Exercise interventions for cognitive function in adults older than 50: a systematic review with meta-analysis

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ABSTRACT

Background Physical exercise is seen as a promising intervention to prevent or delay cognitive decline in individuals aged 50 years and older, yet the evidence from reviews is not conclusive.
Objectives To determine if physical exercise is effective in improving cognitive function in this population.
Design Systematic review with multilevel meta-analysis.
Data sources Electronic databases Medline (PubMed), EMBASE (Scopus), PsychINFO and CENTRAL (Cochrane) from inception to November 2016.
Eligibility criteria Randomised controlled trials of physical exercise interventions in community-dwelling adults older than 50 years, with an outcome measure of cognitive function.
Results The search returned 12 820 records, of which 39 studies were included in the systematic review. Analysis of 333 dependent effect sizes from 36 studies showed that physical exercise improved cognitive function (0.29; 95% CI 0.17 to 0.41; p<0.01). Interventions of aerobic exercise, resistance training, multicomponent training and tai chi, all had significant point estimates. When exercise prescription was examined, a duration of 45–60 min per session and at least moderate intensity, were associated with benefits to cognition. The results of the meta-analysis were consistent and independent of the cognitive domain tested or the cognitive status of the participants.
Conclusions Physical exercise improved cognitive function in the over 50s, regardless of the cognitive status of participants. To improve cognitive function, this meta-analysis provides clinicians with evidence to recommend that patients obtain both aerobic and resistance exercise of at least moderate intensity on as many days of the week as feasible, in line with current exercise guidelines.

INTRODUCTION

Physical exercise shows promise as a modifiable risk factor to reduce the risk of dementia and related neurodegenerative diseases.[1] As cognitive function declines with advancing age, a physically active lifestyle has an important role in reducing such declines,[2 3] as well as the incidence of dementia.[4] It is hypothesised that the neural and vascular adaptations to physical exercise improve cognitive function through promotion of neurogenesis, angiogenesis, synaptic plasticity, decreased proinflammatory processes and reduced cellular damage due to oxidative stress.[5] While lifelong participation in physical exercise may be preferable, the adoption of exercise at any age to delay or reverse cognitive decline is worthwhile given the prevalence of physical inactivity and the increasing proportion of older adults in the population.

Although early meta-analyses, such as a study of aerobic exercise interventions,[6] showed large benefits to cognitive function in older adults, more recent systematic reviews[7] and meta-analytical studies[8–10] are much less conclusive. For example, a recent meta-analysis of aerobic, resistance training and tai chi interventions in people older than 50 showed little benefit of exercise on cognitive function.[9] The discrepancy in findings is partly because existing reviews are excessively restrictive in their inclusion criteria, often considering only one mode of exercise (eg, recent reviews of aerobic training only[10 11]) or a narrow range of publication years. Thus, the numerous meta-analyses published provide incomplete summaries of the available evidence in people aged 50 and over. Studies which prescribe a combination of both aerobic and resistance training components in one intervention (here on called multicomponent training) have not been reviewed in healthy older adults since the 2001 study of Colcombe and Kramer[6] despite global guidelines recommending this type of training in older adults.[12 13] Alternative modes of exercise such as yoga[14] or tai chi[15] may also be beneficial to cognitive function, yet randomised controlled trials (RCTs) of these modes in older adults have not been specifically reviewed. Importantly, prior reviews offer relatively little information about the optimal prescription of physical exercise for cognitive health. Physical exercise provides a complex stimulus for adaptation in the body and its dosage can be modulated by various parameters, including duration, frequency, intensity and the mode or type of exercise. Despite this, many reviews do not take into account the importance of exercise prescription variables in either the analysis or discussion of the literature. Consequently, there is an urgent need for guidelines on the type or amount of exercise a clinician should recommend to their patient.

To deal with these research gaps, we have completed a comprehensive meta-analysis which includes a larger number of studies by imposing no limit on publication date or exercise mode. This study examines four key issues including: (1) the effects of supervised exercise interventions of aerobic, resistance, multicomponent, tai chi and yoga training modes on cognitive function; (2) the influence of exercise training variables, including the duration, frequency, intensity and length of exercise; (3) the differentiation of exercise effects on global cognition and domains of cognition, including attention, executive function, memory working memory; and (4) the impact of study

design, including the nature of the control group and the baseline cognitive status of participants.

