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Physical Activity Interventions in Preventing Cognitive Decline and Alzheimer-Type Dementia

A Systematic Review

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Background: The prevalence of cognitive impairment and dementia is expected to increase dramatically as the population ages, creating burdens on families and health care systems.

Purpose: To assess the effectiveness of physical activity interventions in slowing cognitive decline and delaying the onset of cognitive impairment and dementia in adults without diagnosed cognitive impairments.

Data Sources: Several electronic databases from January 2009 to July 2017 and bibliographies of systematic reviews.

Study Selection: Trials published in English that lasted 6 months or longer, enrolled adults without clinically diagnosed cognitive impairments, and compared cognitive and dementia outcomes between physical activity interventions and inactive controls.

Data Extraction: Extraction by 1 reviewer and confirmed by a second; dual-reviewer assessment of risk of bias; consensus determination of strength of evidence.

Data Synthesis: Of 32 eligible trials, 16 with low to moderate risk of bias compared a physical activity intervention with an inactive control. Most trials had 6-month follow-up; a few had 1- or 2-year follow-up. Evidence was insufficient to draw conclusions about the effectiveness of aerobic training, resistance training, or tai chi for improving cognition. Low-strength evidence showed that multicomponent physical activity interventions had no effect on cognitive function. Low-strength evidence showed that a multidomain intervention comprising physical activity, diet, and cognitive training improved several cognitive outcomes. Evidence regarding effects on dementia prevention was insufficient for all physical activity interventions.

Limitation: Heterogeneous interventions and cognitive test measures, small and underpowered studies, and inability to assess the clinical significance of cognitive test outcomes.

Conclusion: Evidence that short-term, single-component physical activity interventions promote cognitive function and prevent cognitive decline or dementia in older adults is largely insufficient. A multidomain intervention showed a delay in cognitive decline (low-strength evidence).

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Forty-seven million people worldwide live with dementia (1), and this number is expected to triple by 2050 (2). Despite evidence that the overall incidence of dementia has declined in the United States (3, 4), the number of U.S. adults older than 70 years with dementia or mild cognitive impairment (MCI) increases as our population ages (5, 6). Dementia severely erodes functioning and quality of life, creates burden and stress on families, and leads to institutionalization. Dementia-related costs exceed those of heart disease and cancer and often are paid directly by families (7). Therefore, preventing dementia is an urgent public health priority.

Many believe that an active lifestyle may prevent cognitive decline and dementia. Findings of several reviews, primarily those looking at cohort studies, suggest that physical activity may reduce or delay the development of potential modifiable risk factors for cognitive decline, such as obesity, diabetes, and hypertension (8–13). However, the relationships among physical activity, other risk factors, and cognitive decline are complex and interrelated. Findings of associations from cohort studies alone cannot clarify whether physical activity affects cognitive decline directly, indirectly through the reduction of medical risk factors, or both. Previous systematic reviews of randomized controlled trials report some cognitive benefits of physical activity interventions, although the certainty and clinical importance of these findings have not always been clear (14, 15). This systematic review reports a synthesis of the evidence assessing the effectiveness of physical activity interventions in slowing cognitive decline and delaying the onset of cognitive impairment and dementia in adults without diagnosed cognitive impairments.

See also:

Related articles. 39, 52, 63
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Methods

We developed and followed a standard protocol (16). Our full technical report (17) contains details on methods and findings, an analysis of studies addressing secondary prevention in adults with MCI, and an evaluation of comparative effectiveness.

Data Sources and Searches

We searched bibliographic databases, including MEDLINE, EMBASE, and PsycINFO via Ovid, as well as the Cochrane Library, to identify controlled trials published in any language from January 2009 through July 2017. (See Part A of the Supplement, available at Annals.org, for search strategies.) We identified studies published before 2009 by citation searching relevant systematic reviews.

Study Selection

Two investigators independently reviewed titles and abstracts of search results and screened the full text of potentially eligible references. Disagreements about eligibility were resolved by consensus. We included randomized controlled trials of physical activity interventions with any sample size and large (n > 500) prospective quasi-experimental cohort studies with comparator groups if they enrolled adults without diagnosed cognitive impairments, had follow-up of at least 6 months, were published in English, and reported 1 of our preselected primary or intermediate outcomes. We excluded trials enrolling pure subgroups of patients with major medical conditions or conditions that may explain changes in cognitive function (namely stroke, Parkinson disease, cancer, and traumatic brain injury).

