Published in final edited form as:
J Aging Health. 2007 April ; 19(2): 242–259. doi:10.1177/0898264307299299.

Physical Activity and the Risk of Dementia in Oldest Old

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Abstract

Objective—This study evaluated the protective role of physical activity (PA) against cognitive impairment (CI) in the oldest old (age ≥ 85).

Method—Prospective data on 66 optimally healthy, oldest old adults (mean age 88.5) were analyzed using survival analysis.

Results—In all, 12 men and 11 women reported exercising > 4 hours per week, and 38 participants developed CI (mean onset age 93; mean follow-up 4.7 years). The effect of exercise was modified by gender. In more active women (> 4 hours/week), the risk of CI was reduced by 88% (95% confidence interval 0.03, 0.41) compared to those less active. Less active women had 2 times the incidence rate of CI compared to less active men and almost 5 times the rate compared to active women.

Discussion—This study demonstrates the beneficial effects of exercise on healthy brain aging even in the oldest old and emphasizes the importance of increasing PA in older women.

Keywords

oldest old; physical activity; exercise; dementia; cognitive impairment

Rowe and Kahn (1987) proposed that the aging process is not necessarily associated with disease and that many supposed age-related declines could be prevented. In the model proposed by Rowe and Kahn, “successful aging” was characterized by the absence of disease, disability, and risk factors such as high blood pressure, smoking, and obesity; maintenance of physical and mental functioning; and active engagement with life. They emphasized the importance of identifying risk factors associated with successful aging to promote optimal health in older age. Since this model was proposed, the study of “successful aging” has provided evidence that genes do not explain the aging process entirely and that modifiable environmental and lifestyle factors have significant impact on aging (Berkman et al., 1993; Seeman & Chen, 2002; Seeman et al., 1994, 1995; Seeman, Lusignolo, Albert, & Berkman, 2001; Seeman, Unger, McAvay, & Mendes de Leon, 1999). A review of aging studies published from 1985 to 2003 identified smoking status, physical activity level, body mass index, diet, alcohol use, and health practices as important modifiable behavioral determinants of healthy aging (Peel, McClure, & Bartlett, 2005).

Although our understanding of the aging process has significantly expanded during the past two decades, most of what we know about cognitive aging is based on research involving predominantly young old (ages 65 and older, sometimes also known as the third age).

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Recently, the oldest old (ages 85 and older, sometimes referred to as the fourth age) have been recognized as a population distinct from the young old (Baltes & Smith, 2003; Gonzales McNeal et al., 2001; Howieson et al., 1997, 2003; Howieson, Holm, Kaye, Oken, & Howieson, 1993; Kaye et al., 1994; Marquis et al., 2002). Although the oldest old represent the fastest growing segment of the rapidly expanding U.S. population of older adults, in absolute terms the number of people in this population is relatively small (1.6% in 2000) (Federal Interagency Forum on Aging-Related Statistics, 2000). In addition, by this age many adults are already experiencing significant physical and mental declines (high levels of dementia, frailty, dysfunctionality, and multimorbidity) (Baltes & Smith, 2003), limiting their ability to participate in research. Finally, recruiting older adults in this age group who are willing to participate in research presents additional challenge when studying this population (Howieson et al., 1993).

In spite of these issues, research specific to the oldest old population is important because morbidity and mortality risk factors relevant in the young old may not hold in the oldest old. To the extent that different sets of risk factors modify the aging process in these two populations, more risk factor research is needed to guide development of effective interventions and recommendations aimed at improvement of overall health and quality of life of the oldest old.

Given the rapid increase in the number of older adults affected by dementia and the lack of adequate prevention strategies (Laurin, Verreault, Lindsay, MacPherson, & Rockwood, 2001; Podewils et al., 2005; Verghese et al., 2003), there is an urgent need to advance our current understanding of modifiable factors protective against cognitive impairment even in very old age. Severe dementia, such as Alzheimer's disease, affects roughly 50% of North Americans age 85 and older (Gonzales McNeal et al., 2001; Kaye et al., 1994). As the number of oldest old increases, the number of dementia cases is also rapidly increasing. Physical activity is an important, modifiable risk factor for many health outcomes, including dementia (Centers for Disease Control and Prevention, 2005a; Laurin et al., 2001; Podewils et al., 2005). A number of studies have demonstrated a fairly consistent association between participation in physical activities and decreased risk of dementia (Abbott et al., 2004; Fabrigoule et al., 1995; Laurin et al., 2001; Podewils et al., 2005; Verghese et al., 2003; Weuve et al., 2004; Wilson et al., 2002; Yaffe, Barnes, Nevitt, Lui, & Covinsky, 2001). However, the existing research was conducted among the young old, leaving the question of the cognitive protection afforded by physical activity in the oldest old unanswered.

