Title: Youths are less susceptible to exercise-induced muscle damage than adults; a systematic review with meta-analysis

Running head: Youth versus adult EIMD

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Abstract

Purpose; This meta-analysis aimed to 1) provide a comparison of peak changes in indirect markers of EIMD in youths versus adults and 2) determine if the involved limb moderated this effect. Method; Studies were eligible for inclusion if they 1) provided a human youth versus adult comparison, 2) provided data on muscle strength, soreness or creatine kinase (CK) markers beyond ≥ 24 hours, 3) did not provide a recovery treatment. Effect sizes (ES) were presented alongside 95% confidence intervals. Results; EIMD exhibited larger effects on adults than in youths for muscle strength (ES=-2.01; $P<0.001$), muscle soreness (ES=-1.52; $P<0.001$) and CK (ES=-1.98; $P<0.001$). The random effects meta-regression examined the effects of upper- and lower-limb exercise in youths and adults was significant for muscle soreness (coefficient estimate =1.11; $P< 0.001$) but not muscle strength or CK (P>0.05). As such, the between-group effects for muscle soreness (ES=-2.10 versus -1.03; P<0.05) were greater in the upper- than lower-limb. Conclusion; The magnitude of EIMD in youths is substantially less than their adult counterparts, and this effect is greater in upper- than lower-limbs for muscle soreness. These findings help guide practitioners who may be concerned about the potential impact of EIMD when training youth athletes.

1. Introduction

There is a considerable volume of evidence recommending that youths engage in physical activity and long-term athletic development programs (29,46,47). Current guidelines suggest that youths should perform an average of 60 minutes of moderate to vigorous daily physical activity (61). Engaging in physical activity can improve health related outcomes, reduce injury risk, and positively influence fitness variables (1,2,29,57). For youth athletes, fitness variables are, for the most part, positively influenced by the maturation process (57,58) and can be further enhanced by engagement in a variety of strength, hypertrophy, power, speed, and agility training methods (47).

Notwithstanding the positive adaptations that can occur through training, exercise-induced muscle damage (EIMD) occurs if the exercise mode or intensity is novel, high in volume, or eccentrically biased (8,21,30,31,76,77). Though greater in more mature individuals, EIMD occurs irrespective of the maturity status in youths (20,36,73). The "popping-sarcomere hypothesis" (59) proposes that an increased stress per myofibre during eccentric contractions causes non-uniform lengthening of the sarcomeres whereby weaker ones extend beyond their myofilament overlap and fail to re-interdigitate (38,59). Thereafter, disruptions to calcium homeostasis lead to excitation–contraction coupling failure and a prolonged loss of muscle strength and other associated symptoms (15,38,59). Independent of age and maturity, EIMD can manifest in its symptoms which include reductions in muscle function (e.g., strength and power), elevated muscle soreness and pain, and increased intramuscular enzymes in the blood (e.g., creatine kinase; CK; (15)). These symptoms frequently peak between 24 and 48 hours after the initial exercise bout and are recovered (i.e., returned to baseline values) by seven days post-exercise (15,30,31,38,76,77). Moreover, symptoms are highly individualised, not synchronous (35,50), and have been suggested to differ according to age and maturity status (3,12,44).

The magnitude of EIMD is attenuated when individuals possess prior experience of eccentric exercise (37,54). This protection is known as the repeated bout effect (RBE) and is underpinned by neural, mechanical, and biomechanical adaptation after an initial bout of exercise (37,54) and can last up to 6 months (63). Although the RBE has been demonstrated across the lifespan, its effect appears more evident in adults than youths (32,51). This is likely because extent of the RBE is related to the initial magnitude of EIMD with several studies reporting that adults experience greater EIMD than youths (3,12,17,19,32,44,51,72,74). A recent narrative review (26) also concluded that practitioners working with youths populations need not have undue concerns about EIMD due to the lower magnitude they experience. Drury et al. (26) proposed that eccentric training, which induces the most severe EIMD, in youths should be considered a necessity due to the performance-related and injury-protecting benefits. However, strength and conditioning coaches deem scheduling as the most frequent barrier to the implementation of eccentric exercise in youths (25), perhaps due to the perception that EIMD may occur as consequence or the practicalities of implementing such training.

Previous studies in adults have repeatedly shown that the upper-limb is more susceptible to EIMD than the lower-limb (11,13,39,49,62,70). The greater susceptibility of fast-twitch muscle fibres to EIMD, and greater percentage of this fibre type in upper-limbs compared to lower-limb might explain these differences (39,70). Moreover, the daily use of the lower-limb is greater than the upper-limb, and these muscles (i.e., the lower-limb) habitually undergo more eccentric contractions (e.g., downhill walking, walking downstairs), thus a greater protective RBE is elicited (37). Regardless of the mechanism, it is unknown whether the protective effect is greater in adults compared to youth. Such information would be useful to applied practitioners when scheduling upper- and lower-limb exercise that is novel, eccentrically biased, or high-volume. However, whilst individual investigations comparing EIMD in youths and adults exist, a systematic and rigorous pooled statistical analysis of these data has not been conducted. This is an important issue when planning and programming training for youth, as the distinct biological differences mean that youths cannot be treated the same as adults. That EIMD impairs markers of sports performance (e.g., strength and power, change of direction; (31,33) might also have implications for training and competition (22). Therefore, the present paper sought to meta-compare indirect markers (muscle strength, muscle soreness/pain and CK) of EIMD in youths and adults. A secondary aim was to determine if peak changes in EIMD were different between the upper- and lower-limb in youths versus adults.

