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Systematic Review and Meta-Analysis of Skeletal Muscle Fatigue in Old Age

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Abstract

Despite intense interest in understanding how old age may alter skeletal muscle fatigability, a quantitative examination of the impact of study design on age-related differences in muscle fatigue does not exist.

Purpose—The purpose of this study was to conduct a systematic review of the differences in muscle fatigue between young and older adults, with specific examination of moderator variables suggested to contribute to discrepancies across studies: contraction intensity, contraction mode, duty cycle, fatigue index, sex, muscle group, and contraction type.

Methods—The standardized effect of age on muscle fatigue was computed for 37 studies (60 standardized effects). Standardized effects were coded as positive when less fatigue was reported in older individuals compared with young individuals.

Results—The overall standardized effect of age on muscle fatigue was positive (0.56). In studies using dynamic contractions or using muscle power as the index of fatigue, the standardized effect was negative (–0.12 and –2.5, respectively). The standardized effect for all other moderator categories was positive (range = 0.09–0.90), indicating less fatigue in older adults under all other methodological conditions.

Conclusion—This review provides the first quantitative analysis of the effect of study design on age-related differences in muscle fatigue. The results indicate that older individuals develop less muscle fatigue than young individuals, particularly during isometric contractions of the elbow flexor and knee extensor muscles. However, the results also suggest that older adults develop greater fatigue during dynamic contractions, particularly when the decline in power is assessed. Studies that verify this latter outcome are needed, as are studies designed to elucidate the mechanisms of fatigue.

Keywords

AGING; CONTRACTION; QUANTITATIVE REVIEW; ISOMETRIC; POWER

It is well established that advanced age is accompanied by numerous changes in the neuromuscular system, including a decline in muscle size and strength (25,27,38,46). Indeed, strong associations exist between muscular strength and performance of activities of daily living in older individuals (12,22,58). However, also important to the performance of activities of daily living is the ability to perform tasks repeatedly or for prolonged periods of time, which requires the capacity to resist the development of muscle fatigue.

Muscle fatigue is defined as the activity-induced loss of force-producing capability of the muscle (36). This fall of force or power is generally expressed relative to a baseline measure. The importance of fatigue resistance in older individuals has gained increasing recognition in the literature, with a tremendous increase in the number of investigations of age-related differences in fatigue in the past 10 yr. Although there is general agreement about many of the neuromuscular adaptations observed with senescence, age-related differences in the development of muscle fatigue are less clear. Despite the numerous detrimental changes in the neuromuscular system that would seem to put older individuals at a disadvantage, several studies report increased fatigue resistance in older relative to young adults (9,23,37,42,53,55). However, contrary results showing greater levels of fatigue in older individuals compared with young individuals have also been reported (19,21,51), although other reports still indicate no age-related difference in fatigue (3,44,47).

Discrepant findings among studies using different methodological designs suggest that the age-related differences in muscle fatigue may be specific to the task and study population. Factors defining the task that may influence study outcomes include contraction intensity (maximal or sub-maximal), contraction mode (isometric or dynamic), duty cycle (intermittent or sustained contractions), index of fatigue used (endurance time, loss of force, or loss of power), and contraction type (voluntary or stimulated), whereas design characteristics such as the sex of the subjects and muscle group may also influence the outcomes. Although these confounders are often invoked to explain differences in study results, a systematic analysis of the impact of old age on muscle fatigability and each of these factors has not been reported.

Therefore, the purpose of this study was to perform a systematic review to obtain a comprehensive, quantitative analysis of the existing literature on aging and fatigue. Such an analysis will provide, for the first time, quantitative information about the important characteristics modulating muscle fatigue and the conditions under which an age-related difference in muscle fatigue is most prominent. This analysis affords a new perspective on the discrepant results among studies, identifies areas of concurrence, and highlights important parameters for consideration in future studies.

METHODS

Literature search

The analysis included cross-sectional studies rather than clinical trials. Accordingly, it was performed in line with the recommendations of the Meta-analysis of Observational Studies group (59). The literature search was conducted using the Medline online database, the Academic Search Premiere database, and combinations of the following keywords and MeSH headings: “fatigue,” “age,” “aging,” “ageing,” “older,” “elderly,” “muscle,” and “endurance.” No date limit was applied to the search. Additional articles were identified from the reference lists of review articles and book chapters and through communication with authors. The search returned 681 articles that were considered for inclusion. Studies were included if they met the following criteria: i) were available in the English language, ii) reported measures of muscle fatigue in statistics that could be converted to a standardized effect, iii) involved human subjects, and iv) included a young control group.

From the list of 681, articles were removed if they involved whole-body exercise ($n = 102$), were specific to a clinical population ($n = 197$), lacked a young control group or did not study the applicable age group ($n = 129$), were review articles on any fatigue-related topic ($n = 124$), were not human studies ($n = 9$), or were otherwise irrelevant to the review ($n = 66$). From this list, additional studies were removed ($n = 16$) if the data were not reported in

statistics that could be converted to a standardized mean difference (e.g., means, SD or SE, *F*-ratios) and if the corresponding authors could not provide the appropriate values.