Only a small number of older adults participate in regular vigorous exercise, and the level of participation decreases sharply with age (Centers for Disease Control and Prevention, 2005b). Given the limited information on the oldest old from national surveys, it is not clear how many older adults exercise regularly into their ninth decade. To the extent that oldest old adults engage in exercise, does exercise in this group provide similar protection against cognitive decline as observed for the young old? Is the level of exercise among the oldest old sufficient to prevent decline? Do other biological factors overwhelm any influence of behavior? This study presents a unique opportunity to examine the association between participation in physical activity and cognitive health in a prospective cohort of successfully aging oldest old. The Oregon Brain Aging Study (OBAS) cohort includes a number of adults aged 85 and older who were cognitively healthy and free of any comorbid conditions that might affect cognition at baseline. By studying this unique population of the healthiest oldest adults, we will be able to examine whether participation in physical activity (i.e., exercise and walking) reduces risk for cognitive decline even in the very old age.

Methods

Study Population

The Oregon Brain Aging Study is an ongoing open cohort study begun in 1989 as part of the Layton Center for Aging and Alzheimer's Research Center at Oregon Health and Science University (OHSU) (Gonzales McNeal et al., 2001) to investigate the effects of aging on the central nervous system in the optimally healthy elderly 65 years of age and older. OBAS has been previously described in detail elsewhere (Gonzales McNeal et al., 2001; Howieson et al., 1993, 1997, 2003; Kaye et al., 1994; Marquis et al., 2002). Briefly, all participants are cognitively healthy and free of any conditions that might affect cognition (diabetes mellitus; hypertension; angina pectoris; cardiac arrhythmia; myocardial infraction; stroke/transient ischemic attack; chronic pulmonary disease; chronic renal disease; chronic immunosuppression; untreated hypothyroidism; syphilis; vitamin deficiencies; seizure disorders; active cancer; Parkinson's disease; major surgeries such as coronary bypass or carotid endarterectomy; psychiatric disorders such as chronic schizophrenia, major affective disorders, phobias, or chronic anxiety; vision uncorrectable to 20/100 OU; hearing loss that interferes with speech perception; other conditions such as alcohol or drug abuse; significant head injury; unexplained prolonged loss of consciousness; and use of medications impairing cognitive function; Gonzales McNeal at al., 2001; for the complete list of selection criteria refer to Table 1 in Gonzales McNeal at al., 2001). The participants are identified and recruited from retirement homes, senior citizens' organizations, and public relation activities (Howieson et al., 1993). The principal language for all the recruited volunteers is English, and they are required to have adequate hearing and be able to read letters 4 millimeters tall (Howieson et al., 1993). All are community-dwelling, functionally independent older adults (Howieson et al., 1993). After enrollment, all the participants are assessed biannually for medical history, functional independence (measured by Instrumental Activities of Daily Living Scale from the Older American Resources and Services), and cognition (Mini Mental State Examination and Clinical Dementia Rating Scale) and annually for a full physical examination, neurological, neuropsychological, and brain MRI examinations (Gonzales McNeal et al., 2001). Blood samples are collected upon entry to the study and DNA extracted to obtain apolipoprotein E genotypes. Upon death, brain autopsies are performed to make definitive neuropathological diagnosis (Gonzales McNeal et al., 2001). All participants give informed consent, and the study protocol was approved by the human subjects committee at OHSU (Howieson et al., 1997). Although the OBAS cohort includes ages 65 and older, the focus of this study is only the oldest old participants, those 85 years of age and older. They were selected for the study from the overall cohort and represent 56% of the total OBAS population.

Questions about participation in leisure activities, specifically social and physical activities, hobbies, and interests, were introduced into the OBAS intake questionnaire in 1992. For our analyses, first completion of the leisure activity questionnaire was defined as participant's baseline visit. Community-dwelling OBAS participants who were 85 years of age and older (the oldest old) and cognitively intact at baseline were eligible for inclusion in our study if they completed the leisure activity questionnaire. Participants with depression or functional limitations at the visit they first completed the leisure activities questionnaire were excluded. Participants with less than 1 year of follow-up were excluded as well.