Our main outcomes of interest were MCI or dementia. Intermediate outcomes included measures of cognitive function assessed by instruments that tested cognition across several domains or those that specifically tested executive function, attention, and processing speed, or memory. Intermediate outcomes were categorized as follows: broad measures intended to capture several cognitive domains that were either brief cognitive tests (category 1) or more comprehensive multidomain neuropsychological tests (category 2) and domain-specific neuropsychological tests or subscales of broader instruments that assessed executive function, attention, and processing speed (category 3) or memory (category 4). Part B of the Supplement shows a list of the intermediate outcomes reported from the studies and our categorization of those outcomes.

Data Extraction and Quality Assessment

One reviewer extracted the study population, treatment characteristics, and funding source from all eligible studies. Risk of bias was assessed independently by 2 investigators using an instrument developed with guidance from the Agency for Healthcare Research and Quality (AHRQ) (18). Risk of bias for each reported outcome was rated as low, medium, or high on the basis of adequacy of randomization and allocation concealment, masking, attrition, use of intention-to-treat analyses, selectiveness of outcome reporting, and confidence that results were believable given limitations. Outcomes and adverse effects were extracted from eligible trials with low or moderate risk of bias, and a second investigator checked the extraction.

Data Synthesis and Analysis

We grouped studies by type of physical activity intervention and analyzed results by direction of effect and statistical significance. We found it impossible to assess the clinical significance of findings of the intermediate outcomes across all studies, because many different instruments were used and we did not always find information on the degree of change in specific instrument scores or subscores that would indicate clinical importance. (Part B of the Supplement shows the information we did find about clinically important changes in specific instrument scores.) In addition, results were measured, analyzed, and reported in many different ways.

When sufficient data were available (from more than 1 study or 1 study with ≥ 500 participants), 1 investigator assessed the strength of evidence for unique comparisons. These assessments were confirmed through consensus. We assessed strength of evidence by using 5 required domains: study limitations (risk of bias of eligible studies for a given comparison), directness (single, direct link between intervention and outcome), consistency (similarity of effect direction and size), precision (degree of certainty around an estimate that includes attention to small sample sizes with power to detect only large differences), and reporting bias (19). On the basis of these factors, the overall strength of evidence for each outcome from a given intervention was rated as high, moderate, low, or insufficient.

Role of the Funding Source

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RESULTS

Of 32 eligible studies that compared interventions using physical activity components with an inactive control in adults without a cognitive impairment diagnosis (20–51), 16—all of which were randomized trials—were considered to have low to medium risk of bias (20, 23, 25, 29, 30, 33, 35–37, 39, 40, 43, 45, 46, 48, 50). Inactive controls in the trials with low to medium risk of bias included waitlist, usual care, no-intervention, and attention (that is, education and information) groups. Most trials were government funded. Most studies enrolled older adults; some limited enrollment to men or women. Total sample sizes ranged from 42 to 1635 participants. Trials rarely reported adverse effects; those that did showed no differences between groups, with 1 exception. Intervention components, frequency, and duration varied. (Part C of the Supplement contains the literature flow diagram; part D contains evidence tables.)

The Table shows overall conclusions and strength-of-evidence ratings. Details of studies considered to have low to medium risk of bias are described later. For any cognitive outcome, evidence was insufficient to draw conclusions about most interventions (aerobic training, resistance training, tai chi, physical activity with diet, and physical activity with a cognitive component). Low-strength evidence showed that multicomponent physical activity interventions of 1 to 2 years did not improve multidomain neurologic performance; executive function, attention, and processing speed; or memory compared with an attention control. Low-strength evidence showed that an intervention combining physical activity, diet, and cognitive training benefited multidomain neuropsychological test performance and executive function, attention, and processing speed compared with an attention control; however, evidence was insufficient to draw conclusions about the efficacy of this intervention on memory. Moderate-strength evidence showed that more participants in the intervention than the control groups had musculoskeletal pain.