Publication bias was assessed through the construction of a funnel plot of standardized effects versus standard errors. Asymmetries or missing sections within the funnel plot suggest the presence of a publication bias (24). Potential bias was accounted for in the calculation of the overall standardized effect and the standardized effect for each moderator by weighting the effects on the basis of their SE (see the “Calculation of standardized differences in means” section).

Moderator coding

Moderators are variables that the authors have selected as potentially important factors contributing to differences in results across studies. In this case, moderators were selected on the basis of study characteristics that have been suggested to be confounding variables in age-related differences in muscle fatigue (4,36). All moderators were coded as categorical variables, following the procedures recommended by Stroup et al. (59). The following moderators were used in the analysis: contraction intensity (maximal or submaximal), contraction mode (isometric or dynamic), duty cycle (intermittent or sustained), fatigue index (change in force, change in power, or endurance time), sex (male, female, or mixed groups), muscle (elbow flexors (EF), knee extensors (KE), dorsiflexors (DF), abductor digiti minimi, adductor pollicis, plantarflexors, shoulder abductors, or thenar), and contraction type (stimulated or voluntary).

Calculation of standardized differences in means

The calculation of the standardized difference in means (or standardized effect) provides an index of the magnitude of a treatment effect, independent of sample size (29). In the analyses presented in this article, all standardized effects (within and across studies) were calculated as the difference in group means, divided by the pooled SD, using the Comprehensive Meta-Analysis, Version 2.0 (Biostat, Englewood, NJ), as follows:

$$\frac{\bar{X}_{\text{young}} - \bar{X}_{\text{older}}}{SD_{\text{pooled}}}$$

A random effects model was used to assess standardized effects across studies, which assumes that the samples are drawn from different populations and that the true effect varies across studies. This model accounts for differences in variability across studies by weighting each standardized effect on the basis of its SE. The random effects model also accounts for multiple standardized effects from the same study by including a random effect for variation between estimates within each study (30).

The indices of fatigue vary across studies. Most commonly, the change in isometric force during a maximum voluntary contraction (MVC) force was used to quantify fatigue (Table 1), expressed either as the percent decline in force or as the percent of maximal force remaining after the fatigue protocol. Two studies (three standardized effects) used the percent drop in power during a dynamic contraction as the fatigue index. In studies where the fatigue task involved sustaining a contraction until task failure, the endurance time was used to quantify fatigue. The variety of methods of quantifying fatigue produces some confusion in the direction of the effects, with a higher value sometimes indicating less fatigue (e.g., longer endurance times or higher percent force remaining, for example) and other times indicating greater fatigue (e.g., greater drop in force). For consistency,

standardized effects were coded as “positive” when investigators reported less fatigue in older individuals than that in young individuals.

Heterogeneity

If the results of all studies on fatigue and aging were similar, the standardized effects across studies would be homogenous. However, if there is a significant fatigue $\times$ study interaction, in other words, if differences in study design produce different results, the standardized effect will be heterogeneous (60). In the analysis presented here, heterogeneity of standardized effects was tested by calculating the 95% confidence interval (CI) around the mean standardized effect and by the calculation of the Q statistic, using Comprehensive Meta-Analysis. The Q statistic is calculated as the sum of squares of the weighted mean standardized effect of each study over the overall weighted mean standardized effect. The standardized effects are heterogeneous if Q is statistically significant.

RESULTS

Thirty-seven studies were included in this analysis. To characterize the populations across studies, the mean ages and sample sizes for all studies combined were calculated and are presented in Table 1. The average age of young subjects ranged from 21 to 36 yr and that of older subjects ranged from 61 to 84 yr. In determining the number of participants per decade of life, studies were included in the count if the mean age of participants was provided and fell within a particular decade ($n = 28$).

Standardized Effects

A total of 60 standardized effects were calculated from the 37 studies and are presented in Table 2. Where a single study had more than one measure of fatigue, one standardized effect was computed for each measure of fatigue and listed separately Table 2. A positive standardized effect indicates greater fatigue in young compared with older muscle, whereas a negative standardized effect indicates greater fatigue in older compared with young muscle.

The overall standardized effect of age on muscle fatigue was 0.56 (Table 2), indicating less fatigue in older individuals compared with young individuals. As summarized in Table 1, there were a total of 46 standardized effects (from 29 studies) indicating less fatigue in older individuals, 13 standardized effects (from 10 studies) indicating greater fatigue in older individuals, and a single standardized effect indicating no difference between young and older participants (Table 1). It is also evident from Table 1 that the overall greater preponderance of studies showing less fatigue in older individuals is not a result of bias in the methodology used in these studies because all categories of the moderators were used in studies with both positive and negative standardized differences. This observation along with the distribution of the funnel plot (Fig. 1) suggests that the observed effects are not a result of substantial publication bias.