METHODS
This systematic review with meta-analysis was conducted in accordance with established guidelines from Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA).[16]

Search strategy
To direct the design of the search strategy, previously completed meta-analyses[6–9] were reviewed and search terms were piloted to ensure a comprehensive identification of potential articles for inclusion in the systematic review. A computer search of Medline (PubMed), EMBASE (Scopus), PsychINFO and CENTRAL (Cochrane Central Register of Controlled Trials) was then conducted up to November 2016, using medical subject headings (MeSH) for 'exercise' and 'cognition' (box 1). 'Exercise' and 'cognition' search terms were combined with 'AND' and searched in 'All Fields' with the limits human and English language (see online supplementary table A). All returned titles were screened by the first author (JMN) to exclude duplicate or clearly non-relevant studies. The abstract of each remaining study was then independently reviewed by JMN and BR. The preceding stages were overinclusive. Subsequently, the full texts of the remaining studies were independently reviewed by JMN, KLP and DJS against the inclusion and exclusion criteria. Disagreements were discussed and consensus reached among the authors in all cases. Review authors subsequently searched the bibliography of included articles and prior reviews to ensure that relevant articles had been captured by the search strategy. All studies in the systematic review were eligible for inclusion in the meta-analysis.

Inclusion and exclusion criteria
Studies were included from the initial search if they strictly met the following criteria: (1) studies of community dwelling men or women aged 50 years or older. Because criteria for diagnosing cognitive ability (eg, the presence of mild cognitive impairment (MCI)) differ between studies and prior reviews,[8] there were no limitations on baseline cognitive status. However, studies which included clinical samples with other neurological (eg, stroke) or mental illnesses (eg, depression) were excluded. (2) A structured exercise programme of any mode, duration, frequency or intensity. Exercise programmes that were not explicitly stated as fully supervised, or of <4 weeks, were excluded. Studies must have allowed the isolated effects of exercise to be measured. (3) A control group could include no contact, waiting list, attention control, sham exercise or alternative active treatment. (4) At least one outcome measure of cognition, measured at baseline and follow-up by any validated neuropsychological test of cognition. (5) The study design was strictly limited to RCTs. (6) A trial must have been published in a peer-reviewed journal.

Data extraction
Data on the study population, intervention, control group and outcome measures were independently extracted into a standardised form by two review authors (JMN and DJS). Where available, the mean change from baseline, the SD of the mean change and the number of participants at each assessment for all groups were extracted. Where authors reported more than one measured time-point throughout an intervention, only the longest follow-up period in which the exercise intervention was continued was admitted. Data were extracted such that an improvement in performance was coded as a positive change score. Variance information was converted to SD. Where the mean change from baseline was not available, it was calculated from baseline and postintervention cognition scores. Similarly, where change from baseline SD was not available, it was calculated from baseline SD and postintervention SD using the formula: $SD_{change} = \sqrt{(SD^2_{baseline} + SD^2_{postintervention})} - (2 \times Corr \times SD_{baseline} \times SD_{postintervention})$, where $Corr = 0.5$. The value for Corr was imputed on the assumption of a moderate correlation between baseline and postintervention measures. While this may overestimate the change from baseline SD, it represents a conservative approach that is consistent with previous meta-analyses.[8] Sensitivity analysis was performed to assess the impact of including SDs calculated from the imputed Corr value. Unpublished data (mean and SD) were requested from the authors of four studies,[17–20] and clarification of published data was requested from the author of one study.[21] Subsequently, unpublished data from Langlois et al[18] and Tsai et al[20] were included in the quantitative assessment.

Data coding
Descriptive data from each study were coded for inclusion in the moderator analysis (described later).

Exercise moderators
In accordance with objective 2 of the review, the characteristics of the physical exercise intervention were coded into categorical variables. First, the mode of exercise was classified as aerobic, resistance training, multicomponent training (an intervention with both aerobic and resistance training components), tai chi or yoga. Exercise intensity (*low; moderate; high*) was coded in reference to published guidelines that reconcile differences in the terminology used to describe exercise intensity.[22 23] The duration (minutes each session lasted, including any warm-up or cool-down) and length (weeks of exercise: *short*: 4–12 weeks; *medium*: 13–26 weeks; *long*: >26 weeks) of the training period in the exercise and control groups were coded using a prior review as a guide.[6] The coding for duration (*short*: ≤45 min; *medium*: >45 to ≤60 min; *long*: >60 min) was modified from Colcombe and Kramer,[6] who defined a 'short' duration as ≤30 min. The current review modified this cut-off point as it did not include any studies which prescribed exercise for ≤30 min,

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> **Box 1 Search terms for exercise and cognition**
>
> **Exercise search terms combined with 'OR'**
> Exercise
> Aerobic exercise
> Plyometric exercise
> Resistance training
> Strength training
>   Muscle stretching exercises
> Physical conditioning, human
>   Walking
> Tai ji (tai chi)
> Yoga
> **Cognition search terms combined with 'OR'**
> Cognition
> Memory
> Executive function
> Dementia
> Alzheimer disease

possibly owing to differences in the inclusion criteria. In addition, the frequency (number of exercise sessions per week: *low*: ≤2; *medium*: 3–4; *high*: 5–7) of both groups was coded.