2. Methods

This systematic review with meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (66). The literature search was performed by three authors (JFTF, LJW and AFD) with the data extraction and verification performed by two authors (JFTF and LJW).

2.1 Literature search

A systematic search, with no date restrictions, was performed on Google Scholar, PubMed, and Sport Discus in July 2022. Only peer-reviewed articles written in the English language were considered. Using Boolean logic the following terms were searched for in article title, abstracts and keywords; "paediatric" OR "youth" OR "children" OR "adolescent" OR "maturation" AND "muscle damage" OR "exercise-induced muscle damage" OR "exercise-induced muscle injury" OR "contraction-induced injury" OR "muscle soreness" OR "delayed onset muscle soreness" OR "creatine kinase". When selecting studies for inclusion, all relevant article titles were reviewed before an examination of article abstracts and then, full published articles. After the formal systematic searches, additional searches of the eligible papers were conducted. The search process is outlined in Figure 1.

2.2 Eligibility criteria

The following criteria were used to determine the eligibility of studies for the meta-analysis; 1) provided a youths (<18 years) versus adult (≥18 years) comparison, 2) provided muscle strength, muscle soreness/pain or CK markers to at least 24 hours post-exercise, 3) did not provide a recovery aid or strategy (e.g. cold-water immersion; [control groups were included providing they did not receive treatment]) and 4) was conducted in humans. Alterations within 24 hours of exercise could be due to transient fatigue (7), therefore studies were only included if they provided indirect markers of EIMD ≥ 24 hours after the exercise bout.

2.3 Data extraction

Using a standardised form in Microsoft Excel, data were extracted by two reviewers (LJW and JFTF). Any disagreements were resolved via consensus. Where data were not numerically reported, and only visualised, authors were contacted. In the case of authors not responding, ImageJ software was used to manually extract the data (71). Data were extracted on any baseline and post-EIMD measures of muscle strength, muscle soreness/pain and CK. Biometric and physical activity characteristics of the participants, as well as the EIMD bout were also extracted. Note that it was not possible to extract or retrieve CK data from Chen et al. (12). Muscle soreness data in Dos Santos et al. (23) were presented as median values and it was not possible to retrieve the data. Any data reported as standard error were converted to standard deviation for analysis. As differences at baseline were expected between youths and adults for muscle strength, the peak percentage change from baseline was entered for analysis. The standard deviation of the change was calculated as:

$$SD\ of\ the\ change = \sqrt{(a^2 + b^2)} - (2correl. \times a \times b)$$

Equation 1. a = baseline SD; b = peak SD; and correl. = the Pearson's correlation between baseline and 24h post-EIMD muscle strength (r = 0.94) in Fernandes et al. (30).

Where studies implemented multiple youths groups, both were included for analysis (12,44). Previous work (40) has raised concerns that including multiple groups from the same study within a meta-analysis could ignore the within-study correlation. However, the differences in age and maturity of the groups (see Table 2) in Chen et al. (12) and Lin et al. (44) indicate distinct physical and physiological differences which warrant their inclusion. As per the suggestion of Kadlec et al. (40) multiple variables were not included in the same analysis, e.g., both concentric and isometric strength into the muscle strength analysis. Finally, a *post-hoc* ‘quality check’ (i.e., a sensitivity analysis) was performed by individually removing the younger/less mature and then older/more mature groups from each indirect EIMD marker analysis. For muscle strength the removal of the younger/less mature group resulted in a minimal qualitative (i.e., the magnitude, not the direction) effect size change (from -2.01 to -1.78), whilst the removal of the older/more mature group did not alter effect size. For muscle soreness and CK the removal of each group did not change the magnitude of the effect. The authors believe this justifies the inclusion of these groups.

2.4 Analysis and interpretation of results

Jamovi (version 2.3.0.0, MAJOR package) was used to conduct the meta-analysis. Means and standard deviations of baseline and post-exercise markers of EIMD were used to calculate the standardised mean difference (SMD). SMDs expressed the intervention effect within each study using a restricted maximum-likelihood model estimate (42). An inverse-variance random effects model for meta-analyses was used as it allocates a proportionate weight to trials based on the size of their standard errors (16) and facilitates analysis whilst accounting for heterogeneity across studies. Effect sizes are given as SMD and 95% confidence intervals (CIs). The following qualitative criteria were used to interpret the ES; 0.2 = trivial; 0.2–0.59 = small, 0.6–1.19 = moderate, 1.2–1.99 = large, 2.0–3.99 = very large, > 4.0 = extremely large (34). To assess the degree of heterogeneity amongst the included studies, the I^2 statistic was employed. This represents the proportion of effects that are due to heterogeneity as opposed to chance (43). Low, moderate, and high heterogeneity correspond to I^2 values of 25, 50, and 80%, respectively. A random-effects meta-regression with moderator analysis was employed to establish the influence of the involved limb segment (i.e., upper- or lower-limb) on the magnitude of indirect markers in adult and youth. Alpha was set at ≤ 0.05.