Physical Activity Interventions

Multicomponent Physical Activity

Four trials (n = 1885) with low to medium risk of bias examined multicomponent physical activity interventions. Components included flexibility, strength, balance, endurance, and aerobic training (36, 45, 46, 50). Enrollment criteria varied by trial. Sink and colleagues (45) and Williamson and colleagues (50) enrolled sedentary adults older than 70 years, most of whom were white women. Mean Modified Mini-Mental State Examination (MMSE) scores were higher than 90 points (on a scale of 0 to 100 points). Taylor-Piliae and colleagues (46) enrolled adults, mostly white college-educated women, older than 60 years. Napoli and colleagues (36) enrolled frail, obese older adults, most of whom were white women; mean Modified MMSE score was 96 points. Interventions during the trials lasted from 6 months to 2 years.

Sink and colleagues (45) (n = 1635) reported diagnostic outcomes that showed no difference in the incidence of MCI (odds ratio, 1.14 [95% CI, 0.79 to 1.62]) or dementia (odds ratio, 0.96 [CI, 0.57 to 1.63]) between groups at 2 years. A wide range of neuropsychological tests were used to assess intermediate outcomes across the 4 trials. Only 3 of 25 comparisons showed a statistically significant benefit with multicomponent physical activity interventions compared with the attention controls.

Aerobic Activity

Six trials (n = 531) with low to medium risk of bias compared aerobic training with an attention control (20, 30, 35, 39, 40, 43). Four studies enrolled healthy older adults (35, 39, 40, 43), whereas 1 trial enrolled sedentary older men (20) and another enrolled adults with MMSE scores of at least 24 points (on a scale of 0 to 30 points) who also reported memory challenges (30).

Lautenschlager and colleagues (30) (n = 170) reported dementia diagnoses and showed that participants assigned to aerobic training were less likely to receive a dementia diagnosis than those assigned to the attention control group at 18-month follow-up (change from baseline at 18 months in Clinical Dementia Rating Sum of Boxes scores: −0.33 [CI, −0.46 to −0.2] vs. −0.20 [CI, −0.33 to −0.03] point; P = 0.050). Eleven of 35 reported results for intermediate outcomes from the 6 trials showed a statistically significant benefit with aerobic training compared with an attention control, whereas 24 of 35 showed no statistically significant differences between groups.

Resistance Training

Three trials (n = 315) examined the effectiveness of resistance training in preventing cognitive decline (23, 29, 48). Studies enrolled prefrail and frail adults older than 65 years (48), sedentary men aged 65 to 75 years with a minimum MMSE score of 24 points (23), and sedentary older adults with at least 1 disability (29). Mean age of participants was in the early 70s. In an analysis of combined data from 2 separate trials, van de Rest and colleagues (48) compared supervised resistance training twice weekly with usual care. Both trials randomly assigned participants to receive protein supplements or placebo; 1 trial also incorporated resistance training. Both trials lasted for 24 weeks. Cassilhas and colleagues (23) randomly assigned participants to 1 of 3 groups: attention control, high-resistance training, and low-resistance training. Lachman and colleagues (29) randomly assigned participants to the Strong for Life program (home-based, video-directed resistance training) or a waitlist control group.

No trial reported diagnostic outcomes. Less than one third of the results for executive function, attention, and processing speed (32%) and for memory (27%) favored the intervention. Most positive results arose from 1 small 3-group trial (23).

Tai Chi

One small trial (n = 93) with moderate risk of bias compared tai chi with an attention control in adults aged 60 to 79 years with education-adjusted Chinese MMSE scores higher than 26 points (46). Diagnostic outcomes and adverse events were not reported. One of 2 outcomes for executive function, attention, and processing speed showed a benefit with tai chi compared with the attention control, whereas the other did not.