Cognitive moderators

To address objective number 3, neuropsychological tests were classified according to the domain of cognition being assessed, similar to previous reviews.[24] The domains considered were global cognition (eg, The Mini-Mental State Examination), attention (sustained alertness, including the ability to process information rapidly), executive function (a set of cognitive processes responsible for the initiation and monitoring of goal-orientated behaviours), memory (storage and retrieval of information) and working memory (short-term manipulation of encountered information).[24]

Study design moderators

Characteristics of the control group and the baseline cognitive status of the participants were categorised in accordance with objective 4. The control group of each study was organised into four categories, including no contact (eg, instructed to maintain current lifestyle), active (eg, sham exercise intervention such as stretching), educational (eg, health lectures or a computer course) or social (eg, social meeting groups). Finally, the baseline cognitive status of participants was coded with respect to the presence of MCI (yes, no or unclear) using the criteria for MCI adopted by Gates *et al*.[8]

Risk of bias assessment

Two authors (JMN and DJS) independently assessed the risk of bias at the study level of included RCTs in accordance with the Cochrane Collaboration Guidelines.[25] The risk of bias was assessed as being 'low', 'high' or 'unclear' across the following domains: randomisation; allocation concealment; blinding of therapists (intervention supervisors); blinding of participants; blinding of outcome assessors; handling of incomplete data (use of intention-to-treat analysis); selective reporting and any other risk of bias. Discrepancies in the risk of bias assessment were resolved by discussion among review authors.

Statistical analysis

Statistical analysis was conducted with R version 3.2.1[26] using the metafor package 1.9.7.[27]

Meta-analysis

The standardised mean difference (SMD) was calculated using the mean change from baseline, change SD and number of participants for the exercise and control groups. To account for dependency between effect sizes, a multilevel random-effects model was run using a restricted maximum likelihood estimator.[28] Unlike traditional meta-analysis, which requires independence of effect sizes, the use of a multilevel meta-analysis accounted for dependency by fitting the term study as a random factor in the model. The multilevel model was used to estimate an overall effect size of exercise interventions versus control on cognitive function (objective 1). Heterogeneity was assessed using the Q statistic (with $p < 0.10$ suggesting statistically significant heterogeneity).[29] A mixed-effects model was fitted to examine the moderators described above as potential sources of variance. Initially, separate models were fitted to determine the main effects for each exercise (objective 2), cognitive (objective 3) and study design (objective 4) moderator. The analysis of main effects was interpreted using the 95% CI for the point estimates of each level of a moderator and the statistical significance of the omnibus test. Following analysis of main effects, where appropriate, and in accordance with the purpose of the study, moderators found to be significant were added to one model in order to examine possible confounding and to test for interaction effects.[28]