2.5 Quality assessment and risk of bias

The quality of the included studies was determined using the National Institute of Health's Quality Assessment Tool for Before-After (Pre-Post) Studies with No Control Group (60). The assessment tool analyses the following domains 1) study question is clearly stated; 2) eligibility is prespecified and clearly described; 3) study subjects are representative of those who would be of interest; 4) eligible subjects were enrolled; 5) sample size is sufficiently large; 6) intervention is clearly described and evenly applied to subjects; 7) outcome measures prespecified, clearly defined, valid, reliable; 8) assessors were blind to the intervention/outcomes; 9) subject loss was less than 20%; 10) statistical measures assessed pre to post changes; 11) outcome measures were taken multiple times; 12) statistical analysis took into account group level data. Two reviewers (LJW and JFTF) conducted the quality assessment independently with any disputes settled by a third reviewer (LDH).

3. Results

3.1 Study selection

Results from the three database searches identified 744 articles, 74 of which were duplicates (Figure 1). A total of 414 articles were removed after the screening of titles and abstracts, leaving 257 articles available for full text inspection. The authors attempted to retrieve 257 studies and were successful in retrieving and assessing 255 for eligibility. Of the 255 screened, 11 full text manuscripts were included within the final quantitative synthesis. As Dos Santos et al (23) only presented the median data, this study was not included within the meta-analysis.

[INSERT FIGURE 1 HERE]

Figure 1. PRISMA Flow diagram displaying inclusion and exclusion of studies

3.2 Study characteristics

The National Institute of Health Quality Assessment Tool resulted in a mean score of 9.5 ± 0.5. Individual assessments can be found in Table 1 as can the study characteristics. On completion of data pooling, 13 comparisons (from 11 individual studies) were included in the analysis; nine included a marker of muscle function, 11 included a marker of muscle soreness and nine measured creatine kinase. A total of 157 youths and 136 adults were included in the meta-analysis consisting of 49 girls, 108 boys, 35 women and 101 men. Nine comparisons included males only, three studies compared females only and one both males and females. Eight comparisons investigated EIMD in the lower-limb, with the remaining five reporting on EIMD in the upper-limbs. The EIMD interventions included were highly varied; five utilised dynamometry based resistance exercise, three jumping based exercise, two traditional resistance exercise and one aerobic exercise. For both groups peak change in muscle strength occurred at 24 hours in seven of the nine comparisons. In Soares et al. (72) peak muscle strength loss occurred at 48 hours for adults and 72 hours for youth. Gorianovas et al. (32) reported peak muscle strength loss in both groups at 48 hours. Both studies did not measure muscle strength at 24 hours. Muscle soreness peaked at 24 hours in six of the 11 comparisons (for both groups) and at 48 hours in four comparisons (for both groups). In Soares et al (72) peak soreness occurred at 48 hours for adults, and 72 hours for youth. For both groups, CK peaked at 24 hours in three studies, 72 hours in three studies and 96 hours in two studies. In Arnett et al. (3) CK peaked at 24 hours in youths and 72 hours in adults.

[INSERT TABLE 1 AND 2 HERE]

3.3 Exercise-induced muscle damage in youths versus adults

The effects of exercise on muscle strength, muscle soreness and CK are shown in Figure 2. Exercise-induced muscle damage exhibited large and very large effects between adults than in youths for muscle strength (ES = -2.01; 95%CI -2.95,-1.07; Z = -4.20; *P* <0.001), muscle soreness (ES = -1.52; 95%CI -2.15, -0.90; Z = -4.76; *P* <0.001) and CK (ES = -1.98; 95%CI -2.93, -1.04; Z = -4.13; *P* <0.001), indicating greater changes in adults than youths. Heterogeneity was high for all analyses (I^2 = 79-89%), justifying the use of a random effects model. For all analyses the trim and fill method suggested that no studies needed to be removed to reduce publication bias.

[INSERT FIGURE 2 HERE]

Figure 2. Forest plot of studies examining peak changes in muscle strength (A), muscle soreness (B), and creatine kinase (C) after EIMD in youths and adults. Data are presented as the percentage weight each study contributes to the pooled SMD, individual SMD [95% CIs]. Note that symbol size of individual studies is representative of the weighting for the pooled standardised mean difference. The filled diamond indicates overall SMD. RE = random effects. model.

[INSERT FIGURE 3 HERE]

Figure 3. Funnel plots for studies evaluating peak changes in muscle strength (A), muscle soreness (B), and creatine kinase (C) after EIMD in youths and adults.

3.4 Moderator analysis

A random effects meta-regression examined the effects of upper- and lower-limb exercise on muscle strength (coefficient estimate = -0.07; 95% CI range = -2.12 to 1.966; *P* = 0.945) and CK (coefficient estimate = 1.01; 95% CI range = -0.001 to 2.213; *P* =0.285) changes in youths and adults and indicated no relationship. As such the large difference between groups was comparable for the upper- and lower-limbs (see Table 3) and displayed high heterogeneity.

The random effects meta-regression comparing upper- and lower-limb exercise on muscle soreness (coefficient estimate = 1.11; 95% CI range = -0.001 to 2.213; *P* = 0.05) in youths and adults indicated significant relationships. As such, the between-group effects for muscle soreness (SMD = -2.10 versus -1.03; both P <0.05) were heterogenous and greater in the upper- than lower-limb whilst still confirming the main analysis (i.e., greater changes in adults than youth).

