing differences in maximal strength. SMD = standardised mean difference; CI = confidence interval.

Explosive strength

The final analyses included 18 studies^{12,32,37,38,41,48,50–53,55,57–59,61,62,64,65}, with 270 participants performing combined aerobic and strength training and 208 participants performing sole strength training. The observed SMD ranged from -1.60 to 0.22. The estimated average SMD based on the random-effects model was -0.28 (95% CI: -0.48, -0.08, $p = 0.007$) (Figure 3). According to the Q-test there was no significant heterogeneity in the true outcomes

($Q(17) = 26.675$, $p = 0.068$, $\hat{\tau}^2 = 0.068$, $I^2 = 35.81\%$). The studentized residuals indicated Mikkola et al. (2012) ⁶² as a potential outlier that may be overly influential. The sensitivity analyses revealed that by excluding this study the amount of observed heterogeneity was reduced to $I^2 = 0.00\%$ ($Q(16) = 13.860$, $p = 0.061$, $\hat{\tau}^2 = 0.061$).

The subgroup analyses revealed no statistical differences ($p > 0.05$) (Online Supplemental Figures 8-11). When grouping the studies according to aerobic exercise type, the SMD was significant in favour strength training in cycling -0.44 (95% CI: $-0.86, -0.01$, $p = 0.043$) but not running (Supplemental Figure 8). However, after removing the overly influential study by Mikkola et al. (2012) ⁶² this effect was no longer observed (SMD: -0.27 , 95% CI: $-0.58, 0.04$, $p = 0.086$). A similar effect was also shown for low concurrent training volume, with an initial SMD of -0.45 (95% CI: $-0.87, -0.02$, $p = 0.039$) in favour of the sole strength training group (Online Supplemental Figure 9). After removal of the study by Mikkola et al. (2012) ⁶² this was reduced to -0.25 (95% CI: $-0.50, 0.01$, $p = 0.059$). Conversely, when studies were grouped according to training mode, a significant interference effect was observed for studies performing concurrent training within the same session (≤ 20 minutes between aerobic and strength training) (SMD: -0.31 , 95% CI: $-0.62, -0.01$, $p = 0.043$) but not when concurrent training was separated by at least 3 hours (Online Supplemental Figure 11).