Funnel plots of the effect size against the SE of the effect size were visually inspected for small-sample bias and Egger's test values with 95% CI for funnel plot asymmetry were calculated.[30] To run Egger's test, the multilevel random-effects model was modified to include the SE of the effect size as a moderator.[31] Small-sample bias was considered to be present when the funnel plot appeared asymmetrical and the intercept of the Egger's test was significantly different from zero ($p < 0.10$).[30 32]
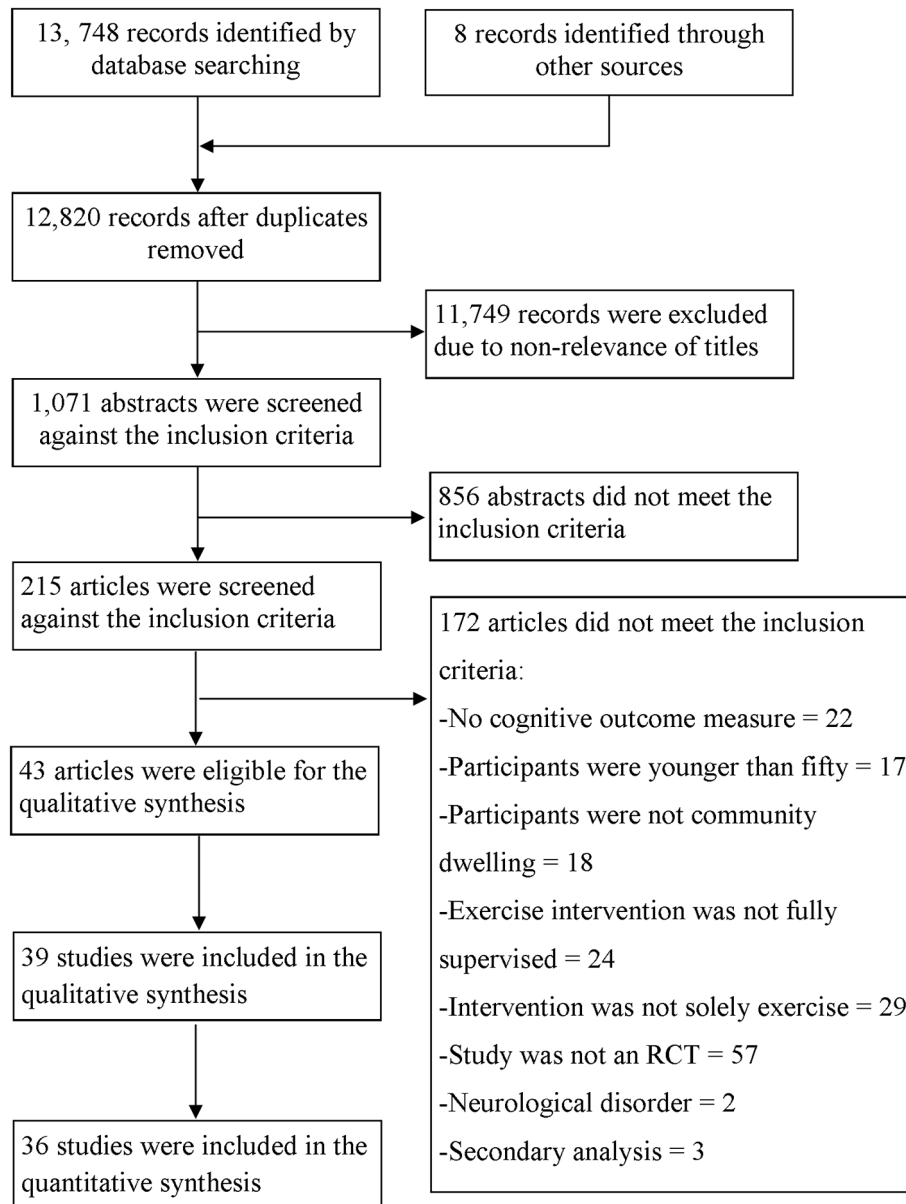
The GRADE guidelines[33] were applied independently by two review authors (JMN and DJS) to evaluate the overall quality of evidence for the comparison of exercise versus control groups for cognitive function. The overall quality of evidence was initially considered 'high' owing to the inclusion criteria, which stipulated that studies must be a RCT. The quality of evidence was downgraded by one level where each of the following four factors applied: (1) high risk of study bias; (2) inconsistency evaluated by a substantial I^2 (>75%). I^2 was calculated with the following formula: $I^2(\%) = (Q - df)/Q) \times 100$; (3) imprecision due to fewer than 400 participants in the outcome and (4) publication bias identified through an evaluation of funnel plot asymmetry. Indirectness was not considered owing to the inclusion criteria of the review.

RESULTS

The flow of records through the review is summarised in figure 1. The initial search strategy returned 12 820 records, of which 215 were retrieved for full-text review. Forty-three articles met the criteria for inclusion in the qualitative analysis. The analysis was conducted on each study. Subsequently, on four occasions when a study produced more than one publication (Blumenthal *et al*[34] and Madden *et al*[35]; Liu-Ambrose *et al*[36] and Liu-Ambrose *et al*[37]; Nagamatsu *et al*[38] and ten Brinke *et al*[39]; and Erickson *et al*[40] and Voss *et al*[41]), they were considered as one study for analysis. Finally, 39 studies were included in the qualitative analysis, with all studies eligible for inclusion in the quantitative analysis. The exercise mode was used to group the studies into interventions of aerobic exercise (k=18),[17 19 34 35 38–52] resistance training (k=13),[20 21 36–39 47 53–59] multicomponent training (k=10),[18 57 60–66] tai chi (k=4)[46 67–69] and yoga (k=2).[34 70] The methodological characteristics of these studies are summarised and available in supplementary table B.

Risk of bias

The risk of bias assessment is summarised in figure 2. The majority of studies did not describe the process of sequence generation or allocation concealment in sufficient detail and were judged as having 'unclear' risk of bias for these domains. In all of the assessed studies it was neither practical nor possible to blind the participants and therapists. It was judged that this presented a low risk of bias for the therapists but a high risk of bias for the participants. Studies were judged to have a high risk of bias for incomplete outcome data if they did not employ intention-to-treat principles in the data analysis or did not account for drop outs. All other domains were judged to have a low to unclear risk of bias.