Moderators of the Effects of Age on Fatigue

The mean standardized effect for each of the moderators is illustrated in Figure 2. For each moderator, this effect represents an average of the standardized effects for all of its categories, weighted by the number of effects in each category. The mean standardized effect was positive for all moderators (range = 0.51–0.76), indicating that, on average, older adults are likely to fatigue less than young, regardless of the moderator. However, to provide a clearer understanding of the impact of each of the moderators, the categories of each moderator were further examined.

The standardized effects for each of the moderator categories are presented in Table 3, along with the 95% CI and the *P* value for the *Q* statistic (test of heterogeneity). The *Q* statistic was significant for all categories of all moderators, with the exception of power as an index of fatigue, indicating a generally high level of heterogeneity among studies.

Contraction intensity—The intensity of the contraction during each protocol was categorically coded as maximal or submaximal. Limitations in the number of studies using a particular submaximal intensity prevented further categorization of submaximal intensities. The standardized effect was positive for both maximal and submaximal contractions, although it was larger for maximal contractions (Table 3).

Contraction mode—Studies involving isometric or dynamic contractions show different effects of the influence of old age on the development of muscle fatigue. Although the use of isometric contractions had a positive standardized effect, the standardized effect for dynamic contraction protocols (including those using isometric torque, dynamic torque, or power as the index of fatigue, *n* = 16 studies) was negative (Table 3).

Duty cycle—The duty cycle of the fatigue protocols was categorically defined as sustained or intermittent contractions. The standardized effect was positive for both intermittent and sustained contractions (Table 3).

Fatigue index—The quantification of fatigue varied across studies, with some studies using a decrement in force, others using a decrement in power, and still others using endurance time as the index of fatigue. The fatigue index was therefore categorized as force, power, or endurance. The standardized effect for endurance and force were both positive (Table 3). However, the standardized effect was negative for the index of power. Although the number of studies reporting a change in power was small (three standardized effects in two studies), there were no standardized effects that indicated less fatigue in older individuals compared with young individuals, using this index of fatigue (Table 1).

It is important to consider that the units of the indices of fatigue can differ. Decreases in force or power are expressed on a relative scale (as a percentage of an initial or maximal value), whereas endurance times are expressed on an absolute scale (time). The different units used to quantify the level of fatigue may impact the computed standardized effects. Therefore, the standardized effects were recalculated independently for each fatigue index, and the results are illustrated in Figure 3. Because declines in force and power are on the same relative scale, studies using these two fatigue indices were grouped for this recalculation. The mean standardized effects for each moderator were all positive and generally were similar across the two indices of fatigue. The most apparent difference was for muscle group, which had a somewhat lower standardized effect for endurance tasks (Fig. 3B) than for those in which fatigue was expressed as a drop in force or power (Fig. 3A).

Sex—A total of 29 standardized effects were calculated from studies involving men only, whereas 8 standardized effects were computed for studies of women only and 16 for combined data for men and women (Table 3). There were three studies (seven standardized effects) in which the sex of the participants was not reported. Studies with a combined male and female group had a positive standardized effect, similar to that of studies involving only women (Table 3). Studies involving only male participants had a smaller, but still positive, standardized effect (Table 3).

Muscle—For clarity of presentation, only those muscles that were examined in at least five studies are presented in Table 3. The standardized effects for KE and EF were positive. The

standardized effects for DF were smaller but still slightly positive (Table 3). The large range of standardized effects across the different muscle groups (0.09–0.94) highlights that the selection of muscle group can impact the magnitude of the observed age-related difference in muscle fatigue.

Contraction type—The standardized effect was positive for both voluntary and stimulated contractions, indicating less fatigue in older individuals compared with young individuals. Note that the standardized effect was somewhat higher for voluntary contractions (0.67) than for stimulated contractions (0.37; Table 3).

DISCUSSION

The aim of this study was to provide a quantitative analysis of the existing literature concerning age-related differences in muscle fatigue. The information provided by this systematic review can help identify knowledge gaps and guide future research. We have shown that the overall effect of age on muscle fatigue was positive for both human and animal studies, indicating that the majority of the literature reports less muscle fatigue in older individuals compared with young individuals. The mean standardized effect for all moderators investigated was positive, suggesting that, on average, older adults fatigue less than young under all conditions. However, a closer evaluation of the categories within each moderator revealed that methodology does indeed influence the magnitude of the difference in fatigue between young and older individuals, as has previously been suggested, but not quantified. This result is consistent with the well-accepted concept of task specificity as a key factor in the development of muscle fatigue. Each of the moderators and their respective categories analyzed here are discussed in the following sections, along with recommendations for future studies.

Contraction intensity

The intensity of the contraction used in the protocols impacted the magnitude of the age-related difference in muscle fatigue, as indicated by the positive mean standardized effect (Fig. 2). Both maximal and submaximal contraction intensities resulted in less fatigue in older adults. However, the standardized effect for maximal contractions was more than double that for submaximal contractions (Table 3). This result indicates that during maximal contractions, there is a strong propensity for older adults to fatigue less than young. There are several studies indicating that voluntary activation of the muscle is similar in young and older adults in a variety of muscle groups (6,18,37), suggesting that a lack of effort is not contributing to this age-related fatigue resistance. However, future studies should consider normalizing baseline and fatigue measures to muscle size to more fully address any potential impairments in activation.