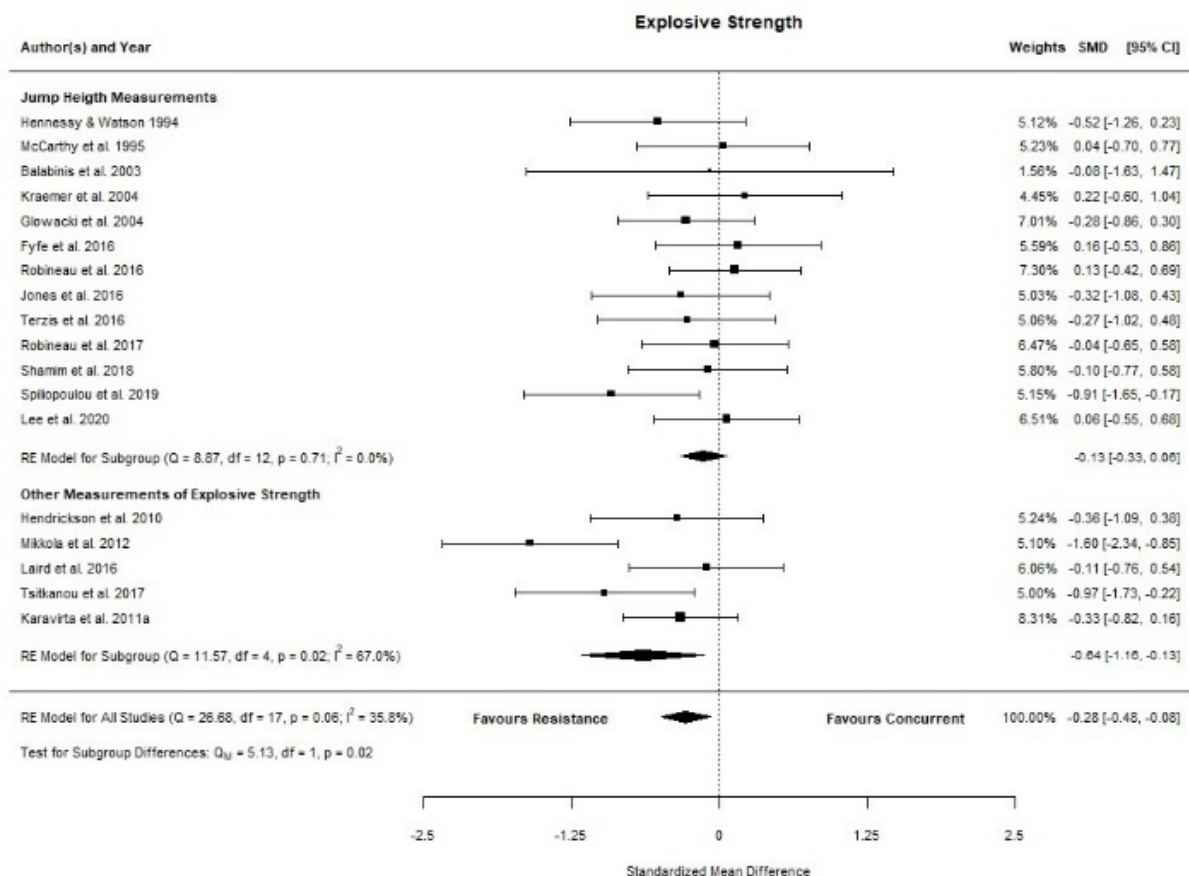


Figure 3. Forest plot of studies comparing differences in explosive strength. SMD = standardised mean difference; CI = confidence interval.

Muscle hypertrophy

The final analyses included 15 studies ^{11,12,31,44-46,48,53,54,58,61,66-69}, including 201 participants performing combined aerobic and strength training and 188 participants performing sole strength training. The observed SMD in the individual studies ranged from -0.67 to 0.28. The estimated average SMD based on the random-effects model was -0.01 (95% CI: -0.16, 0.18, $p = 0.919$) (Figure 4). According to the Q-test there was no significant heterogeneity in the true outcomes ($Q(14) = 4.687$, $p = 0.990$, $\hat{\tau}^2 = 0.000$, $I^2 = 0.00\%$). An examination of the studentized residuals showed that there was no potential outlier in the context of this model. According to the Cook's distances no study could be considered overly influential. The subgroup analyses revealed no statistical differences ($p > 0.05$) (Online Supplemental Figures 12-14).