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┌──────────────────────────┐      ┌──────────────────────────┐
│ 13, 748 records identified│      │ 8 records identified     │
│ by database searching    │      │ through other sources    │
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        ┌──────────────────────────┐
        │ 12,820 records after     │
        │ duplicates removed       │
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                                    │ 11,749 records were      │
                                    │ excluded due to          │
                                    │ non-relevance of titles  │
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        ┌──────────────────────────┐
        │ 1,071 abstracts were     │
        │ screened against the     │
        │ inclusion criteria       │
        └──────────────────────────┘
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                                    │ 856 abstracts did not    │
                                    │ meet the inclusion       │
                                    │ criteria                 │
                                    └──────────────────────────┘
        ┌──────────────────────────┐
        │ 215 articles were        │
        │ screened against the     │
        │ inclusion criteria       │
        └──────────────────────────┘
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172 articles did not meet the inclusion criteria:
- No cognitive outcome measure = 22
- Participants were younger than fifty = 17
- Participants were not community dwelling = 18
- Exercise intervention was not fully supervised = 24
- Intervention was not solely exercise = 29
- Study was not an RCT = 57
- Neurological disorder = 2
- Secondary analysis = 3

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        ┌──────────────────────────┐
        │ 43 articles were eligible │
        │ for the qualitative      │
        │ synthesis                │
        └──────────────────────────┘

        ┌──────────────────────────┐
        │ 39 studies were included │
        │ in the qualitative       │
        │ synthesis                │
        └──────────────────────────┘

        ┌──────────────────────────┐
        │ 36 studies were included │
        │ in the quantitative      │
        │ synthesis                │
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Figure 1 PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) flow diagram of each stage of the study selection. RCT, randomised controlled trial.

Effect of exercise on cognition

The multilevel meta-analysis provides an estimate of the difference between physical exercise and control on cognitive function for 333 dependent effect sizes across 36 studies. The SMD was 0.29 (95% CI 0.17 to 0.41; $p < 0.01$) and there was significant heterogeneity present ($Q_{332} = 811.00$; $p < 0.01$). The funnel plot of included studies is presented in figure 3. Visual inspection of the funnel plot and a non-significant Egger's regression intercept ($p = 0.175$) suggests the absence of funnel plot asymmetry.

According to the GRADE guidelines, the evidence for this outcome was classified as moderate quality. The evidence was conservatively downgraded owing to the level of uncertainty across each domain of the risk of bias tool (figure 3).
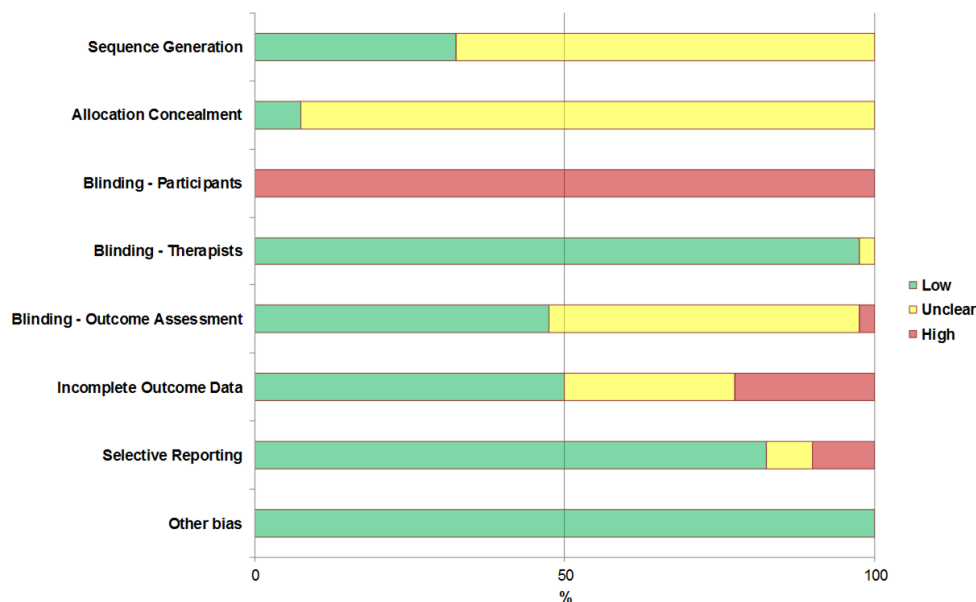
Moderator analysis

To investigate potential sources of variance, moderators were analysed one at a time in separate models. The results from this stage of analysis are summarised in table 1 and described below.