Physical Activity Combined With Other Interventions

Physical Activity and Diet

Two trials (n = 79) compared interventions combining physical activity and diet with attention controls (33, 36). Both studies enrolled overweight or obese adults. Napoli and colleagues (36) randomly assigned obese, sedentary adults with a minimum MMSE score of 24 points to a calorie-restricted diet plus multicomponent

Table. Conclusions: Physical Activity Versus Inactive Comparisons in Adults

Outcome	Conclusion	Strength of Evidence (Justification)
Multicomponent physical activity vs. attention control (*k* = 4; *n* = 1885)		
Dementia	Unable to draw conclusion	Insufficient (medium study limitations, imprecise, unknown consistency)
MCI	Unable to draw conclusion	Insufficient (medium study limitations, imprecise, unknown consistency)
Brief cognitive test performance	No benefit (*n* = 155; 6 mo–1 y)	Insufficient (medium study limitations, indirect, imprecise, inconsistent)
Multidomain neuropsychological performance	No benefit (*n* = 1635; 2 y)	Low (medium study limitations, indirect, unknown consistency)
Executive function/attention/processing speed	No benefit (*n* = 1885; 6 mo–1 y)	Low (medium study limitations, indirect, imprecise)
Memory	No benefit (*n* = 1836; 6 mo–1 y)	Low (medium study limitations, indirect, imprecise)
Aerobic training vs. attention control (*k* = 6; *n* = 531)		
Dementia	Limited data	Insufficient (limited data)
MCI	No data	Insufficient (no data)
Brief cognitive test performance	No benefit (*n* = 162; 6 mo–1 y)	Insufficient (medium study limitations, indirect, imprecise)
Multidomain neuropsychological performance	Limited data	Insufficient (limited data)
Executive function/attention/processing speed	Unable to draw conclusion	Insufficient (medium study limitations, indirect, imprecise, inconsistent)
Memory	Unable to draw conclusion	Insufficient (medium study limitations, indirect, imprecise, inconsistent)
Resistance training vs. attention control (*k* = 3; *n* = 315)		
Dementia	No data	Insufficient (no data)
MCI	No data	Insufficient (no data)
Brief cognitive test performance	No data	Insufficient (no data)
Multidomain neuropsychological performance	No data	Insufficient (no data)
Executive function/attention/processing speed	No benefit (*n* = 120; 6 mo)	Insufficient (medium study limitations, indirect, imprecise, inconsistent)
Memory	No benefit (*n* = 172; 6 mo)	Insufficient (medium study limitations, indirect, imprecise, inconsistent)
Tai chi vs. attention control (*k* = 1; *n* = 93)		
Dementia	No data	Insufficient (no data)
MCI	No data	Insufficient (no data)
Brief cognitive test performance	No data	Insufficient (no data)
Multidomain neuropsychological performance	No data	Insufficient (no data)
Executive function/attention/processing speed	Limited data	Insufficient (limited data)
Memory	No data	Insufficient (no data)
Physical activity plus diet vs. attention control (*k* = 2; *n* = 79)		
Dementia	No data	Insufficient (no data)
MCI	No data	Insufficient (no data)
Brief cognitive test performance	Limited data	Insufficient (limited data)
Multidomain neuropsychological performance	No data	Insufficient (no data)
Executive function/attention/processing speed	Unable to draw conclusion	Insufficient (medium study limitations, indirect, imprecise, inconsistent)
Memory	Limited data	Insufficient (limited data)
Physical activity plus protein supplementation vs. attention control (*k* = 1; *n* = 58)		
Dementia	No data	Insufficient (no data)
MCI	No data	Insufficient (no data)
Brief cognitive test performance	No data	Insufficient (no data)
Multidomain neuropsychological performance	No data	Insufficient (no data)
Executive function/attention/processing speed	Limited data	Insufficient (limited data)
Memory	Limited data	Insufficient (limited data)
Physical activity and cognitive training (*k* = 1; *n* = 134)		
Dementia	No data	Insufficient (no data)
MCI	No data	Insufficient (no data)
Brief cognitive test performance	Limited data	Insufficient (limited data)
Multidomain neuropsychological performance	Limited data	Insufficient (limited data)
Executive function/attention/processing speed	No data	Insufficient (no data)
Memory	No data	Insufficient (no data)

