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Physical Activity and Cognitive Health

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Abstract

Background: The industrialized nations are experiencing a demographic revolution due to the continuing increase in longevity and the rapid rise in the percentage of the population over 65 years old. Interventions that promote healthy aging will continue to gain significance as efforts to delay disability and loss of function intensify.

Methods: Since physical activity has been implicated in promoting healthy aging, here we review a large body of research that examines physical activity and cognitive health. Specifically, we focus on the associations of physical activity with cognitive function and dementia, including prevention, delay or slowing down of disease progression. Thus, we have prepared a descriptive review of the literature including various types of publications, prospective cohort, case-control, clinical trial and meta-analysis papers, published since 1999 in peer-reviewed journals.

Results: Based on currently available data, we conclude that the relative risk of cognitive decline with aging may diminish in individuals who are physically active; however, this has not been definitively demonstrated thus far.

Conclusions: Further research is needed to determine conclusively the effects of physical activity on cognitive function and dementia and to elucidate the basis for this linkage.

Keywords

Cognitive function; cognitive health; cognitive decline; dementia; Alzheimer's disease; physical activity(ies); exercise; fitness

1. Introduction

In the United States, we are experiencing nothing short of a demographic revolution. Two segments of the population are growing exponentially: those age 85 and older or the “oldest-old” and those born between 1946 and 1964, the “Baby Boomers” (1,2). It is estimated that between 2000 and 2030 those age 65 and older will double and that by 2050 there will be five

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times the number of those age 85 and older compared to the year 2000 (3). In addition, not only are people living longer, disability rates are declining as well (4). Given the demographic shift that we in the US and other industrialized countries are experiencing, the challenge of the future will be to continue to support and augment this trend towards lower disability rates thereby enabling individuals the optimal opportunities to age successfully. Without vigorous commitment to these goals, which are certainly within our grasp provided there are sufficient resources dedicated to accomplishing them, our healthcare and economic systems will be overwhelmed.

When considering a prescription for healthy, successful aging, the vital role of physical activity is immediately apparent, and, this role is increasingly supported by data from a variety of epidemiological, health outcomes and experimental studies. Physical activity not only lowers the risk of mortality (5) but is associated with decreased morbidity from many chronic diseases like cardiovascular disease, stroke, coronary heart disease, cancer (6,7), depression (8) and diabetes (9,10,11). Research has shown a positive association between physical activity and both cognitive function (12,13) and physical function (14). In this article, we review a large body of research that examines physical activity and cognitive health. Although cognitive health can be defined in many different ways, for the purposes of this paper we use a broad definition that includes improvement, maintenance, or minimal decline, of cognitive function and absence, delay of onset, or slowing the progression of dementia. Specifically, we focus on the associations of physical activity with (or effects of physical activity on) cognitive function and dementia. Our definition of physical activity is also broad and includes exercise, as well as usual daily activities, such as household chores and walking, and physical leisure activities, such as playing golf or tennis. To be as comprehensive as possible we have not performed a meta-analysis which would considerably limit the type and number of studies that we could include for review and analysis here. Instead we have prepared a descriptive review of the literature including various types of publications, prospective cohort, case-control, clinical trial and meta-analysis papers, published recently (1999 or later) in peer-reviewed journals (see Tables 1 and 2 for a brief tabulation and summary of the studies examined here). Through this systematic descriptive review, we examine the current state of knowledge about any putative beneficial effects of physical activity on both cognitive function and dementia. Key questions that we have used to structure our examination of the current literature are:

1. Does engagement in physical activity result in improvement or maintenance of cognitive function?
2. Does engagement in physical activity result in a lower risk for dementia?

2. Cognitive function

There is a growing body of research, predominately prospective cohort studies, which have examined the connections between cognitive function and physical activity (see Table 1). Results have overwhelmingly shown an association between the two.

2.1 Evidence from prospective cohort studies

Two studies of women only show strong associations between physical activity and cognitive function (13,15). Both include walking, have large sample sizes, controlled for typical potential confounding factors and have long follow-up periods.

Using data from the Nurses' Health Study, Weuve et al. included 18,766 women ages 70 to 81 to ascertain whether or not greater participation in leisure-time physical activities, as measured by energy expenditure (mean of biennial reports over 8 to 15 years), resulted in better cognitive function, as measured by a global cognitive function score, created by combining scores from six different tests. Analyses controlled for potential confounders (i.e. age, education, etc.).

Results indicated that cognitive scores were higher for women who expended more energy ($p < .001$ for trend). Furthermore, easy walking, at a pace of about 21 to 30 minutes per mile, for at least 1 and ½ hours per week resulted in scores that were at least .06 units higher than those of subjects walking less than 38 minutes per week ($p = .007$ for trend), indicating that exercise may not need to be vigorous to have an effect. Although .06 may not appear to be much of a difference, it approximates the difference in cognitive functioning of women differing by about 1 and ½ years in age (13).