Unfortunately, there were not enough studies performed at a particular submaximal intensity to further separate standardized effects on the basis of contraction intensity. As a result, it is possible that the lower standardized effect observed for submaximal contractions was due to, in part, the range of relative contraction intensities used in the various studies, which could introduce variability across these studies. To help clarify this issue, future studies should examine fatigue at various contraction intensities within the same individuals.

Contraction mode

Although the mean standardized effect of contraction mode was positive (Fig. 2), examination of the categories of mode used in the analysis (Table 3) revealed that contraction mode also impacts the age-related difference in fatigue. The standardized effect for isometric contraction protocols was positive in contrast to protocols using dynamic

contractions in which the standardized effect was negative (Table 3). These results suggest that older muscles develop less fatigue than young muscles during isometric contractions but that this age-related fatigue resistance is not present during dynamic contractions. It is notable that this interpretation is reflected in Table 1, which shows that far more studies using isometric contractions show less fatigue in older individuals compared with those showing more fatigue. In contrast, the number of standardized effects using dynamic contraction protocols indicates a much more balanced result (i.e., nine standardized effects show less fatigue in older individuals, whereas seven standardized differences show more).

It is likely that differences in contraction intensity, loading, velocity, and duty cycle contribute to greater variability across studies using dynamic contraction protocols, which will contribute to a lower standardized effect. However, it is also likely that a lack of age-related fatigue resistance during dynamic contractions is related to the marked decline in power production in older adults (discussed in the next section). Although the isometric MVC was used to quantify fatigue in most dynamic protocols, the requirement for power production during the task may be associated with the development of greater fatigue. Additional studies involving dynamic contractions are needed to resolve this issue and should characterize fatigue on the basis of the decline in power rather than (or in addition to) the decline in isometric MVC.

Duty cycle

The mean standardized effect of duty cycle on the age-related difference in fatigue was positive (Fig. 2). In general, both intermittent and sustained protocols produce less fatigue in older individuals compared with young individuals, as evidenced by the positive standardized effects for both categories of duty cycle (Table 3). It appears that the index used to quantify the level of fatigue has a greater impact on the magnitude of the age-related difference in fatigue than does the duty cycle used to produce the fatigue.

Fatigue index

The average standardized effect of the fatigue index on the age-related difference in muscle fatigue was positive (Fig. 2). However, it appears that the overall effect was likely influenced by the low number of studies using power as the index of fatigue. Although several studies involved dynamic contractions, in which power was produced, only two studies (three standardized effects) used the decline in power as the index of fatigue. Notably, the decline in power as the index of fatigue was the only category of any moderator to unequivocally result in a negative effect, indicating greater fatigue in older individuals. Unfortunately, however, the strength of this result is tempered by the low number of studies that used this index of fatigue.

Because baseline muscle power has been shown to be highly predictive of future morbidity (52) and strongly related to measures of physical function (16,48), further investigation of muscle fatigue using power as the index of fatigue is clearly warranted. It is possible that the mechanisms of fatigue during power-based contractions may be important in understanding the decline of physical performance over the course of the day (i.e., “fatigability”), which is often reported by older individuals (unpublished report, *Idiopathic Fatigue of Aging*, National Institute on Aging, 2008).

Sex

In young adults, sex-based differences in muscle fatigue have been reported (56), and the mechanisms for this difference are under investigation by several research groups. Although some authors have reported an age $\times$ sex interaction in the development of muscle fatigue (23,32), the standardized effects for male, female, or mixed groups of participants were all

positive in this systematic review. Although the standardized effect was higher in the female (0.75) and mixed groups (0.76) than that in the male group only (0.49), it can be concluded that older individuals tended to fatigue less than young individuals, regardless of sex. However, it should be noted that the number of standardized effects for the male group ($n = 29$) was much greater than that for female ($n = 8$) or mixed groups ($n = 16$). In the future, assessment of muscle fatigue should be made in both sexes in studies focused on understanding muscle fatigue in senescence. Studying both sexes with sufficient sample sizes will provide further insight into the potential confounding effect of sex on the age-related difference in muscle fatigue. This is particularly important given the greater susceptibility of women for frailty and loss of functional capacity with advanced age (1).

Muscle group

As has been suggested (4,9,36) but not quantified, it appears that the choice of muscle can impact the study outcome (Table 1, Fig. 2). Of the three muscle groups with at least five standardized effects (Table 3), the EF and the KE showed the largest standardized effects. Although all muscle groups analyzed had a positive standardized effect, this difference across muscle groups suggests some degree of muscle specificity for the effect of age on muscle fatigue. These muscle differences may be related to differences in fiber type composition, muscle architecture, or patterns of use. For example, the KE and the EF muscles, which are used mainly for locomotion, have a more mixed fiber type composition and complex architecture than the ankle DF (35,61).