[INSERT TABLE 3 HERE]

4. Discussion

It is well documented that EIMD routinely occurs because of strenuous or novel exercise, particularly after eccentrically biased actions. Whether a differential EIMD response is evident in youths compared to adults is yet to be fully elucidated. Therefore, the aim of this meta-analysis was to compare peak perturbations of indirect markers of EIMD in youths and adults after muscle-damaging exercise, and to determine if these perturbations between groups are different in the upper- and lower-limb. The key findings from this study demonstrate that after EIMD; 1) youths experience smaller changes in peak indirect markers of EIMD compared to adults and, 2) the age effect for muscle soreness and CK is greater in the upper- than lower-limb. The present study adds meta-analytical confirmation to the literature on the effect of age on EIMD. These data are encouraging for practitioners concerned about the negative impact of EIMD on youth athletes' performance and quality of training. A better understanding of the magnitude of EIMD symptoms in youth athletes can help practitioners in managing these symptoms potentially using recovery aids or changes in scheduling and programming of training.

While the finding that adults exhibit greater peak decrements in muscle strength than youths after muscle-damaging exercise is not novel, our study is the first to offer a pooled analysis on such data and a meta-analytical magnitude of effect (i.e., very large) to the knowledge base. Unfortunately, we are unable to provide insight into the underpinning physiological mechanism(s) evoking such age-related effects. In some studies, despite standardised *relative* intensity (i.e., number of body mass vertical jumps), youths would experience a reduced *absolute* mechanical stimulus because of a lower body mass resulting in small symptoms of EIMD (32,51). Another possible explanation is that due to the reduced body mass of youths compared to adults, less force is generated per muscle fibre unit during concentric and eccentric contractions, resulting in a smaller amount of structural muscle damage after exercise (18,32,51,74). This is supported by the finding that although absolute strength decrements are larger in adults, this relationship is attenuated or reversed when strength data are presented relative to body mass (18). Youths also exhibit increased flexibility compared to adults (51). This leads to greater relative strength at longer muscle lengths (51), suggesting the popping sarcomere hypothesis of muscle damage would be less evident at a given joint angle for youths compared to adults (52). Differential responses may also be related to muscle fibre characteristics in that fast-twitch (i.e., type II) muscle fibres are proposed to be more susceptible to damage and preferentially disrupted during eccentrically biased exercise (44). Given that youths tend to have a higher proportion of slow-twitch muscle fibres and fewer fast-twitch fibres, their skeletal muscles may be less susceptible to EIMD, resulting in a smaller strength decrement post-exercise (51). A lower maximal volitional muscular force in youths compared to adults, even when accounting for body- and muscle-size differences (5) might reduce their capacity to recruit fast-twitch motor units (24) and thus attenuates EIMD magnitude. Furthermore, within a group of youth athletes, maturity status may also affect EIMD symptoms and recovery. In the present meta-analysis, six of 11 studies assessed maturity status, and only two studies compared maturity status against adults (12,44). Given that maturation can result in significant changes in physiology and physical qualities (e.g. increases in body mass, muscle mass, limb-lengths, absolute strength) (1,2,56,58) this is something that future studies must consider. Nonetheless, practitioners should be aware that youths exhibit reduced losses in muscle strength after EIMD than their adult counterparts. These findings suggest that training which requires high force contractions (e.g. resistance exercise, sprinting) should be avoided in the presence of EIMD as the quality of these is likely to be reduced. Similarly, the reductions in muscular strength with EIMD negatively affect markers of sports performance ((31,33), thus novel or eccentrically biased exercise should be avoided close to competitions.

Our meta-analysis indicates that youths experience lower peak increases in muscle soreness than adults with EIMD, with the magnitude of the difference deemed large. In addition to structural damage, muscle soreness can also result from connective tissue damage and inflammation (38). Many of the mechanisms discussed above which are responsible for smaller strength decrements are also likely to contribute to less muscle soreness experienced by youths compared to adults. Youths may also experience less soreness as they are less susceptible to microdamage of the connective tissue around the working joints. It has been reported that musculo-tendinous stiffness is lower in youths compared to adults (41). During exercise, the reduced musculo-tendinous stiffness leads to a more 'compliant' tendon (51) that can then act as a buffer to reduce mechanical strain on both fascicles and muscle fibres (44). This finding is practically meaningful as increased muscle soreness can result in decreased physical activity adherence (55). Indeed, physical activity has physical, mental, and social benefits of exercise (69) and withdrawal from physical activity can negate these benefits. Given younger individuals experience less muscle soreness with EIMD, they are more likely to continue with subsequent physical activity and may require less recovery time between exercise bouts compared to adults. This would be pertinent to applied practitioners developing periodised training programmes for youth athletes, particularly during competition phases or when in-season. However, the potential for negative consequences of exercise (e.g., non-functional overreaching, overtraining) are still present in youths (53,75) and repeated exposure to EIMD with insufficient recovery could lead to this. Practitioners should ensure that youths' physical activity experiences are positive, so that their well-being and adherence to long-term participation are maximised (64).