In another study of women only, Yaffe et al. followed 5,925 women age 65 and older for 6 to 8 years to determine whether or not walking and kilocalories (or energy) used during physical activity (assessed at baseline) were associated with less cognitive decline, as measured by the modified Mini-Mental State Examination (mMMSE). The women, part of the Study of Osteoporotic Fractures, were all cognitively unimpaired at baseline. After adjusting for potential confounders such as age, education, functional limitations, etc., at follow up women in the highest quartile of blocks-walked-per-week (median = 175, range = 113-672), compared to those in the lowest quartile (median = 7, range = 0-22), were 34% (odds ratio = .66, 95% confidence interval = .54-.82) less likely to experience cognitive decline, defined as a score on the mMMSE ≥ 3 points lower than at baseline. One block was estimated to be about 160 meters, so women in the highest quartile walked approximately 17.4 miles per week. Those in the highest quartile for kilocalories expended, compared to those in the lowest quartile were 26% (odds ratio = .74, 95% confidence interval = .60-.90) less likely to have cognitive decline at follow up (15).

Several studies have examined the relationship between physical activity and cognitive function for men only. Both studies have small sample sizes which might explain the weaker links between physical activity and cognitive function that their results indicate.

In one such prospective cohort study, 295 men, part of the Finland, Italy, and the Netherlands Elderly or FINE Study, age 70 and older were assessed at baseline and 10 years later for both physical activity, such as walking, bicycling, gardening, chores, etc., and cognitive function, using the MMSE. A cutoff point of over 18 on the MMSE, which the authors note as “not severely cognitively impaired”, was used as part of inclusion criteria along with an absence of stroke, diabetes, cancer and heart attack. Physical activity data were not available from Finish subjects at the 10-year follow-up, leaving 243 subjects for those analyses. After adjusting for potential confounders such as age, education, etc., measures of neither duration nor intensity of physical activity at baseline were associated with differences in baseline cognitive functioning. However, results indicated linear trends between cognitive decline and changes in both duration of activity ($p = .02$) and intensity of activity ($p = .002$). A strength of this study is the long follow-up period of 10 years; however, the sample size for these analyses was quite small. In addition only those who were “severely cognitively impaired” were excluded from the analyses (16).

In another study of men only, 347 men from the Netherlands who were part of the Zutphen Elderly Study were followed for 3 years. Subjects were considered more active if they engaged, at baseline, in self-reported physical activity for over an hour per day; less active subjects reported physical activity of an hour or less per day. Cognitive decline was defined as a decrease greater than 3 points, over the 3 year period, on the Dutch version of the MMSE, wherein the highest score is a total of 30 points. Analyses of those with and without the apolipoprotein e4 allele were also performed. After adjusting for possible confounders such as age, education, etc., comparing all more active men to all less active men, those who were less active were twice as likely to experience cognitive decline, although this finding was not significant (odds ratio = 2.0, 95% confidence interval = 0.9-4.8). However, men with the apolipoprotein e4 allele who were less active were 3.7 times (95% confidence interval = 1.1-12.6) more likely to

experience cognitive decline, in adjusted models, at follow up when compared to those who were more active. It should be noted that the sample size for this study is small and there were only 37 carriers of the e4 allele in the less active group and 47 in the more active group (17).

In a study of Chinese elderly who were followed for 3 years, Ho et al. found an association between not exercising (self-report) at baseline and incident cognitive impairment, as measured by questions extracted from the CAPE (Clifton Assessment Procedure for the elderly). Analyses were adjusted for age and education and the odds ratio was 2.1 (95% confidence interval = 1.3-3.3). When the data were analyzed separately for men and women, the relationship held for women only (odds ratio = 2.2, 95% confidence interval = 1.2-3.8). Of note the women in this sample of 988 study subjects age 70 and older were quite different than their male counterparts. All women and men were cognitively unimpaired at baseline, but the women compared to the men, at baseline, had less education and were more financially dependent on others. The women also reported poorer health and had greater functional limitations. At follow-up, 6.7% of the men in the sample had cognitive impairment, but 22.2% of the women were cognitively impaired; women were 2.7 times (95% confidence interval = 1.6-4.4) more likely to be cognitively impaired at follow-up. The sample size for this study was just under 1,000 subjects and when compared to the sample sizes of Weuve et al. (13) and Yaffe et al. (15), it could be considered relatively small (18).

The studies described above are all based on self-reported physical activity. To overcome the limitations associated with self-reported data, such as potential errors due to recall, Barnes, et al. examined possible associations between cognitive function and fitness by measuring peak oxygen consumption, a measure of physical fitness, using a sample of 349 adults age 55 and older. Levels of fitness as well as cognitive function, as measured by the mMMSE, were assessed at baseline. They found no association between mMMSE scores and peak oxygen consumption at baseline ($p = .22$ for trend). Six years later, subjects were given a full battery of cognitive tests, including the full MMSE. After adjusting for gender, study subjects who were less fit at baseline experienced greater cognitive decline ($p = .002$ for trend) and had lower cognitive scores at follow up, when compared to those who were more fit (19).

The diverse group of prospective cohort studies outlined above include samples that are not comparable across studies, and they do not use common measures for physical activity or cognitive function while the timeframes for follow up also vary. These and other differences among these studies notwithstanding we can cautiously infer that the studies with large sample sizes (> 1,000) identified strong associations between physical activity and cognitive function while studies with smaller sample sizes had less definitive results.