Continued on following page

Table–Continued

Outcome	Conclusion	Strength of Evidence (Justification)
Physical activity, diet, and cognitive training vs. attention control (*k* = 1; *n* = 1260)		
Dementia	No data	Insufficient (no data)
MCI	No data	Insufficient (no data)
Brief cognitive test performance	No data	Insufficient (no data)
Multidomain neuropsychological performance	Intervention comprising physical activity, diet, and cognitive training improves multidomain neuropsychological test performance (*n* = 1260; 2 y)	Low (indirect, unknown consistency)
Executive function/attention/processing speed	Intervention comprising physical activity, diet, and cognitive training improves executive function/attention/processing speed (*n* = 1260; 2 y)	Low (indirect, unknown consistency)
Memory	Unable to draw conclusion (*n* = 1260; 2 y)	Insufficient (indirect, imprecise, inconsistent)
Musculoskeletal pain	Musculoskeletal pain is higher with intervention comprising physical activity, diet, and cognitive training	Moderate (unknown consistency)

MCI = mild cognitive impairment.

exercise for 90 minutes, 3 times weekly, for 1 year. Martin and colleagues (33) randomly assigned overweight adults aged 25 to 50 years to a calorie-restricted diet plus group aerobic training for 6 months. Neither trial reported diagnostic outcomes. Only 2 of the 22 cognitive tests reported showed a benefit with combined physical activity plus diet versus the attention controls.

Physical Activity and Protein Supplementation

In an analysis of combined data from 2 separate trials, van de Rest and colleagues (48) compared physical activity and protein supplementation with usual care (*n* = 58). The original trials did not report outcomes pertinent to our review (52, 53). Both trials randomly assigned participants to receive protein supplements or placebo; 1 trial also incorporated resistance training. In both trials, the interventions lasted 24 weeks. Participants were older than 65 years and prefrail or frail according to measures of physical function. Trial inclusion criteria did not specifically address cognitive status; mean MMSE scores at baseline were higher than 27 points (52, 53).

One of 11 tests of executive function, attention, and processing speed and none of 6 memory tests showed a statistically significant difference favoring physical activity and protein supplementation after the intervention.

Physical Activity Plus Cognitive Training

Hars and colleagues (25) (*n* = 134) compared physical activity plus cognitive training with a waitlist control. Adults aged 65 years and older with an increased fall risk were randomly assigned to a structured, music-based exercise program or a waitlist group (25). The intervention consisted of 6 months of weekly 60-minute multitasking exercise classes during which participants followed instructions for pattern changes according to cues in the music as the cognitive training component.

Diagnostic outcomes were not reported. Brief cognitive test performance was not statistically different between groups after the intervention. Results from 1 of 2 tests of executive function, attention, and processing speed showed a postintervention difference between groups favoring the intervention, whereas the other test did not.

Physical Activity, Diet, and Cognitive Training

In the FINGER (Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability) trial, Ngandu and colleagues (37) (*n* = 1260) compared an intervention program comprising components addressing several risk factors simultaneously with an attention control. Adults aged 60 to 77 years with CAIDE (Cardiovascular Risk Factors, Aging and Dementia) dementia risk scores of at least 6 points and cognition near or slightly below that expected for age were randomly assigned to receive nutritional counseling, multicomponent exercise, and cognitive training or an attention control (general health advice). The intervention involved individual and group sessions to foster tailored dietary changes, 1 to 3 aerobic exercise and 2 to 5 resistance training sessions per week, and group and individual cognitive training. Intention-to-treat analysis at 2 years included 1190 participants (94% of those randomly assigned).

Diagnostic outcomes were not reported. Improvement in multidomain neuropsychological test performance was 25% greater with the intervention versus the control at 2 years. The mean change in 2 measures of executive function, attention, and processing speed also was greater with the intervention versus the control. Mean improvement in executive function, attention, and processing speed was 83% greater with 1 measure and 150% higher with the other. No statistically significant difference was observed between the changes in memory outcomes. Several adverse events were reported, including musculoskeletal pain, stress, challenges related to time commitment, death, and "other." However, only musculoskeletal pain affected as many as 5% of the participants in either group. Results showed a difference between groups, with participants receiving the intervention reporting a significantly higher rate of pain (5%) than those in the control group (0%).