Increases in CK concentration are commonly used as proxy measures for structural skeletal muscle damage (4). Findings from the present study reveal large differences in CK after exercise with youths experiencing lower peak CK increases compared to adults. However, it is well-reported that resultant CK is modified by several factors including sex, ethnicity, maturation, and age (4), and exhibits large inter-individual variation (9). Therefore, CK results reported herein should be interpreted with caution (6), although in conjunction with the strength and soreness data it could be inferred that a lower CK activity also reflects a smaller magnitude of EIMD observed in youths compared to adults after eccentrically biased or novel exercise. Notwithstanding the issues surrounding CK's ability to reflect the magnitude of damage experienced by an individual, increased CK represents a greater cell membrane disruption after the initial insult (15,38). It is probable that youths experience less cell membrane disruption for the reasons already outlined such as reduced mechanical load, increased flexibility, greater proportion of slow-twitch muscle fibres, and reduced muscle fibre activation. These factors would result in a reduced structural damage and resultant cell membrane disruption, translating to a lower peak CK activity in youths than adults. Whilst this finding is important to note from a mechanistic perspective, the practical utility of these data is limited. It is unlikely that practitioners working with youth athletes would routinely use invasive measures such as blood sampling to monitor training, report on recovery status, or programme physical activity.

Moderator analysis revealed effects that were greater for the upper-limb for muscle soreness than for the lower-limb. Essentially, although both youths and adults will be experience EIMD, the magnitude of the difference between groups is larger after upper-limb exercise than lower-limb exercise in adults than in youth. This finding supports previous literature (13,39,70) however, no study has reported on the susceptibility to upper- and lower-limb exercise between adults and youth. The mechanisms underpinning these observations remain unclear. It is plausible that daily activities that youths engage in include a greater amount of upper-limb activation than their adult counterparts. Indeed, youth physical activity programmes regularly encourage the use of play type movements that include animal shapes (e.g., bear crawls, alligator walks), hanging and swinging, all of which active the upper-limbs (28,67); it is unlikely that untrained adults (included in nine out of 13 comparisons) engage in such activities. A more physiological explanation might be sought from the fibre type differences between youths and adults. Maturation is associated with an increase in fast-twitch fibres (27,68), which are more susceptible to EIMD (48) and of higher proportions in the upper-limb than lower-limb (39,70). Therefore, youths might have a tissue makeup in the upper-limb that makes them less susceptible to structural and connective tissue damage and inflammation, which underpin changes in muscle soreness. Practitioners should be mindful that peak symptoms of EIMD will be different in youths and adults, which is particularly important in scenarios where youths and adults exercise concurrently (e.g. teams sport).

This meta-analysis has highlighted several avenues for future research. Firstly, other than Webber et al. (74), no studies included in this review utilised an ecologically valid exercise protocol, and instead predominantly focused on vertical jump or single joint resistance training protocols. EIMD in youths has been investigated after competitive soccer match-play (73), although no youth versus adult comparison has been reported. Future studies should implement exercise protocols that better reflect a) the dynamic nature of physical activity and/or competitive sport, such as self-directed play or simulated games and b) the training methods used in strength and conditioning settings. Secondly, girls and women accounted for 32.1 and 25.7% of the research participants, with only two studies solely recruiting female participants (3,44), and one both combined males and females without reporting sex-specific results (74). As is the case with sport and exercise science research more generally, there is a dearth of EIMD literature in female youth athletes which reflects the patriarchal nature of sport and exercise research (10,65). It has previously been suggested that there are sex-specific differences in the susceptibility to, and recovery from, symptoms of EIMD (38). Future work must ensure that girls and women are benefiting from the same quality and quantity of EIMD research (14). Thirdly, maturation may also impact EIMD symptoms and recovery (73) yet only two studies have reported on the maturity status of participants in response to EIMD (12,44). Youths who are the same chronological age can differ markedly in maturity status and biological maturity influences the neural, muscular, and cardiorespiratory systems (45). As such, it would be pertinent to directly compare males and females across the lifespan, to better understand the physiological and performance related responses to EIMD. Finally, nine of the 13 comparisons included untrained participants, and one which failed to describe the training status. Although the RBE is less expressed in youths than adults (32,51) future studies must determine how training status influences EIMD in youth. Indeed, recently there has been an increase in the appreciation of physical activity and exercise for youth physical development and long-term athletic development. Data on the EIMD response in well-trained youths would be practically beneficial to those working with youth athletes in high demanding environments. Such a study should include girls and EIMD protocols which are ecologically valid.

5. Conclusion

The findings from this meta-analysis provide a clear overview of the responses of youth athletes to EIMD. The data strongly indicates a lower EIMD magnitude in youths after eccentric and/or novel exercise, when measured by changes in muscle strength, muscle soreness and CK. The magnitude of this effect is also greater in the upper- than lower-limbs. By understanding peak responses, and the potential performance impact, practitioners can effectively programme for young athletes to ensure optimal training adaptations, recovery between sessions, and performance outcomes. Practitioners should be mindful that although youths experience less EIMD, it still occurs and that recovery between bouts of exercise is necessary. Moreover, insufficient recovery can lead to non-functional overreaching/overtraining which can have a negative effect on youths performance and well-being. We therefore encourage practitioners to be cognisant of these data and engage youths in physical activity that maximises their enjoyment and development. Future research should explore EIMD in female youths by employing more ecologically valid muscle-damaging protocols and accounting for both maturity and training status.