2.2 Evidence from randomized trials

All three of the identified randomized trials support the prospect that engagement in physical activity will result in improvement or maintenance of cognitive function. Two studies (20, 21) found that aerobic, vs. anaerobic, activity resulted in improved executive function and one study (22) found that overall cognitive function improved for subjects who engaged in aerobic activity even though the intervention lasted for only 2 months.

In a randomized trial of 124 sedentary older adults (age 60 to 75 years old), Kramer et al. were able to show an impact of aerobic exercise on executive functioning (i.e. planning, problem-solving, scheduling, etc.). Following a pretest, study subjects were randomly assigned to either a walking (aerobic) intervention or a stretching and toning (anaerobic) intervention. After participating in the exercise interventions for 6 months, subjects were given a posttest. Results indicated that the scores on cognitive tests requiring greater executive processing improved for the group assigned to the aerobic intervention but not for the anaerobic group. For cognitive

tests requiring less executive control (e.g. reaction time to a command to stop), both groups showed similar results (20).

In a later study conducted by Colcombe, Kramer et al. 29 adults, age 58 to 77 years old were again randomly assigned to an aerobic (walking) or anaerobic (stretching and toning) exercise intervention group. Both the aerobic group and the anaerobic group met 3 times a week for 6 months. Aerobic sessions initially lasted for 10 to 15 minutes, then increased 1 minute each session to a maximum of 40 to 45 minute sessions. Participants were at the maximum level for approximately the last half of the intervention. Anaerobic sessions followed the same schedule as aerobic sessions and also increased in level of difficulty. Pre- and posttests were administered prior to and following the interventions. The pre- and posttests this time consisted of asking subjects to respond to both congruent and incongruent cues. Reaction times were measured and a comparison of reaction times for incongruent cues and congruent cues was made as follows: increase in reaction time to incongruent cues (as a percentage) over reaction time to congruent cues, resulting in a measure of executive function. The aerobic group experienced an 11% reduction between pre- and posttests ($p < .04$), while the anaerobic group had only a 2% reduction, which was not statistically significant (21).

In a related study, Colcombe et al. enrolled 41 older adults, assessed their physical fitness and divided them into two groups: those with a higher level of fitness and those with a lower level. Study subjects took the same cognitive performance test noted above and reaction time scores were computed. Although both groups made relatively few errors, those in the higher level fitness group handled the incongruent cues better ($p < .02$) than those in the lower level fitness group (21).

Fabre et al. undertook a randomized trial of 32 adults, age 60 to 76 years old, for which subjects were randomly assigned to one of 4 groups, resulting in 8 study subjects per group. The 4 groups were: individualized aerobic training intervention, cognitive training intervention, a combined cognitive and individualized aerobic training intervention and a control group. Aerobic training (for both the aerobic training and combined aerobic and cognitive training groups) consisted of 2 sessions each week for a period of 2 months. Each session was an hour long, including a 5-minute warm up and a 10-minute cool down, and was individually tailored, gradually increasing in intensity. Subjects were given a pretest and then participated in the various interventions for 2 months. Those in the control group also met over the 2 month period following the pretest. At the end of the 2 month period, all study subjects were given a posttest. Results from the Wechsler memory scale indicated that subjects in the 3 intervention groups all improved between the pre- and posttests ($p < .01$), while the control group showed no statistically significant improvement. Further, participants in the combined cognitive and aerobic intervention group, showed greater improvement than all of the other groups ($p < .001$), intervention and control. The cognitive training intervention group improved scores by 7.4%, the aerobic group by 8.5% and the combined aerobic and cognitive training group by 9.2% (22).

2.3 Evidence from a meta-analysis of early randomized trials

A recent meta-analysis of 18 randomized trials published between 1966 and 2001, including Kramer et al, 1999 described above, indicated that aerobic exercise training can positively impact cognitive function for healthy, nonexercising older adults, average age of 55 and older ($p < .05$). Impact was greatest for executive function ($p < .05$) when compared to other cognitive processes and interventions with exercise sessions less than 30 minutes long had no effect ($p < .05$). In addition, the effects of a combined (aerobic and strength) intervention were greater than a pure aerobic intervention ($p < .05$) alone (12).

Although most of the research available is from prospective cohort studies, and therefore shows association and not causation, and the number of randomized trials is limited, evidence to suggest that physical activity or fitness could be linked by some mechanistic process to offset aging-related declines in cognitive function is growing. A few thoughts on exercise prescription emerge from the findings outlined above and can be incorporated into future research in this area. For example, walking was found to be associated with better cognitive function in a number of studies including some designed as randomized trials (13,15,20,21). Kramer et al. found in their meta-analysis that exercise sessions needed to be at least 30 minutes long to be effective (12). Although the authors of just one randomized trial by Fabre et al. were able to see cognitive improvement after just 2 months of an aerobic intervention, this implies that improvements may be realized quite quickly (22). In the next section we review studies examining any potential effect of physical activity to prevent, delay or slow the progression of dementia, including dementia due to brain degeneration caused by Alzheimer's disease (AD).