Note that the EF, the KE, and the DF muscles were studied in approximately 69% of the calculated standardized effects. Part of the reason these muscles are studied is that potential confounders, such as contributions from other muscles to force production, can be controlled. However, other muscle groups, such as the ankle plantarflexors, are important in balance and walking (43) yet are underrepresented in the literature. Therefore, future studies of older adults should consider additional muscle groups, particularly those important in performing activities of daily living.

Contraction type

The mean standardized effect for contraction type was positive (Fig. 2), although there were far more standardized effects using voluntary than stimulated contractions (Table 3). The larger standardized effect for voluntary contractions (0.60), compared with stimulated (0.37, Table 3) suggests that an age-related fatigue resistance is more prominent during voluntary protocols. It is reasonable to assume that differences in stimulus location, intensity, frequency, and duration contribute to variability across studies and reduce the overall magnitude of the standardized effect for stimulated protocols. In addition, although stimulated contractions can be useful in elucidating muscle contractile properties, the nonphysiological nature of these contractions may contribute to this difference in standardized effects.

Additional factors

In this systematic review, we sought to examine the most common factors suggested by various investigators to mediate differences in age-related fatigue outcomes across studies. It is recognized that the factors examined here may also have some interdependence in their mediation of an age-related effect on fatigue. Unfortunately, there were not enough degrees of freedom in the studies available to date to adequately use a multivariate model or a meta-regression to examine the levels of interdependence between moderators.

It is also acknowledged that additional factors such as the age and physical activity level of the participants require consideration. Very few studies, aside from that of McNeil and Rice

(51), have examined skeletal muscle fatigue across a range of ages. These investigators (51) showed an age-dependent increase in fatigability, such that older individuals (64 yr) had greater fatigue during dynamic DF contractions than young individuals (26 yr), and very old individuals (84 yr) had even greater fatigue (51). This result suggests that the age of the older population that is studied can impact the measure of fatigue. In the studies included in this systematic review, there were 5 studies with an average age in the sixth decade, 13 studies with an average age in the seventh decade, and 3 studies with an average age in the eighth decade. The majority of these studies included a range of ages that spanned two or three decades.

With few studies examining individuals in a single decade of life, a systematic analysis of the impact of different older age groups on muscle fatigue was not possible here. However, the notion that the age of the subjects is a potential confounder cannot be discounted. Future studies should consider the age of the older participants more carefully, decrease the range of ages studied, and/or draw further comparisons among individuals in different decades of life. Studies examining muscle fatigue across the life span, including middle-aged participants and those in the ninth decade and beyond, will undoubtedly prove useful in clarifying the magnitude and the mechanisms of muscle fatigue in senescence.

The health and habitual physical activity level of participants may also be confounders in studies of age-related differences in muscle fatigue. Most of the studies in this analysis did not quantify the physical activity level of participants but generally reported participants to be “healthy” and “sedentary,” “recreationally active,” or “community dwelling.” It is unknown whether the results reported here will hold in older individuals who maintain a high level of physical activity or in those with poor health or impairments in physical function. Future studies that identify the impact of changes in activity level, health status, and functional capacity on muscle fatigue in aging men and women are sorely needed.

Potential mechanisms

In studies showing less fatigue in older individuals, authors have proposed that a greater proportion of Type I muscle fibers and/or slower contractile characteristics of the older muscles are potential mechanisms of fatigue resistance (23,53). However, the exact mechanisms underlying this age-related increase in fatigue resistance are still not well understood, and it is likely that neural, morphological energetic, and contractile factors are important in dictating the degree of fatigability in elders (36). Future studies should continue to elucidate the mechanisms of muscle fatigue in aging and begin to address how any physiological advantage in fatigue resistance might be used to improve or extend physical capacity in older adults.

It should not be ignored that approximately 17% of the studies investigated here had a negative standardized effect, indicating greater fatigue in older individuals when compared with young. The results of this review highlight the potential role of dynamic contractions and measures of power in clarifying the particular conditions under which age-related fatigue resistance is diminished.

CONCLUSIONS

This systematic review provides the first quantitative support for the often-invoked conclusion that discrepant results across studies of age-related differences in muscle fatigue are due to, in part, differences in study design. The results show that a preponderance of the literature indicates less fatigue in older individuals compared with young individual under a variety of testing conditions. It is apparent that a protocol involving isometric, voluntary contractions of EF and KE muscle groups is likely to yield the greatest fatigue resistance in

older individuals. However, the use of dynamic fatigue protocols and the use of a decline in power as the index of fatigue appear to result in greater fatigue in older individuals compared with young individuals, although this later conclusion awaits further verification.