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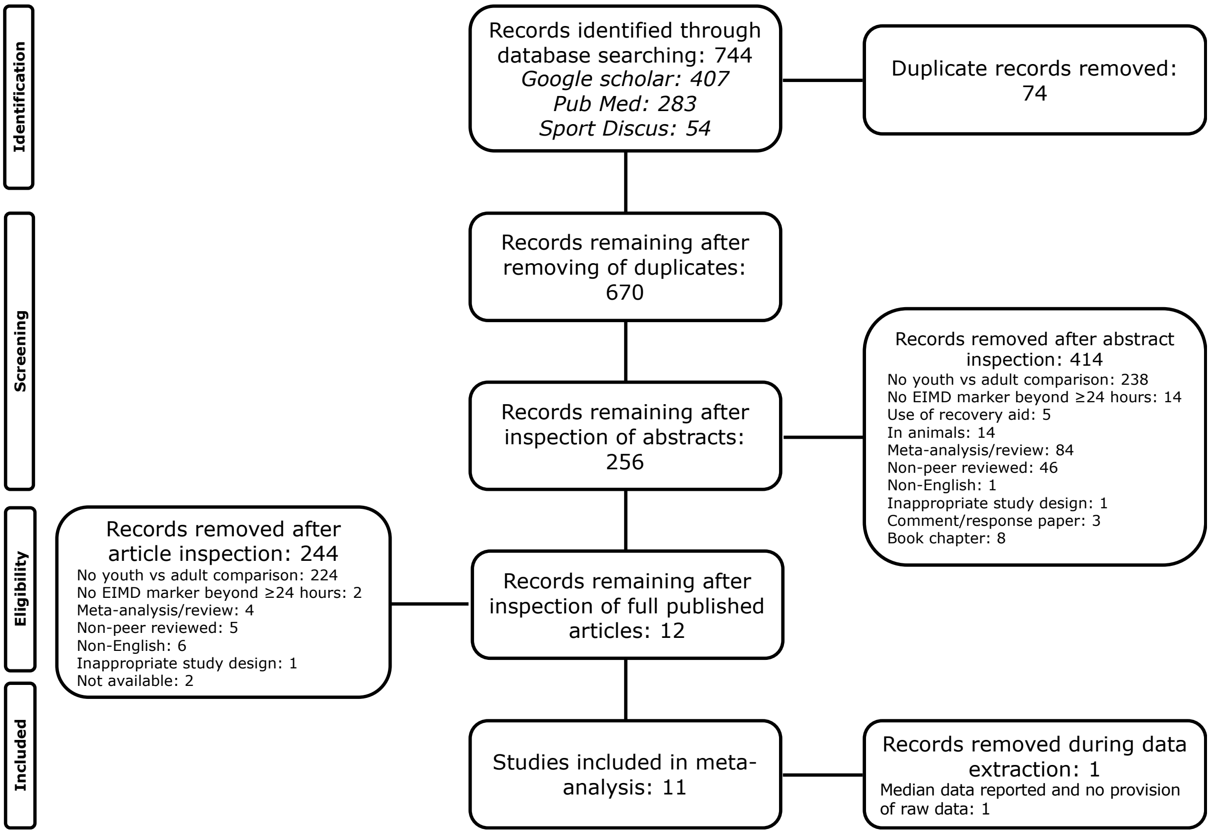