3. Dementia

The vast majority of the recent research that has sought to determine if there is evidence for any potential benefit of physical activity on the prevention, delay or slowing down of disease progression for AD and other dementias comes from prospective cohort studies (see Table 2). The evidence to date on this subject is not as strong as that examining the effects of physical activity on cognitive function, and the associations between them, and almost no studies have sought to conduct prospective, randomized trials of physical activity as an intervention for dementia.

In a prospective cohort study Larson et al. followed 1,740 dementia-free study subjects, age 65 and older, from the Adult Changes in Thought (ACT) Study for a mean of a little over 6 years. At baseline, participants were asked how often they participated in physical exercise, activities like walking, aerobics, swimming, stretching, etc. Regular exercisers were defined as those who exercised at least 3 times a week (at least 15 minutes per session). After adjusting for possible confounders such as age, gender, cerebrovascular disease, coronary heart disease, having the apolipoprotein e4 allele, etc., results indicated that regular exercisers were less likely (hazard ratio = .68, 95% confidence interval = .48-.96, $p = .03$) to have dementia at follow-up when compared to subjects who exercised less than 3 times per week (23).

Another large prospective study with a similar follow-up timeframe, but in this instance using AD as the outcome variable, found a similar risk reduction of just over 30%. Lindsay et al. carried out a prospective study, aimed at identifying risk factors for AD using the Canadian Study of Health and Aging (CSHA) cohort, all age 65 or older at baseline. Of the 4,088 participants included in this analysis, 194 were diagnosed with incident AD at follow-up, 5 years later (on average). After controlling for age, gender and education, regular exercise, assessed via a baseline yes/no question regarding exercising regularly, was associated (odds ratio = .69, 95% confidence interval = .50-.96) with a lower risk of AD (24).

In another study that used the CSHA cohort ($N = 4,615$ for this analysis), Laurin et al. examined the association between exercise and incident cognitive impairment-no dementia (CIND) and dementia (any type). At follow-up, 436 subjects were diagnosed with CIND, 194 with AD, 61 with vascular dementia and 30 with other dementias. Exercise was rated, using frequency and intensity, as high, moderate or low. High consisted of exercise, carried out at least three times a week, that was more intense than walking; moderate was exercise at least three times a week but equal to the intensity of walking; low included all other combinations of intensity and frequency; those who reported no exercise were classified as such. Controlling for age, education and gender, they found that subjects whose exercise rating was higher (more often and with greater intensity) had a lower risk for both CIND ($p < .001$ for trend) and dementia

($p = .04$ for trend). For those with a “high” rating, the odds ratio of developing CIND was .58 (95% confidence interval = .41-.83) and for dementia it was .63 (95% confidence interval = .40-.98). Further analysis by gender resulted in a statistically significant association for women in the study between exercise and CIND ($p = .003$ for trend) and AD ($p = .05$ for trend) but not for dementia of any type ($p = .18$). For men there were no statistically significant associations between exercise and CIND, AD or dementia of any type. The authors note that this lack of association for men may be the result of a small number of cases (25).

Using data from the Cardiovascular risk factors, Aging and Incidence of Dementia (CAIDE) study, Rovio et al. followed 1,251 participants for an average follow-up of 21 years. A total of 61 subjects were diagnosed with dementia at follow-up. During the baseline exam, completed at 50.6 (mean) years of age, study subjects completed a questionnaire which included an item regarding “leisure-time physical activity”. Specifically they were asked how frequently they engaged in such activity, for at least 20 minutes, causing “breathlessness and sweating”. Responses ranged from “daily” to “not at all” and responses were grouped and categorized as at least two times per week (active) and all others (sedentary). After controlling for age, education, gender, cholesterol levels, blood pressure, smoking, apolipoprotein e4 carrier status, etc., analyses resulted in a finding that those in the active group were less likely to have a diagnosis of dementia at follow-up (odds ratio = .48, 95% confidence interval = .25-.91) when compared to those in the sedentary group. When data for men and women were analyzed separately, associations were no longer statistically significant. However, Rovio et al. note that this may be due to such small sample sizes for these analyses. The effects of being a carrier of the apolipoprotein e4 allele were also examined. Active carriers may have a reduced risk of dementia compared to sedentary carriers. Adjusting for some variables (i.e. age, education, cardiovascular risk factors, etc.) resulted in an odds ratio of .38 and 95% confidence interval of .15-.99 for active carriers compared to sedentary carriers; however, the fully adjusted model which included smoking and alcohol consumption was not significant (odds ratio = .41, 95% confidence interval = .16-1.06). For noncarriers of the apolipoprotein e4 allele, there was no statistically significant association between being active, compared to sedentary, and dementia risk (26).