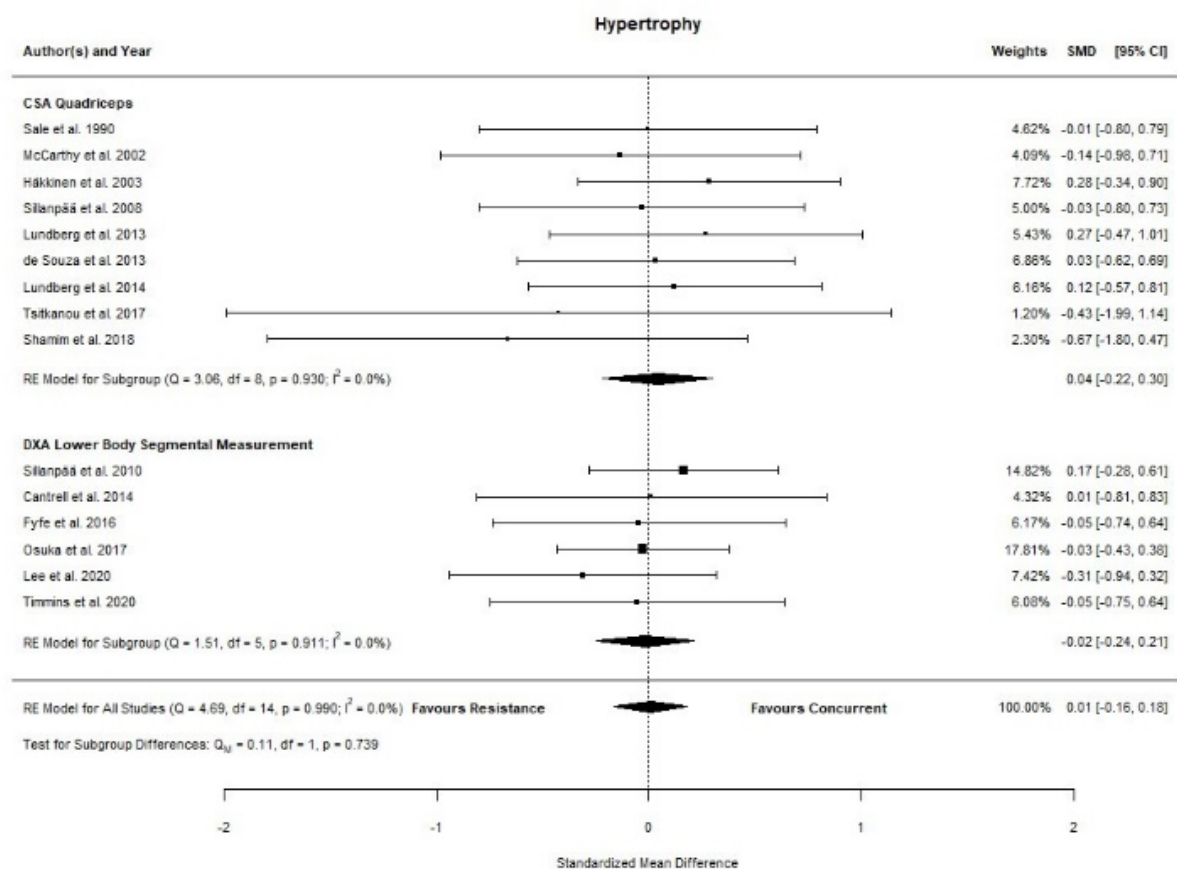


Figure 4. Forest plot of studies comparing differences in muscle hypertrophy. SMD = standardised mean difference; CI = confidence interval.

DISCUSSION

The recent updated physical activity guidelines from the WHO, which encourage all adults to perform concurrent aerobic and strength training, place a strong emphasis on the dose-response relationship between exercise volume and health benefits with little discussion of the compatibility of contrasting exercise modalities. Likewise, whether concurrent exercise can be performed by athletes without compromising strength adaptations is still a matter of debate. We therefore conducted a comprehensive meta-analysis to provide systematic and evidence-based appraisal on whether aerobic training interferes with adaptations to strength training in terms

of muscle function (maximal and explosive strength) and muscle mass. In addition, we assessed the impact of important mediating covariates such as aerobic exercise type, training modality, exercise order, training frequency, age, and training status. The main finding was that concurrent aerobic and strength training, compared with volume-matched isolated strength training, does not interfere with maximal strength development and muscle hypertrophy. However, the development of explosive strength was negatively affected by concurrent training. Our subgroup analysis revealed that this negative affect was exacerbated when concurrent training was performed within the same session as compared to when aerobic and strength training was separated by at least 3 hours.

An important goal of this meta-analysis was to deliver evidence that may be translated into optimised and fine-tuned exercise recommendations for fitness and health purposes. Our results generally support the benefits of including both aerobic and strength training into the same training programme, especially in terms of maximal strength gains and muscle hypertrophy. While our findings generally are in line with those reported by Wilson et al. a decade ago¹⁵, these authors considered anaerobic performance measures such as Wingate performance as indicators of explosive strength. Since we purposefully included only direct measures of explosive strength (i.e. jump performance, isometric rate of force development and dynamic leg press power), our findings reinforce that concurrent aerobic and strength training may compromise strength qualities requiring rapid neural activation.

The mechanism for compromised explosive, but not maximal strength is interesting and warrants further research. Our findings are supported by an early study showing that muscle hypertrophy and maximal strength were uncompromised by concurrent training, while rate of force development was blunted, likely due to interference in rapid voluntary neural activation¹¹. More specifically, while the maximal neural activation was not compromised, the increase in the integrated Electromyographic signal (iEMG) during the first 500 ms was attenuated in the group performing both aerobic and strength training. As the speed of recruitment and maximal discharge of motor neurons largely determine the maximal rate of force development⁷⁰, it seems that motor unit recruitment and discharge speed are particularly sensitive to the interference effect from aerobic training. It could be speculated that residual fatigue induced by aerobic training affects the corticospinal inputs received by the motor neurons before force is generated, which would subsequently compromise rapid force generation. The latter may potentially reduce the quality but not the quantity of the strength training sessions performed concurrently with aerobic training, and thereby possibly reduce the development of explosive strength but not maximal strength or muscle hypertrophy. This, in turn, may have implications for programme design as it appears that concurrently improving both cardiorespiratory fitness and rapid force production through rather generic exercise recommendations is physiologically challenging.

In line with this, our subgroup analysis revealed that the magnitude of interference in explosive strength development was dependent on the programming of exercise sessions, with significant interference being observed when aerobic and strength training were performed within the same training session. Previous studies have indicated that neuromuscular interference may be more pronounced when strength training is immediately preceded by aerobic training both in young⁷¹ and older individuals⁷². Our pooled analysis, however, does not provide evidence for an order-specific effect but rather highlights that combining aerobic and strength training within close proximity attenuates adaptations in explosive strength irrespective of the exercise order. Apart from limitations in rapid neural drive¹¹, previous studies have also indicated that adaptations in pennation angle and fascicle length⁵³ or patella tendon cross-sectional area⁷³ could be possible mechanistic explanations for these findings.