Exercise moderators

When exercise mode was examined as a moderator, all modes of exercise produced significant ($p < 0.01$) and positive effect estimates, except for yoga ($p = 0.27$). Studies where the duration of exercise was medium (>45 min to ≤60 min; $p < 0.01$) were associated with significant estimates in comparison with short- and long-duration exercise, which were not statistically significant. Moderate ($p = 0.02$) and vigorous ($p < 0.01$) intensities had similar sized effect estimates, whereas low intensity was not significant ($p = 0.11$). The frequency and length of the exercise intervention produced significant estimates across all three categories. For each exercise moderator analysis, the omnibus test was significant and the 95% CI for each factor overlapped.

Cognitive moderators

The effect of exercise on cognition was statistically significant for all domains, except global cognition. As prior reviews have indicated the effects of exercise on cognition may vary

Figure 2 Analysis of the risk of bias in included studies in accordance with the Cochrane Collaboration guidelines.

depending on the mode of exercise and cognitive domain, we included both these moderators as an interaction term in a separate model. Studies of resistance training had significant interaction effects on executive function (SMD=0.49, 95% CI 0.20 to 0.78; p<0.01), memory (SMD=0.54, 95% CI 0.23 to 0.85; p<0.01) and working memory (SMD=0.49, 95% CI 0.16 to 0.82; p<0.01). There was also a significant tai chi x working memory interaction (SMD=−0.70, 95% CI −1.21 to −0.19; p=0.01). All other interaction terms were non-significant.

Study design moderators

The type of control group was associated with differences in the statistical significance of the effect size estimated. When the control group involved either no contact (eg, waiting list, usual care; p<0.01) or education (eg, computer course, health lectures; p=0.01) the estimate was statistically significant. Where the control condition was exposed to an active control (eg, stretching; p=0.17) or social group (p=0.62), the effect

size was still positive but no longer statistically significant. As shown in table 1, the cognitive status of the study participants did not change the overall result of the meta-analysis. To test the differential effect of exercise on cognitive domain dependent on cognitive status, both moderators were entered with an interaction effect. There were no significant cognitive status x domain interaction effects. In addition, cognitive status and exercise mode were entered into a separate model with an interaction term. There was only one significant interaction effect for tai chi x unclear (SMD=1.11, 95% CI 0.16 to 2.07; p=0.02)

DISCUSSION

This study conducted the most comprehensive systematic review of RCTs in adults >50 years of age to date. Importantly, it did not limit the inclusion of studies by exercise mode or publication date and incorporated a multilevel meta-analysis method that included exploration of moderator variables and formal assessment of small-study effects. The key finding from this study is that physical exercise interventions are effective in improving cognitive function in adults aged >50 years, regardless of cognitive status.

Exercise mode

Of the traditional modes of exercise, studies incorporating a component of aerobic or resistance training showed similar effect size estimates. Aerobic exercise has previously been associated with large improvements in complex cognitive tasks such as executive function.[6] Although the size of the effect estimates reported here is smaller than reported by Colcombe et al,[6] our study also suggests that aerobic exercise is beneficial to the cognitive functioning of older adults. This finding is of importance as the results of more recent reviews[8–10] collectively provided little evidence of aerobic training benefits and contradicted exercise recommendations for this age group. An important feature differentiating this study from more recent reviews of aerobic exercise is the multilevel analysis model used and the absence of restrictions on publication date. As a result of these differences, this review was able to conduct a robust investigation, with greater statistical power and included a large number of otherwise relevant studies not eligible for these recent reviews.
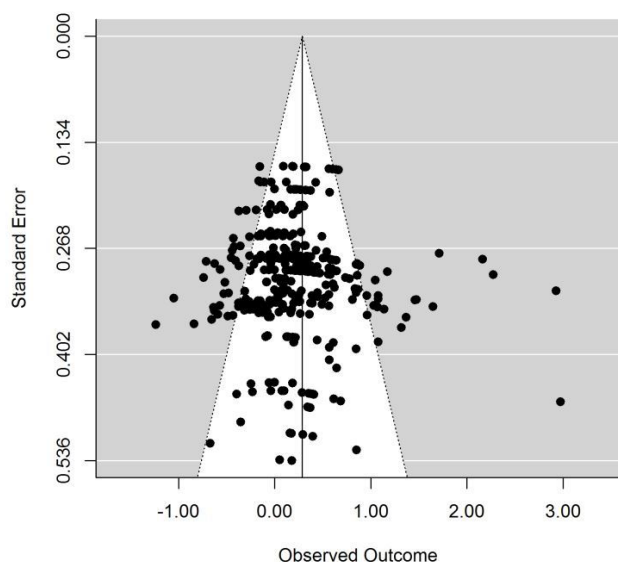
Figure 3 Funnel plot of included dependent effect sizes (k=333).