Abbott et al. followed 2,257 dementia-free men, age 71 to 93, from the Honolulu-Asia Aging Study to examine the effects of walking on incident dementia. After an average of almost 7 years of follow-up, 158 men were diagnosed with dementia. Men who walked over 2 miles per day at initial assessment for this analysis were compared to men categorized as walking shorter distances per day. After controlling for possible confounders such as age, education, diabetes, cardiovascular risk factors, apolipoprotein e4 carrier status, etc., an association was found between walking less than ¼ mile per day (relative hazard = 1.93, 95% confidence interval = 1.11-3.34, $p = .02$) and walking ¼ to 1 mile per day (relative hazard = 1.75, 95% confidence interval = 1.03-2.99, $p = .04$) and incident dementia. There was no difference in risk between men who walked > 1 mile to 2 miles per day compared to men who walked over 2 miles per day (27).

The cohort in the Cardiovascular Health Cognition Study (CHCS), all age 65 and older, was asked to complete a modified version of the Minnesota Leisure Time Activity Questionnaire during the baseline interview and calculations were made for the number of physical activities undertaken within a two week period and energy expenditure per week. After an average follow-up period of almost 5 ½ years, 480, out of 3,375, subjects developed dementia. Although after adjusting for age, education, gender, apolipoprotein e4 carrier status, baseline mMMSE score, etc. greater energy expenditure was not associated with a lower risk of dementia, those with more activities over the two-week period were less likely to develop dementia ($p = .004$ for trend; hazard ratio for ≥ 4 activities compared to 0 to 1 activity = .58 (95% confidence interval = .41-.83)). Further, Podewils et al. found that in adjusted models noncarriers of the

apolipoprotein e4 allele who expended greater energy per week had a decreased risk of dementia ($p = .01$ for trend) and risk was also decreased for noncarriers who participated in at least four activities (hazard ratio = .44 (95% confidence interval = .28-.69) over the two-week period covered by the leisure activity questionnaire (28).

Friedland et al. conducted a case-control study with participants from the Alzheimer's Disease Case-Control Study population at Case Western Reserve University. They collected retrospective data directly from the control subjects ($N = 358$) and from surrogates for the cases ($N = 193$), asking whether or not 26 activities were undertaken at least once a month. For each activity undertaken, respondents were asked the number of hours spent doing the activity each month in early adulthood (20s and 30s) and during mid adulthood (40s and 50s). Activities were then grouped as physical, intellectual or passive. Scores on diversity (number of activities undertaken in each group divided by total number of activities in that group) and intensity (number of hours per month spent doing the activities in each group) were calculated. After controlling for potential confounders such as age, education, gender, etc., cases participated in fewer activities compared to controls ($p < .001$). Although those with greater diversity of physical activities were less likely ($p \leq .001$) to be included as a case (have AD) even after controlling for possible confounders, physical activity intensity (number of hours per month) was not associated with a decreased likelihood of having AD in adjusted analyses. One reason for the lack of association between AD and hours spent participating in physical activities might be the difficulties of reporting such detailed recalled information from earlier periods of one's life. For surrogate reporting, we can assume that this problem would be magnified (29).

In a prospective cohort study using data from the Bronx Aging Study (currently Einstein Aging Study), Verghese et al. followed 469 subjects, over age 75, who were free of dementia at baseline, for up to 21 years, with a median follow-up of just over 5 years. During the initial interview, subjects were asked about their participation in 6 cognitive activities and 11 physical activities (tennis or golf, swimming, bicycling, dancing, group exercises, team sports such as bowling, walking, climbing stairs, housework and babysitting). They were also asked about the frequency of their participation which was then calculated as activity-days per week. For example, subjects received 7 points if they participated in an activity each day and 0 points if participation was monthly or less. A total of 124 study subjects were diagnosed with dementia by the end of the study. The composite score for physical activity was not associated with a lower risk of dementia. However after adjusting for possible confounders such as age, gender, education, etc., dancing was (hazard ratio = .24, 95% confidence interval = .06-.99), since those who danced frequently (at least several days per week) were less likely to have been diagnosed with dementia compared to those who rarely (once a week or less) danced (30).

Wilson, Mendes de Leon et al. followed 733 subjects, at least 65 years old and with no dementia at baseline, in the Religious Orders Study to ascertain any association between incident AD, as well as cognitive decline, and physical activity (exercise such as bicycling, swimming, walking, calisthenics and yardwork). Study participants were asked how much time they spent doing each activity in the 2 weeks prior to the baseline evaluation. From this information, a score of hours per week spent doing physical activities was computed. Subsequent to an average follow-up of 4.5 years, 111 study subjects had been diagnosed with AD. After adjusting for age, education and gender, there was no association between physical activity and incident AD or decline in cognitive function (31).

Wilson, Bennett et al. used the Chicago Health and Aging Project to evaluate any association between participation in physical activities and incident AD. All 835 study participants were age 65 and older and did not have AD at baseline. They were asked, at the baseline interview, about their participation in 9 physical activities (i.e. swimming, walking, dancing, calisthenics, yardwork, etc.) and a score of hours per week engaged in physical activities was calculated. A

total of 139 subjects were diagnosed with AD after a mean follow-up of just over 4 years. Controlling for apolipoprotein e4 carrier status and demographic characteristics, Wilson, Bennett et al. found no association between physical activity participation and incident AD (32).