The moderators, including training volume, type of exercise, age, and training status, neither significantly influenced adaptations in maximal and explosive strength, nor muscle hypertrophy. Thus, our results differ from the recently published meta-analysis focusing solely on the effect of training status on maximal strength during concurrent training¹⁶. In that study the 1RM for leg press and squat exercise was negatively affected by concurrent training in trained individuals but not in moderately trained or untrained individuals compared with strength training alone. Moreover, their subgroup analysis suggested that the negative effect observed in trained individuals only occurred when aerobic and strength training were conducted within the same training session. However, due to lack of consistent reporting we decided not to group active participants into moderately or well-trained athletes and this may have diluted possible significant effects. Furthermore, albeit the exact calculations were not published by Petré et al. 2021¹⁶, their analysis appears to differ from our approach. Apart from the fewer number of studies included (27 vs. 37 studies), studies consisting of multiple intervention groups with only one comparator were included multiple times within the same analysis, potentially inflating power⁷⁴. However, although the results did not reach statistical significance, our subgroup analysis for training status indicated a similar direction for the SMD in trained compared to untrained participants as reported by Petré et al.¹⁶.

In previous concurrent training research, numerous studies have focused on the potential interference mechanisms in terms of muscle hypertrophy⁷⁵. The rationale for these studies stem from rodent and cell models indicating a possible inhibition of mechanistic targeted of rapamycin (mTOR) signalling through activation of the AMP-activated protein kinase (AMPK) following aerobic training⁷⁶⁻⁷⁹. However, subsequent human studies have failed to confirm these findings when exploring physiological mechanisms such as metabolic stress and AMPK activation^{68,80} or protein synthesis⁸¹ following concurrent training. Based on our systematic review, this is not surprising given that none of the identified studies reported a significant interference effect on muscle hypertrophy. While Wilson et al. concluded from their subgroup analysis that there was a negative relationship between the effect size for hypertrophy and both the aerobic training frequency and duration¹⁵, our results do not confirm these observations. There are several potential explanations for this disagreement apart from the obvious fact that our analysis was done almost a decade later and thus included more studies. First, the inclusion criteria differed since Wilson et al. included fibre hypertrophy as an outcome parameter and studies without a sole strength training control group were also included. Secondly, in the analytical approach we performed our analysis based on an inverse variance-weighted random-effects model in a pre-test post-test control group design¹⁹, whereas Wilson et al. estimated effect sizes of every individual group, leading to a total of 72 effect sizes for muscle hypertrophy. The reported aerobic training duration and intensity were then correlated with the effect sizes, potentially leading to significant positive correlations.

While the current meta-analysis provides updated and novel information, there are some limitations that should be acknowledged. Meta-analyses are generally limited to the information provided within the included individual studies. Even though authors have been contacted with requests of additional information, the response rate was low. Therefore, to avoid speculations we decided to include only clearly defined moderators. For example, aerobic training intensity was not included due to the lack of consistent reporting within the included studies. Yet, it is possible that aerobic training intensity may impact the compatibility of aerobic and strength training. A previous meta-analysis explored the effects of concurrent high-intensity interval training (HIIT) and strength exercise and reported that lower-body strength development was compromised by concurrent training compared with strength training alone, even though the authors noted that any possible negative effect on lower body strength may be ameliorated by incorporating running-based HIIT and longer inter-modal rest periods⁸². This was further supported by a recent narrative review reporting that HIIT may minimise the risk for

neuromuscular interference and that this effect is further pronounced when HIIT is replaced by sprint-interval training⁸³. However, it should be acknowledged that based on previous research the overall health benefits of concurrent training other than muscle function and size appear to be greater than those achieved with single-modality training of either aerobic or strength training in isolation^{84,85}, and the overall risk of interference effects is rather low. Thus, most individuals, including recreational athletes, can enjoy complementary benefits from including both aerobic and strength training into their training programme.

In summary, this updated meta-analysis shows that concurrent aerobic and strength training does not interfere with the development of maximal strength and muscle hypertrophy, compared with strength training alone. However, the notion of reduced development of explosive strength with concurrent training, especially when aerobic and strength training is performed within the same session, suggests that practitioners prioritizing explosive strength could benefit from separating aerobic and strength training bouts to achieve optimal adaptations.

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COMPETING INTERESTS

The authors do not have competing interests to declare.

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