Table 1 Results of moderator analysis

Moderator	No. of effect sizes	Estimate Mean (95% CI)	Q statistic	Omnibus test of moderators
Exercise moderators				
Mode			$Q_{328}=781.68$; $p<0.01$	$Q_5=39.53$; $p<0.01$
Aerobic	153	0.24 (0.10 to 0.37)		
Resistance training	80	0.29 (0.13 to 0.44)		
Multicomponent training	47	0.33 (0.14 to 0.53)		
Tai chi	25	0.52 (0.32 to 0.71)		
Yoga	28	0.13 (−0.10 to 0.36)		
Duration			$Q_{318}=789.68$; $p<0.01$	$Q_3=27.83$; $p<0.01$
Short (≤45 min)	36	0.09 (−0.28 to 0.46)		
Medium (>45 to ≤60 min)	263	0.31 (0.16 to 0.46)		
Long (>60 min)	24	0.33 (−0.04 to 0.65)		
Frequency			$Q_{329}=804.58$; $p<0.01$	$Q_3=24.12$; $p<0.01$
Low (≤2)	92	0.32 (0.13 to 0.52)		
Medium (3–4)	229	0.24 (0.07 to 0.40)		
High (5—7)	13	0.69 (0.10 to 1.28)		
Intensity			$Q_{207}=264.61$; $p<0.01$	$Q_3=13.55$; $p<0.01$
Low	71	0.10 (−0.02 to 0.23)		
Moderate	57	0.17 (0.03 to 0.33)		
High	83	0.16 (0.04 to 0.27)		
Length			$Q_{330}=807.48$ $P<0.01$	$Q_3=23.32$; $p<0.01$
Short (4–12 weeks)	78	0.31 (0.09 to 0.54)		
Medium (13–26 weeks)	170	0.28 (0.10 to 0.47)		
Long (>26 weeks)	86	0.27 (0.03 to 0.52)		
Cognitive moderators				
Cognitive domain			$Q_{303}=795.06$; $p<0.01$	$Q_5=28.08$; $p<0.01$
Global cognition	6	0.16 (−0.14 to 0.47)		
Attention	87	0.27 (0.14 to 0.41)		
Executive function	94	0.34 (0.20 to 0.47)		
Memory	81	0.36 (0.22 to 0.50)		
Working memory	36	0.29 (0.12 to 0.45)		
Study design moderators				
Control group			$Q_{328}=785.37$; $p<0.01$	$Q_4=25.52$; $p<0.01$
Active	120	0.13 (−0.06 to 0.32)		
Education	17	0.48 (0.14 to 0.82)		
No contact	189	0.34 (0.17 to 0.51)		
Social	7	0.20 (−0.58 to 0.98)		
Cognitive status			$Q_{330}=797.56$; $p<0.01$	$Q_3=21.62$; $p<0.01$
MCI - Yes	197	0.28 (0.11 to 0.44)		
MCI - No	41	0.36 (0.04 to 0.68)		
Unclear	96	0.28 (0.05 to 0.51)		

MCI, mild cognitive impairment.

This study confirms previous suggestions that resistance training may play an important role in improving cognitive function in older adults.[8] The moderator analysis showed significant interaction effects for resistance training with executive function, memory and working memory. Although this does not show that resistance training is better than other modes of exercise, it does suggest that this type of training has particularly pronounced effects on these domains of cognitive function. In contrast to our results, a previous meta-analysis which tested the effect of resistance training found no benefit to cognition in older adults.[9] However, our review contained a greater number of resistance training trials than the previous meta-analysis[9] by including studies published before 2002[47 56] and those published since their census date in 2012.[37–39 57–59] Although prior reviews showed that the addition of resistance training to an aerobic intervention may have additional benefits to cognition compared with aerobic exercise alone,[6 24] this is the first review to specifically investigate the

effect of multicomponent training on cognitive function in this age group. As exercise guidelines for this age group recommend obtaining both aerobic exercise and resistance training to improve health and reduce the risk of disease,[12 13] it was important for this type of intervention to be reviewed for its effect on cognition. Our meta-analysis provides positive evidence for the prescription of both aerobic and resistance training (ie, multicomponent training), in accordance with exercise recommendations, for this age group to specifically improve cognitive functions.