Study subjects from the Kungsholmen Project, all age 75 and older, who were not diagnosed with dementia by the time of the first follow-up and who agreed to participate (N = 732) were followed for 3 additional years. By the second follow-up, 123 subjects were diagnosed with incident dementia. At baseline subjects had been asked what activities they do and how often they participate in them. Responses were categorized as physical (swimming, walking, gymnastics), mental, social, productive (i.e. housekeeping, gardening, volunteering, etc.) or recreational (television viewing or listening to the radio). After controlling for potential confounders such as age, gender, education, etc., Wang et al. found no association between participation in physical activity (everyday vs. less than everyday vs. never) and incident dementia. However, it should be noted that only 3 subjects with dementia exercised everyday, only 6 exercised less than everyday and 114 did not exercise at all (33).

Although data from the studies summarized above are not consistent enough to allow one to state definitively that exercise can lower the risk of, or prevent, delay or slow the progression of dementia, the evidence presented above does provide a foundation for future, more nuanced research in this area to dissect out the relationship between physical activity and aging-related cognitive impairments that progress to dementia. It should be noted that the studies that found no association between physical activity and dementia (29,30,31,32,33) all had relatively small sample sizes (< 1,000) compared to those that found an association (23,24,25,26,27) and perhaps the sample sizes were not large enough to identify an association.

Some thoughts that can inform future research regarding an exercise prescription emerge as well. Several studies (23,25) found associations between exercising at least 3 times per week and a lower risk of dementia. One study (26) found an association between exercise at least twice a week and a lower risk of dementia; however, exercise sessions needed to be vigorous, causing “breathlessness and sweating” and lasting at least 20 minutes. In addition, one randomized trial which tested the effects of exercise on cognitive function (described above in the section on physical activity and cognitive function) used an intervention lasting 40 to 45 minutes 3 times a week and found a positive effect (21). In another randomized trial of the effects of exercise on cognitive function (also described above), subjects participated in 2 sessions per week but each was 1 hour long. The results of this trial were positive as well (22). Given this evidence, next steps might include studying exercise interventions prescribed for 3 times a week or twice a week if exercise is vigorous or sessions are lengthy.

Walking was beneficial in a study examining risk of incident dementia for men (27), but those who experienced a decreased risk walked over 2 miles per day. Since there was no statistically significant difference in risk identified in this study for those walking over 2 miles per day compared to those walking in the range of over 1 to 2 miles per day, walking at least 1 mile a day may be the cut point for experiencing benefit. Of course, this would need to be tested further. Walking was also found to be associated with, or responsible for with the randomized trials, better cognitive function in a number of studies described above in the section on physical activity and cognitive function (13,15,20,21). In addition, dancing, at least several days a week, was found to be beneficial in one study (30).

4. Summary

Two recent reviews have highlighted the potential for physical activity and other life style practices as possible intervention strategies to prevent, delay or slow the progression of dementia (34,35). In addition, using a transgenic mouse model of AD-like A β pathologies,

Adlard et al. were able to demonstrate that a voluntary exercise intervention resulted in a statistically significant decrease of “AD-like neuropathology” (36). Evidence-based support for using exercise as a potential intervention to lower the risk of dementia, or slow its progression, is growing; however, more research is needed before definitive recommendations can be made to consumers and health care providers. Although many studies have found an association between physical activity and better cognitive function and a lower risk of dementia, some studies have not. In addition, cause and effect have not been sufficiently demonstrated. It is not clear whether participation in physical activities results in improved cognitive function and a lower risk of dementia or do those with better cognitive function and a lower risk of dementia participate in physical activities. It is also possible that the associations are a result of other unmeasured, and uncontrolled for, variables. For example, variations in the constitutive levels of trophic factors or other endogenously produced substances could account for these associations if high levels of these factors or substances act to both stimulate physical activity and enhance cognition.

If physical activity does have a beneficial effect on cognitive function and can lower the risk of dementia, how this might be brought about is still unclear. There are several leading theories regarding how physical activity might reduce the risk of cognitive decline, including (a) reduction of cardiovascular risk; (b) reduction of inflammation, (c) increasing trophic factor production and (d) through neurogenesis. It has also been suggested that some of these mechanisms may work in combination. There is a growing body of research linking risk of dementia and cardiovascular disease and risk factors (37,38), leading to the theory that dementia risk is heightened as cardiovascular risk is heightened (e.g. when level of physical activity is low). It has also been posited that physical activity may reduce inflammation which has been identified as a possible contributory factor of dementia (39). Finally, it has been hypothesized that physical activity can be neuroprotective by increasing levels of trophic factors or by neurogenesis, as this has been shown in animal models (40,41). Although most of our data on physical changes to the brain after participation in physical activity come from animal models, a recent study demonstrated that older adults who participated in an aerobic exercise intervention for 6 months boosted brain volume, both gray and white matter, suggesting that the human brain can be enhanced through aerobic activity (42). More research is needed to identify the pathway(s) by which physical activity may impact cognitive function.

Even if it was clear that physical activity improves cognition and lowers the risk of dementia and we knew how that happened, there are many unanswered questions about exercise. No specific or clear guidelines about what kinds of exercise are the most beneficial currently exist. Walking was identified in several studies as being beneficial (13,15,20,21,27), but swimming might be just as effective and jogging might be even better, for example. In one randomized trial, walking improved cognitive function while stretching and toning did not (21). On the other hand in the meta-analysis described above, a combined intervention of aerobic plus strength training was more effective than just an aerobic intervention alone (12).