This review has also identified some critical gaps in the literature that can help guide future research. In terms of subject characteristics, studies that focus on differences in fatigue across a range of older ages include more women and draw comparisons across a wider range of health and physical activity levels will be valuable. Although recognizing that some muscles are not conducive to well-controlled mechanistic studies of fatigue, efforts should be made to incorporate additional muscle groups that substantially impact physical function, which will provide novel information about the specificity of these effects. Finally, because of the importance of muscle power in maintaining physical function in old age, study designs that assess the fall in power in response to fatigue are needed. All of this information will enhance our understanding of the underlying mechanisms of muscle fatigue and any age-related differences therein and the potential impact of these differences on physical function in our aging population.

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FIGURE 1.

Funnel plot of SE and standardized effect for each study. Each of the 60 standardized effects and their associated SE (from Table 2) are represented by open circles. The angled lines define the area in which 95% of the standardized effects are expected to fall, in the absence of publication bias. The vertical line defines the middle of the funnel. Symmetry within the funnel on either side of the midline indicates a lack of publication bias.

FIGURE 2.

Standardized effect for each moderator variable (mean $\pm$ SE). The standardized effects are the weighted average across all categories of each moderator. All standardized effects were positive, indicating less fatigue in older individuals compared with young individuals.

FIGURE 3. Standardized effect for each moderator variable (mean $\pm$ SE) for each fatigue index. A, Standardized effects when a drop in force or a drop in power was used ($n = 38$ standardized effects) as the fatigue index. B, Standardized effects when endurance time ($n = 22$ standardized effects) was used as the fatigue index.

TABLE 1

Study characteristics: source of standardized effects for all studies.

	Less Fatigue in Older Individuals (Positive Standardized Effect)	Same Fatigue in Young and Older Individuals	More Fatigue in Older Individuals (Negative Standardized Effect)
Number of effects (number of studies)	46 (29)	1 (1)	13 (10)
Sample size per study (mean $\pm$ SD)			
Young	12.9 $\pm$ 6.1	8	13.7 $\pm$ 6.6
Older	12.1 $\pm$ 5.6	8	13.2 $\pm$ 6.2
Ages studied			
Sixth decade	5 (5)		6 (5)
Seventh decade	20 (13)	1 (1)	3 (3)
Eighth decade	2 (2)		2 (2)
Moderators			
Contraction intensity			
Maximal	20 (14)	1 (1)	3 (3)
Submaximal	26 (14)	0 (0)	10 (7)
Contraction mode			
Isometric	37 (23)	1 (1)	6 (5)
Dynamic	9 (6)	0 (0)	7 (5)
Duty cycle			
Intermittent	29 (16)	0 (0)	10 (7)
Sustained	17 (12)	1 (1)	3 (3)
Fatigue index			
Endurance	19 (11)	0 (0)	3 (3)
Force	27 (18)	1 (1)	7 (5)
Power	0 (0)	0 (0)	3 (2)
Sex			
Male	21 (15)	1 (1)	7 (4)
Female	7 (7)	0 (0)	1 (1)
Combined	12 (10)	0 (0)	4 (3)
Unspecified	6 (2)	0 (0)	1 (1)
Muscle			
EF	14 (9)		1 (1)
KE	9 (6)		4 (3)
DF	9 (5)	1 (1)	4 (2)
PF	2 (2)		3 (2)
APB	5 (3)		1 (1)
ADM	1 (1)		
FDI	1 (1)		
Thenar	1 (1)		
Shoulder	4 (1)		
Contraction type			

	Less Fatigue in Older Individuals (Positive Standardized Effect)	Same Fatigue in Young and Older Individuals	More Fatigue in Older Individuals (Negative Standardized Effect)
Voluntary	40 (25)	1 (1)	9 (7)
Stimulated	6 (4)	0 (0)	4 (3)

The total number of standardized effects (with the number of studies in parentheses) that indicated less fatigue in older individuals, similar fatigue in young and older individuals, and more fatigue in older individuals are shown. The number of standardized effects calculated for each category of each moderator (with the number of studies in parentheses) is also provided.

DF, dorsiflexors; EF, elbow flexors; KE, knee extensors; PF, plantar flexors; APB, abductor pollicis brevis; ADM, abductor digiti minimi; Combined, males and females combined for analysis.

TABLE 2

Individual standardized effects for each study.