DISCUSSION

This systematic review found that evidence for the effectiveness of single-component physical activity interventions in preventing cognitive decline is largely insufficient. The only exception is low-strength evidence of no effect for multicomponent physical activity in preventing cognitive decline. The intervention with sufficient evidence of benefit on cognitive function comprised physical activity, diet, and cognitive training, addressing several risk factors simultaneously.

Although our results predominantly showed no cognitive benefit from interventions comprised solely of physical activity, several cognitive results favored physical activity over controls for aerobic training, resistance training, and multicomponent physical activity interventions. We believe that those findings provide a signal that physical activity offers cognitive benefit but that the studies conducted were not long enough or sufficiently powered to show the true long-term effect of a physically active lifestyle, which many cohort studies suggest is beneficial. To be effective, regular physical activity may need to begin earlier in life and be sustained as a lifestyle. Short-term interventions begun after decades of high-risk behavior likely are insufficient to reduce dementia incidence.

Physical activity may slow cognitive decline directly through increased blood flow or indirectly by reducing other risk factors (namely, cardiovascular disease, obesity, and diabetes). The cognitive benefits demonstrated in the FINGER trial are intriguing. Because the intervention included components addressing several risk factors, isolating the benefits attributable to the physical activity component was not possible. However, given the complex relationship between identified and interrelated risk and factors that protect against cognitive decline and dementia, interventions addressing many risk factors at once might offer the best approach to successful prevention, especially if initiated in older adults already at higher risk for MCI and dementia. Although evidence of effectiveness was low strength, harms were not serious, and benefits from physical activity, diet, and cognitive training for other health conditions and functioning are more firmly established. Therefore, clinical approaches to incorporate similar interventions likely are warranted.

Our results are consistent with those of previous systematic reviews identified in our searches (8–15). However, our analysis and conclusions may not be as optimistic as others. This difference seems largely to be the result of interpretation. We saw many results with no statistically significant differences compared with inactive controls. That minority of statistically significant results often was interpreted as evidence of effectiveness in other reviews. Our review also had stricter inclusion criteria, requiring a minimum follow-up of 6 months, so many other reviews included studies not eligible for this one.

Our review has several limitations. Most trials were small and did not follow participants long term. The type, frequency, intensity, and duration of physical activity interventions varied widely. Most trials enrolled sedentary adults, yet how sedentary status was defined or measured was not always clear. Trials used many different cognitive tests and often repeated tests more frequently than appropriate. Many studies measured cognitive outcomes with various instruments and did not correct for multiple comparisons. Ideally, our analysis would assess effect size and the point at which interventions demonstrated a statistically significant effect. However, because many studies did not use instruments with demonstrated clinical thresholds or provide sufficient information to calculate standard effect sizes, we relied on statistical significance. Often when results showed no significant differences, it was unclear whether the insignificance was the result of a lack of effectiveness or of underpowered studies. In these cases, the imprecision of the estimates led us to assess the evidence as insufficient. Checks for treatment fidelity rarely were mentioned, and participant adherence was not always reported. In addition, the question of publication bias was challenging to assess for this topic. Trials of physical activity interventions often measured cognitive outcomes as secondary to others, such as cardiovascular disease outcomes. Studies of physical activity interventions, especially older trials, are not consistently registered. We did not identify unpublished trials at ClinicalTrials.gov potentially eligible for this review.

Future research should seek to identify population traits (such as age at which physical activity began, intervention duration, and baseline activity level) and intervention characteristics (such as type, frequency, duration, and intensity) that trend toward positive outcomes among these trials. Studies then could be designed appropriately to test identified characteristics for research and knowledge purposes. Long-term trials enrolling younger adults with interventions sustained for longer periods would benefit the field and provide important insight on prevention. On the basis of the evidence from this review, it seems that preventing cognitive decline in older adults may be best accomplished by addressing several lifestyle risk factors simultaneously, as demonstrated in the FINGER trial.

Although a physically active lifestyle often is proposed as a way to prevent cognitive decline and reduce risk for cognitive impairment and dementia, we found little evidence to determine whether single-component physical activity interventions offer cognitive benefits. However, clinical practice largely encourages physical activity to prevent or manage other chronic conditions, and this practice should continue, because it may offer benefits for preventing cognitive decline as well. Recommending multidomain interventions may prove even more beneficial.

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