Figure 1. PRISMA Flow diagram displaying inclusion and exclusion of studies

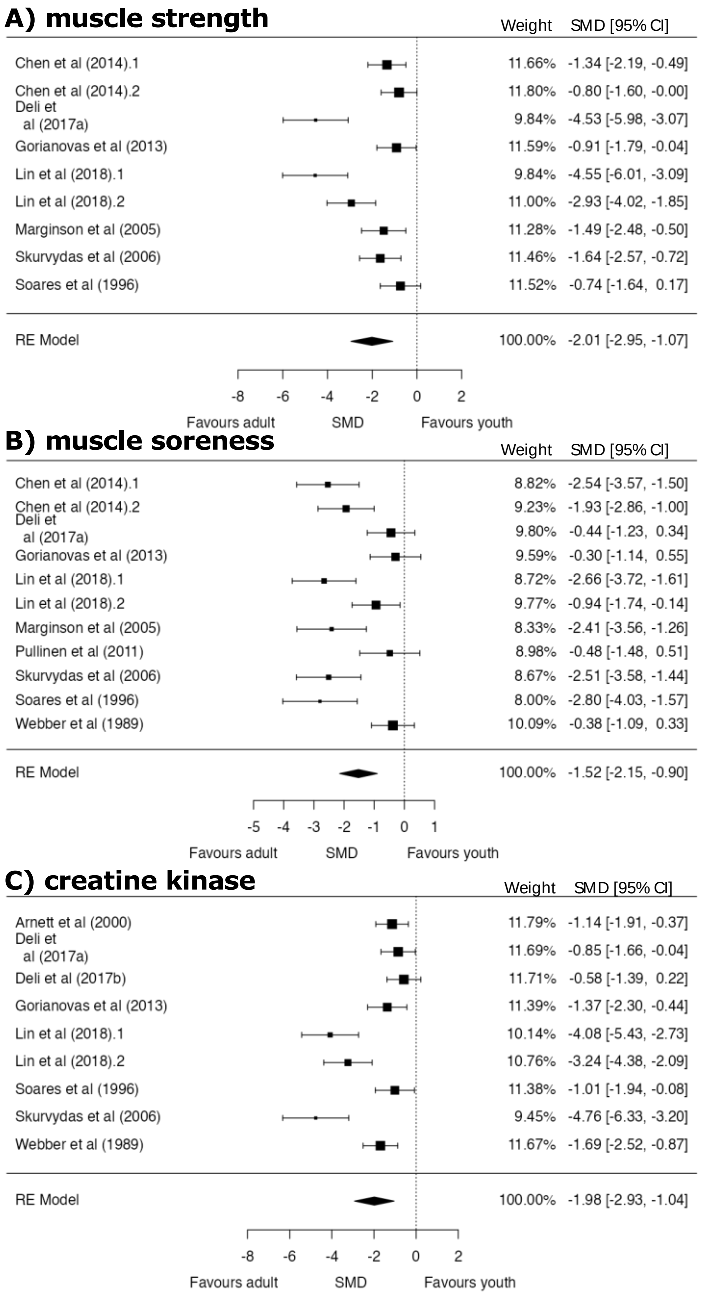

Figure 2. Forest plot of studies examining peak changes in muscle strength (A), muscle soreness (B), and creatine kinase (C) after EIMD in youths and adults. Data are presented as the percentage weight each study contributes to the pooled SMD, individual SMD [95% CIs]. Note that symbol size of individual studies is representative of the weighting for the pooled standardised mean difference. The filled diamond indicates overall SMD. RE = random effects. model.

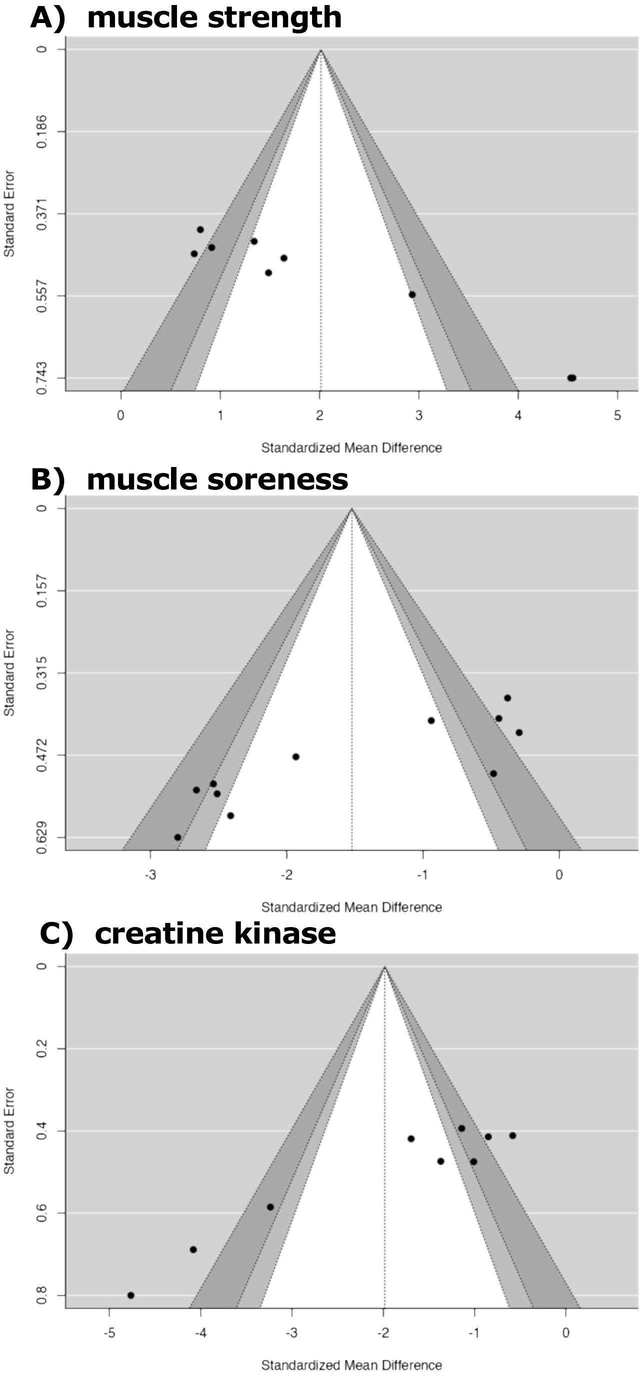

Figure 3. Funnel plots for studies evaluating peak changes in muscle strength (A), muscle soreness (B), and creatine kinase (C) after EIMD in youths and adults.

Table 1. The National Institute of Health quality assessment ratings.