There are no unequivocal directions regarding the recommended dose of exercise, i.e. how many times per week, for what length of time and how intense. Results of the meta-analysis indicate that sessions lasting less than 30 minutes are not effective for cognitive function (12). However, is 30 minutes the optimal amount of time and how many sessions per week are needed? Is 45 minutes twice a week as effective as 30 minutes 3 times a week? Further, there is a need for more research on approaches to exercise and exercise routines that will result in the greatest levels of compliance among participants (43). A better understanding of screening criteria for determining the safety of exercise prescriptions for older individuals (7) and identification and testing of approaches to training health care practitioners that will encourage their recommendation of and screening for exercise prescriptions for their older patients (43)

are also needed. Estimates of current exercise programs for older adults indicate that a sizeable increase in their number will also be required (44).

Although the strength of the evidence falls short of what is needed for definitive recommendations about physical activity and cognitive health and a good deal of research remains to be done, there are several emerging themes from this body of work that should be highlighted since they point to promising areas of inquiry:

- Evidence related to a possible link between physical activity and cognitive health continues to grow and strengthen.
- Aerobic activity appears to be beneficial for cognitive health.
- Walking seems to be an effective aerobic strategy for impacting cognitive health.
- Engagement in physical activity may have the greatest effect on executive function, compared to other cognitive processes, for example speed-related tasks.
- Exercise sessions may need to be at least 30 minutes long to be of benefit for cognitive health.

Given the demographic imperative of our aging population (3), it is essential that effective strategies to lower the risk of dementia, or slow its progression, are identified in the near future. Exercise, if proven to be one such strategy, can be carried out by most people and has other health benefits (6,7,8,9,10,11). Additional research studies, including secondary analyses of existing databases and especially randomized trials, are needed to test the effectiveness of this relatively low cost, easily attainable, lifestyle intervention. In addition, more research is needed to identify the characteristics of effective exercise interventions and match them to specific populations that could benefit from them; to address safety concerns and appropriate screening for participation and to retool or reinvent interventions if necessary; and to identify strategies that will maximize participation and compliance in exercise interventions among all populations.

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Table 1

Cognitive Function and Physical Activity/Fitness

Authors and Publication year	Subjects	Study type	Physical activity/ Fitness	Outcome measure(s)	Results
Weuve, Kang, Manson, et al., 2004	18,766 women, age 70 to 81; Nurses' Health Study	Prospective cohort	Leisure-time physical activities (i.e. running, walking, swimming, etc.)	Cognitive function	Association between cognitive function and physical activities ($p < .001$)
Van Gelder, Tijhuis, Kalmijn, et al., 2004	295 men, age 70 and over; FINE Study	Prospective cohort	Walking, bicycling, sports, odd jobs, etc.	Cognitive decline	Association between cognitive decline and decrease in duration ($p = .02$) and intensity ($p = .002$) of physical activities
Colcombe, Kramer, Erickson, et al., 2004	Study 1: 41 older adult participants; Study 2: 29 participants age 58 to 77	Clinical trial	Study 1: Level of fitness (Rockport 1-mile walk protocol); Study 2: Walking (intervention) vs. stretching and toning (control)	Cognitive function	Study 1: More highly fit participants performed better on the cognitive tests ($p < .02$); Study 2: Walkers performed better from pre- to posttests ($p < .04$) and those in the control group did not
Barnes, Yaffe, Satariano, et al., 2003	349 participants, age 55 and over; Sonoma, CA Study	Prospective cohort	Cardiorespiratory fitness	Cognitive function	Association between cognitive function and cardiorespiratory fitness ($p = .002$)
Colcombe, Kramer, 2003	Subjects in 18 intervention studies, average age 55 and over	Meta- analysis	Aerobic and aerobic + strength training interventions	Cognitive function	Both exercise ($p < .01$) and control ($p < .05$) groups improved cognitive function but exercise groups improved more ($p < .05$)
Fabre, Chamari, Mucci, et al., 2002	32 participants, age 60 to 76	Clinical trial	Aerobic training, mental training, aerobic and mental training (no training for control group)	Cognitive function	Logical memory ($p < .05$), paired associates learning ($p < .05$) and memory quotient ($p < .01$) improved for the intervention groups
Ho, Woo, Sham, et al., 2001	988 Chinese elderly (≥ 70)	Prospective cohort	Exercise	Cognitive impairment	Risk of cognitive impairment was doubled for women not exercising at baseline (odds ratio = 2.2, 95% confidence interval = 1.2-3.8)
Schuit, Feskens, Launer, et al., 2001	347 Dutch men, age 65-84; Zutphen Elderly Study	Prospective cohort	Physical activity for > 1 hour/day vs. ≤ 1 hour/day	Cognitive decline	For men with the apolipoprotein e4 allele, risk of cognitive decline more than tripled with ≤ 1 hour/day of physical activity vs. those with > 1 hour/day (odds ratio = 3.7, 95% confidence interval = 1.1-12.6)
Yaffe, Barnes, Nevitt, et al., 2001	5,925 women, age 65 and over; Study of Osteoporotic Fractures	Prospective cohort	Walking and kilocalories used during physical activity	Cognitive decline	More walking and more kilocalories spent were both associated with decreased odds of cognitive decline: walking,