Our meta-analysis also showed that tai chi improved cognitive function in this age group, as suggested in previous studies.[15] However, this finding should be considered in the context of the small number of tai chi studies included in this review. Further evidence is required from large well-designed RCTs to confirm this effect. Nevertheless, it is an important finding because non-traditional modes of exercise, such as tai chi, may be suitable for less functional populations.

Exercise prescription

An important objective of this review was to investigate the role of physical exercise training principles on changes in cognitive function. The moderator analysis in this study showed that exercise of between 45 and 60 min in duration, of moderate or vigorous intensity and of any frequency or length is beneficial to cognitive function. Although the moderator analysis suggested statistical differences in the effect estimates between levels of each moderator, the overlapping 95% CIs made it difficult to discern the practical significance of these differences. While there are statistical methods to identify these differences (namely pairwise comparisons), there is a risk of inflated type I errors and the possibility of false-positive or false-negative results with the application of correction factors. As this review provides evidence of the beneficial effect of physical exercise on cognitive function, future RCTs must instead move beyond investigating effectiveness and begin to refine the prescription of training to promote the greatest benefits to cognitive function.

Trial design moderators

Several trial design characteristics were investigated as moderating factors. First, the presence of MCI in study participants did not change the overall findings of the meta-analysis. This is important owing to the increased risk of transitioning to a diagnosis of Alzheimer's disease or dementia with the presence of MCI.[72] Although higher levels of physical activity are associated with reduced disease progression in MCI,[73] it is important to know how exercise interventions delay or reverse cognitive decline in a population where activity levels may be low. Previous meta-analyses have shown both negligible[8] and positive[11] effects on cognitive function in populations with MCI. Although it is not clear whether exercise is more or less effective in cognitively impaired or intact patients, the results of our analysis provide additional evidence that physical exercise has a positive effect on cognitive function in patients with MCI. Second, when the control group used no contact (eg, usual care, waiting list) or an education programme (eg, health lectures, computer course), the effect estimates were all significantly beneficial in comparison with either an active or social control. This finding is of interest as it suggests that education alone is not sufficient to promote changes in lifestyle habits which can be of measurable benefit in the short term.

Strengths and limitations

A major strength of this study is that it provides an up-to-date summary of supervised RCTs of physical exercise for cognitive function in adults aged >50 years and advances previous and recent reviews by employing a multilevel design and not limiting exercise mode or publication date. Despite this, the findings of the review must be considered in the context of a number of limitations. First, the search strategy was limited to English language publications and thus there is a possibility of a language bias in the systematic review. Second, studies were included only if exercise was the sole intervention. Consequently, a large number of studies which used exercise as an adjunct component to another intervention (eg, combined cognitive and physical exercise; see Law *et al*[74]) were excluded. As the objectives of this review were to examine the effect of physical exercise, it was not appropriate to include such studies. Additionally, the RCTs included here were strictly limited to fully supervised exercise interventions. This inclusion criterion was implemented as it is important to acknowledge the methodological and conceptual differences between a supervised and unsupervised intervention. From a public health perspective, however, the effect of unsupervised exercise or a comparison between supervised and unsupervised exercise interventions would be of great value. Future meta-analyses designed to specifically answer this question are required.

CONCLUSIONS

This meta-analysis showed that physical exercise interventions are effective at improving the cognitive function of older adults, regardless of baseline cognitive status. Interventions of aerobic, resistance training, multicomponent training and tai chi were similarly effective. The findings suggest that an exercise programme with components of both aerobic and resistance-type training, of at least moderate intensity and at least 45 min per session, on as many days of the week as possible, is beneficial to cognitive function in adults aged >50 years.

What are the new findings?

► Physical exercise interventions significantly improved cognitive function in adults older than 50 years, regardless of baseline cognitive status.
► Positive benefits to cognition occurred with an exercise intervention that included tai chi, or resistance and aerobic training, prescribed either in isolation or combined.
► When exercise training variables were considered, interventions that included exercise with a minimum duration of 45 min and at moderate to vigorous intensity showed improvements to cognitive function.

How might it impact on clinical practice in the near future?

► This meta-analysis provides positive evidence that a combination of aerobic and resistance type exercise of at least moderate intensity on as many days of the week as feasible is beneficial to cognitive function.
► Tai chi may be a promising intervention aimed at brain health for the over 50s, although further high quality randomised controlled trials are required to confirm the benefits shown in this study.
► The dosage of physical exercise is important and clinicians should ensure their exercise recommendations are individualised and provide a sufficient training stimulus.

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