Item	Arnett et al (2000)	Chen et al (2014a)	Deli et al (2017a)	Deli et al (2017b)	Gorianovas et al (2013)	Lin et al (2018)	Marginson et al (2005)	Pullinen et al (2011)	Skurvydas et al (2006)	Soares et al (1996)	Webber et al (1989)	**Studies fulfilled**
1) Was the study question or objective clearly stated?	1	1	1	1	1	1	1	1	1	1	1	11 (100%)
2) Were eligibility/selection criteria for the study population prespecified and clearly described?	1	1	1	1	1	1	1	1	1	1	1	11 (100%)
3) Were the participants in the study representative of those who would be eligible for the intervention in the general or clinical population of interest?	1	1	1	1	1	1	1	1	1	1	1	11 (100%)
4) Were all eligible participants that met the prespecified entry criteria enrolled?	1	1	1	1	1	1	1	1	1	1	1	11 (100%)
5) Was the sample size sufficiently large to provide confidence in the findings?	1	1	1	1	1	1	0	0	0	0	0	6 (54.5%)
6) Was the intervention clearly described and delivered consistently across the study population?	1	1	1	1	1	1	1	1	1	1	1	11 (100%)
7) Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?	1	1	1	1	1	1	1	1	1	1	1	11 (100%)
8) Were the people assessing the outcomes blinded to the participants' interventions?	0	0	0	0	0	0	0	0	0	0	0	0 (0%)
9) Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?	1	1	1	1	1	1	1	1	1	1	1	11 (100%)
10) Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p values for the pre-to-post changes?	1	1	1	1	1	1	1	1	1	1	1	11 (100%)
11) Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention?	0	0	0	0	0	0	0	0	0	0	0	0 (0%)
12) If the intervention was conducted at a group level did the statistical analysis take into account the use of individual-level data to determine effects at the group level?	1	1	1	1	1	1	1	1	1	1	1	11 (100%)
Criterion fulfilled	10 (83.3%)	10 (83.3%)	10 (83.3%)	10 (83.3%)	10 (83.3%)	10 (83.3%)	9 (75.0%)	9 (75.0%)	9 (75.0%)	9 (75.0%)	9 (75.0%)	

Table 2. Characteristics of included studies

	Youth			Adult						
	Age	n	Maturity status	Age	n	Sex	Activity level	Muscle	EIMD protocol	EIMD markers
Arnett et al. (2000)	10.5 ± 1.1	15	NS	23.4 ± 6.9	15	F	Untrained	KF	6 x 10 ECC at 110% CON 1RM	CK
Chen et al. (2014)	9.4 ± 0.5	13	Tanner stage 1	22.6 ± 2.0	13	M	Untrained	EF	5 x 6 ECC at 90 deg°s^{-1}	Strength, soreness
	14.3 ± 0.4	13	Tanner stage 3-4				Untrained			
Deli et al. (2017a)	11.0 ± 0.66	11	Tanner stage 2	35.3 ± 8.52	15	M	Untrained	KE	5 x 15 ECC at 60 deg°s^{-1}	Strength, soreness, CK
Deli et al. (2017b)	11.0 ± 0.66	11	Tanner stage 2	34.9 ± 8.61	14	M	Untrained	KE	5 x 15 ECC at 60 deg°s^{-1}	CK
Gorianovas et al. (2013)	11.8 ± 0.9	11	NS	20.8 ± 1.9	11	M	Physically active	KE	100 intermittent drop jumps	Strength, soreness, CK
Lin et al. (2018)	10.3 ± 0.7	13	BA = 9.9 ± 0.3	21.3 ± 1.3	13	F	Untrained	EF	5 x 6 ECC at 60% MIVC	Strength, soreness, CK
	14.4 ± 0.5	14	BA = 14.9 ± 0.3			F	Untrained			
Marginson et al. (2005)	9.9 ± 0.3	10	NS	22.2 ± 2.7	10	M	NS	KE	8 x 10 countermovement jumps	Strength, soreness
Pullinen et al. (2011)	14.0 ± 0.0	8	Tanner stage 3-5	31.0 ± 7.0	8	M	Physically active	KE	3 x max repetitions at 40% 1RM	Soreness
Skurvydas et al. (2006)	13.4 ± 0.6	12	NS	25.4 ± 1.7	12	M	Untrained	KE	5 x 10 countermovement jumps	Strength, soreness, CK
Soares et al. (1996)	12.1 ± 0.2	10	NS	28.3 ± 3.5	10	M	Untrained	EE	5 x max repetitions at 80% 1RM	Strength, soreness, CK
Webber et al. (1989)	10.4 ± 4.8	16	Pre-pubescent*	27.2 ± 8.91	15	M & F	Physically active	KE	30 mins running at -10% gradient	Soreness, CK

Note: NS = not stated; BA= bone age; *=determined via maturity questions and paediatric cardiologist; F = female; M = male; KF = knee flexors; EF = elbow flexors; KE = knee extensors; EE = elbow extensors; ECC = eccentric; CON = concentric; RM = repetition maximum; MIVC = maximal isometric voluntary contraction; CK = creatine kinase.

Table 3. Effect of moderator variables with 95% confidence intervals

		Youths (n)	Adult (n)	Z	*P*	SMD (95% CIs)	I^2 (%)
Muscle strength	Upper limb (n=5)	63	62	2.84	0.004	-2.00 (-3.37, -0.62)	88.06
	Lower limb (n=4)	44	48	2.71	0.007	-2.06 (-3.55, -0.57)	89.91
Muscle soreness	Upper limb (n=5)	63	62	-5.47	<0.001	-2.10 (-2.82, -1.38)	61.80
	Lower limb (n=6)	68	71	-2.47	0.014	-1.03 (-1.84, -0.21)	79.63
Creatine kinase	Upper limb (n=3)	37	36	-2.94	0.003	-2.73 (-4.54, -0.91)	87.07
	Lower limb (n=6)	76	82	-3.01	0.003	-1.62 (-2.67, -0.56)	87.96

**Low, moderate, and high heterogeneity correspond to I^2 values of 25, 50, and 80%, respectively*