Authors and Publication year	Subjects	Study type	Physical activity/ Fitness	Outcome measure(s)	Results
Kramer, Hahn, Cohen, et al., 1999	124 adults, age 60 to 75	Clinical trial	Walking (intervention) vs. stretching and toning (control)	Executive function, other cognitive functions	odds ratio = .66 (95% confidence interval = .54- .82) and kilocalories, odds ratio = .74 (95% confidence interval = .60- .90) Executive function improved for intervention group but not control group; other cognitive functions were similar for both groups (statistical significance not reported)

Table 2

Dementia and Physical Activity/ Fitness

Authors and Publication year	Subjects	Study type	Physical activity/ Fitness	*Outcome measure(s)	Results
Larson, Wang, Bowen, et al., 2006	1,740 participants, age 65 and older; Adult Changes in Thought (ACT) Study	Prospective cohort	Exercise (i.e. walking, weight aerobics, weight training, stretching, etc.)	Incident dementia	Association between lower incidence of dementia and exercising 3 or more times/week ($p = .03$)
Rovio, Kareholt, Helkala, et al., 2005	1,251 participants, age 65-79 at reexam; Cardiovascular risk factors, Aging and Incidence of Dementia (CAIDE) Study	Prospective cohort	Frequency of participation in leisure-time physical activities, for at least 20 minutes, during midlife	Dementia	Association between lower risk of dementia and physical activity participation at least 2 times/week (odds ratio = .48, 95% confidence interval = .25-.91)
Podewils, Guallar, Kuller, et al., 2005	3,375 participants, age 65 and over; Cardiovascular Health Cognition Study	Prospective cohort	Physical activities (i.e. walking, biking, household chores, yardwork, etc.)	Incident dementia	Association between lower risk of dementia and participation in ≥ 4 activities in past 2 weeks ($p = .004$); hazard ratio = .58 (95% confidence interval = .41-.83)
Abbott, White, Ross, et al., 2004	2,257 men, age 71-93; Honolulu-Asia Aging Study	Prospective cohort	Walking	Incident dementia	Association between incident dementia and shortest distance walked/day (relative hazard = 1.93, 95% confidence interval = 1.11-3.34) and next shortest distance (relative hazard = 1.75, 95% confidence interval = 1.03-2.99)
Vergheze, Lipton, Katz, et al., 2003	469 participants, age 75 to 85 years old; Bronx Aging Study	Prospective cohort	Physical activities (i.e. swimming, walking, housework, babysitting, etc.)	Incident dementia	Association between more frequent dancing and lower risk of incident dementia (hazard ratio = .24, 95% confidence interval = .06-.99); no association between incident dementia and composite physical activity score
Wang, Karp, Winblad, et al., 2002	732 participants, age 75 and older; Kungsholmen Project	Prospective cohort	Physical activities (i.e. swimming, walking, gymnastics)	Incident dementia	No association between incident dementia and physical activities
Wilson, Bennett, Bienias, et al., 2002	835 participants, age 65 and older; Chicago Health and Aging Project	Prospective cohort	Physical activities (i.e. swimming, jogging, walking for exercise, etc.)	Incident Alzheimer's disease (AD)	No association between incident AD and physical activities

Authors and Publication year	Subjects	Study type	Physical activity/ Fitness	* Outcome measure(s)	Results
Wilson, Mendes de Leon, Barnes, et al., 2002	733 participants, age 65 and over; Religious Orders Study	Prospective cohort	Exercise (i.e. walking, swimming, etc.) or gardening/yardwork Regular exercise	Incident AD	No association between incident AD and physical activities
Lindsay, Laurin, Verreault, et al., 2002	4,088 participants, age 65 and over; Canadian Study of Health and Aging	Prospective cohort	Regular exercise	Incident AD	Association between regular exercise and a reduced risk of AD (odds ratio = .69, 95% confidence interval = .50-.96)
Friedland, Fritsch, Smyth et al., 2001	551 participants; Alzheimer's Disease Case-Control Study at Case Western Reserve University	Case-control	Physical activity	AD	Greater diversity of physical activities undertaken was associated with a decreased likelihood of having AD ($p \leq .001$); more time spent undertaking physical activities was not associated with a lower likelihood of having AD
Laurin, Verreault, Lindsay, et al., 2001	4,615 participants, age 65 and over; Canadian Study of Health and Aging	Prospective cohort	Exercise frequency and intensity	Incident cognitive impairment and dementia	Association between greater physical activity and less risk of cognitive impairment-no dementia ($p < .001$) and less risk of dementia ($p = .04$)

* Notes: For some studies the outcome measure was dementia, of various types, and for some the focus was on Alzheimer's disease (AD). Incident dementia refers to dementia that was diagnosed during the study and subjects were dementia free at baseline.