Study	Age (yr)		Comment	Hedges's <i>g</i>	SE	95% CI	Difference (%)	<i>P</i>
	Young	Older						
Allman and Rice (3)	24 ± 2	84 ± 2		0.42	0.51	-0.57 to 1.41	3.51	0.409
Allman and Rice (5)	25 ± 1	84 ± 1		0.58	0.55	-0.49 to 1.65	1.79	0.285
Allman and Rice (6)	27 ± 1	78 ± 1	CF	1.01	0.48	0.07 to 1.95	3.58	0.035
Allman and Rice (6)	27 ± 1	78 ± 1	NF	3.09	0.68	1.75 to 4.43	8.93	<0.001
Allman et al. (2)	27 ± 1	78 ± 1	CF	1.07	0.48	0.12 to 2.02	4.54	0.026
Allman et al. (2)	27 ± 1	78 ± 1	CI	1.25	0.49	0.28 to 2.21	5.50	0.012
Baudry et al. (7)	24-47	72-87	Concentric	-0.88	0.36	-1.59 to -0.17	-34.81	0.015
Baudry et al. (7)	24-47	72-87	Eccentric	-1.09	0.37	-1.81 to -0.36	-38.20	0.003
Bazzucchi et al. (8)	23-25	70-72	30% MVC	0.26	0.54	-0.78 to 1.31	4.82	0.620
Bazzucchi et al. (8)	23-25	70-72	50% MVC	1.71	0.64	0.46 to 2.96	73.63	0.007
Bazzucchi et al. (8)	23-25	70-72	80% MVC	1.26	0.59	0.10 to 2.42	83.14	0.033
Blodeau et al. (11)	26 ± 3	71 ± 4		1.49	0.49	0.53 to 2.45	162.63	0.002
Blodeau et al. (10)	23-32	65-86		1.32	0.47	0.41 to 2.24	69.44	0.005
Callahan et al. (13)	26 ± 1	71 ± 1	Dynamic	0.081	0.34	-0.59 to 0.76	2.33	0.814
Callahan et al. (13)	26 ± 1	71 ± 1	Isometric	4.55	0.66	3.25 to 5.85	24.56	<0.001
Carlson and Smyth (14)	26-53	65-78		-2.61	0.54	-3.68 to -1.54	-48.94	<0.001
Chan et al. (15)	30 ± 6	70 ± 9		1.36	0.49	0.40 to 2.33	38.30	0.006
Christie and Kamen (17)	24 ± 4	76 ± 6		-0.68	0.49	-1.64 to 0.27	-40.09	0.163
Chung et al. (18)	26 ± 5	72 ± 4	Free flow	1.01	0.42	0.19 to 1.83	19.90	0.016
Chung et al. (18)	26 ± 5	72 ± 4	Ischemia	0.90	0.41	0.086 to 1.71	28.52	0.030
Davies et al. (20)	22 ± 2	69 ± 3	Female	-2.65	0.62	-3.86 to -1.44	-40.32	<0.001
Davies et al. (20)	22 ± 2	70 ± 3	Male	-0.48	0.36	-1.19 to 0.22	-22.39	0.180
Ditor and Hicks (23)	24 ± 2	69 ± 5	Female	0.77	0.45	-0.11 to 1.65	30.42	0.085
Ditor and Hicks (23)			Group	1.18	0.34	0.52 to 1.84	37.31	<0.001
Ditor and Hicks (23)	25 ± 2	72 ± 6	Male	1.85	0.52	0.83 to 2.87	45.86	<0.001
Hakkinen (26)	25 ± 2	69 ± 3		0.49	0.48	-0.45 to 1.43	27.13	0.306
Hara and Findley (28)	20-35	63-81		0.56	0.49	-0.40 to 1.51	23.30	0.253
Huang et al. (31)	20-28	65-78		0.89	0.39	0.13 to 1.64	25.75	0.021

Study	Age (yr)		Comment	Hedges's g	SE	95% CI	Difference (%)	P
	Young	Older						
Hunter et al. (34)	26 ± 4	73 ± 3		2.28	0.51	1.28 to 3.28	44.78	<0.001
Hunter et al. (33)	18–31	67–76		1.42	0.53	0.37 to 2.47	73.85	0.008
Hunter et al. (32)	18–35	65–80	Female	0.32	0.43	–0.53 to 1.17	16.39	0.465
Hunter et al. (32)	18–35	65–80	Mixed	1.003	0.32	0.38 to 1.62	58.33	0.002
Hunter et al. (32)	18–35	65–80	Male	1.98	0.49	1.01 to 2.94	123.15	<0.001
Kent-Braun et al. (37)	33 ± 6	75 ± 6	Female	1.18	0.47	0.26 to 2.093	18.92	0.012
Kent-Braun et al. (37)	33 ± 6	75 ± 6	Male	0.74	0.43	–0.11 to 1.59	11.11	0.089
Klein et al. (39)	25 ± 4	66 ± 2		–0.27	0.47	–1.20 to 0.65	–22.22	0.559
Lanza et al. (41)	27 ± 3	70 ± 5		1.057	0.34	0.39 to 1.72	11.66	0.002
Lanza et al. (40)	22 ± 1	75 ± 5		<0.001	0.47	–0.93 to 0.93	0.00	1.00
Lanza et al. (42)	26 ± 4	72 ± 4	Dynamic	1.11	0.49	0.16 to 2.06	66.67	0.022
Lanza et al. (42)	26 ± 4	72 ± 4	Isometric	0.69	0.46	–0.23 to 1.59	16.67	0.143
Lenmarken et al. (45)	36 ± 3	48 ± 2	Female	2.47	0.54	1.40 to 3.53	43.33	<0.001
Lenmarken et al. (45)	34 ± 2	67 ± 2	Male	–4.02	0.64	–5.27 to –2.76	–71.43	<0.001
Lindstrom et al. (47)	28 ± 6	73 ± 3	Female	0.73	0.49	–0.23 to 1.70	12.73	0.134
Lindstrom et al. (47)	28 ± 6	73 ± 3	Male	–0.47	0.43	–0.38 to 1.31	–8.77	0.280
Mademli and Arampatzis (49)	32 ± 7	64 ± 4		0.94	0.44	0.074 to 1.81	98.12	0.033
Mademli and Arampatzis (50)	30 ± 7	65 ± 3		1.40	0.43	0.56 to 2.23	63.45	0.001
McNeil and Rice (51)	26 ± 4	64 ± 2	Old	–2.71	0.55	–3.80 to –1.62	–21.82	<0.001
McNeil and Rice (51)	26 ± 4	84 ± 3	Very old	–4.92	0.81	–6.51 to –3.33	–41.56	<0.001
Narici et al. (53)	20–29	70–79		2.15	0.55	1.08 to 3.23	25.43	<0.001
Petrella et al. (54)	27 ± 1	64 ± 1	Force	0.39	0.28	–0.15 to 0.93	42.23	0.157
Petrella et al. (54)	27 ± 1	64 ± 1	Power	–0.14	0.27	–0.68 to 0.39	–25.49	0.599
Russ et al. (56)	25 ± 4	73 ± 4	Female	0.63	0.47	–0.29 to 1.56	18.91	0.181
Russ et al. (56)	24 ± 6	74 ± 3	Male	0.38	0.49	–0.58 to 1.34	11.78	0.441
Schwendner et al. (57)	22 ± 1	71 ± 1		–0.11	0.26	–0.63 to 0.40	–3.06	0.672
Yassierli and Nussbaum (62)	18–25	55–65	30% MVC, 20 s	0.25	0.28	–0.31 to 0.81	5.70	0.380
Yassierli and Nussbaum (62)	18–25	55–65	30% MVC, 40 s	0.39	0.29	–0.17 to 0.95	12.94	0.172
Yassierli and Nussbaum (62)	18–25	55–65	40% MVC, 20 s	0.89	0.30	0.31 to 1.48	64.38	0.003
Yassierli and Nussbaum (62)	18–25	55–65	40% MVC, 40 s	0.92	0.30	0.34 to 1.51	67.96	0.002

Study	Age (yr)		Comment	Hedges's <i>g</i>	SE	95% CI	Difference (%)	<i>P</i>
	Young	Older						
Yoon et al. (63)	22 ± 4	70 ± 4	20% MVC	2.04	0.44	1.17 to 2.90	104.86	<0.001
Yoon et al. (63)	22 ± 4	70 ± 4	80% MVC	0.55	0.36	-0.16 to 1.26	33.33	0.127
Mean				0.63	0.14	0.36 to 0.91	23.63	<0.001

The standardized effect, SE of the standardized effect, 95% CI, and percent difference in means for old versus young. The mean ± SD age values of the young and older groups are given for each study. Where the mean was not available for a particular study, the age range is instead provided. If more than one measure of fatigue was reported within a study, a separate standardized effect was calculated for each fatigue measure, and the study is listed more than once. A description of the difference between multiple entries for the same publication is given in the “Comment” column.

CF, constant frequency stimulation; NF, normalized frequency stimulation; CI, catch-like inducing stimulation; MVC, maximum voluntary contraction.

TABLE 3

Standardized mean differences for each category within each moderator variable.

Moderator	Category	n	Standardized Effect	95% CI	P Value for Q
Contraction intensity	Maximal	24	0.90	0.62 to 0.97	<0.001
	Submaximal	36	0.34	-0.03 to 0.71	<0.001
Contraction mode	Isometric	44	0.84	0.41 to 0.98	<0.001
	Dynamic	16	-0.12	-0.34 to 1.5	<0.001
Duty cycle	Intermittent	39	0.48	0.14 to 0.81	<0.001
	Sustained	21	0.73	0.17 to 1.28	<0.001
Fatigue index	Force	35	0.68	0.29 to 1.1	<0.001
	Power	3	-2.5	-5.2 to 0.19	1.00
Sex	Endurance	22	0.73	0.51 to 0.83	<0.001
	Male	29	0.40	-0.11 to 0.92	<0.001
Muscle	Female	8	0.74	0.27 to 0.85	0.004
	Mixed group	16	0.76	0.43 to 0.74	<0.001
	DF	14	0.09	-0.75 to 0.56	<0.001
	EF	15	0.94	0.39 to 1.48	<0.001
Contraction type	KE	13	0.94	0.37 to 1.51	<0.001
	Voluntary	50	0.60	0.48 to 0.70	<0.001
	Stimulated	10	0.37	0.06 to 0.69	<0.001

The number of standardized effects included in the analysis (*n*), the standardized effect and SE ($g \pm SE$), 95% CI, and the significance (*P*value) of the *Q* statistic of heterogeneity are presented. DF = dorsiflexors; EF = elbow flexors; KE = knee extensors; *n* = number of standardized effects; *Q* = test of heterogeneity.