Assessment of Physical Activities

Information about participation in physical activities was self-reported in the Personal and Family History questionnaire. The participants were asked to provide information on how many city blocks they walk daily (12 blocks = 1 mile), how many hours per week they participate in light physical exercise, such as walking, biking, dancing, golfing, and

gardening, and strenuous physical exercise, such as running, jogging, swimming, hunting, wood splitting, working with livestock or other strenuous farm work, skiing, tennis, hiking, and strenuous yard work or home maintenance.

For the analysis, the total physical exercise was calculated for each participant. It represents the sum of hours spent in light and strenuous exercise. Because of its clinical importance based on physical activity recommendations to exercise approximately 30 minutes on most days, 4 hours/week was selected as a cutoff point for the categorization of the exercise variable. Consequently, the participants were categorized as either low (≤ 4 hours/week) or high (> 4 hours/week) exercisers.

The number of blocks walked was addressed separately in the analysis. In addition to its continuous form, the total number of blocks walked was categorized by quartiles as well.

Assessment of Cognitive Impairment

Cognitive impairment was assessed during the face-to-face interview using the Mini Mental State Examination (MMSE; Folstein, Folstein, & McHugh, n.d.) and the Clinical Dementia Rating Scale (CDR; Gonzales McNeal et al., 2001).

The MMSE is a short quantitative assessment of cognitive status with the maximum score of 30 (Folstein et al., n.d.). This clinical instrument is widely used for fast detection of cognitive impairment and assessment of its severity. It is also used to monitor cognitive changes over time (Folstein et al., n.d.).

The CDR is a clinical instrument for staging of dementia. Information on six areas of cognitive and functional performance is obtained and assessed in a semistructured interview with a participant. The score of 0 is assigned if no impairment is detected, 0.5 for very mild or questionable dementia, and 1 to 3 for different severity levels of definite dementia. In addition, a reliable collateral informant, such as family member or friend, is interviewed to verify the information reported by the participant in the interview. The information reported by the collateral informant is also assessed and assigned the scores of 0.5 to 3 (Gonzales McNeal et al., 2001).

Cognitive impairment was defined as repeated abnormal scores on the MMSE (< 24) or the CDR (= 0.5) on two consecutive assessments (Gonzales McNeal et al., 2001). This definition, developed by the Layton Center for Aging & Alzheimer's Research Center at OHSU, relies on two consecutive assessments rather than one to account for the possibility of one abnormal score resulting from the reasons unrelated to the change in cognitive status, such as a bad day, personal reasons, and so on.

The age of onset of cognitive impairment was defined as the age at the time the participant received the first of the two consecutive MMSE < 24 or CDR ≥ 0.5 scores.

Covariates

Previous research (Aartsen, Smits, van Tilburg, Knipscheer, & Deeg, 2002; Ball et al., 2002; Bassuk, Glass, & Berkman, 1999; Fratiglioni, Wang, Ericsson, Maytan, & Winblad, 2000; Friedland et al., 2001; Gonzales McNeal et al., 2001; Howieson et al., 1997, 2003; Marquis et al., 2002; Scarmeas, Levy, Tang, Manly, & Stern, 2001; Seeman et al., 2001; Verghese et al., 2003; Wang, Karp, Winblad, & Fratiglioni, 2002; Wilson, Bienias, Berry-Kravis, Evans, & Bennett, 2002) has identified certain covariates as important confounders of the relationship of physical and leisure activities with cognitive function. Covariates in this analysis were selected based on these studies.

At the baseline, the information on participants' age, race, sex, years of education, socioeconomic status, place of residence (home/apartment, retirement community), and living arrangements (alone, not alone) was collected. Socioeconomic status was assessed using validated method that assigns points on the basis of education, occupation, sex, and marital status and derives the score by calculating the weighted average of the assigned points. To validate the index, the correlation of median years of schooling with occupational score was examined (correlation coefficient for women = .85, correlation coefficient for men = .84). In addition, correlation of the occupational scores with another previously accepted scale, the National Opinion Research Center Scale, was calculated (correlation coefficient = .93) (Hollingshead, 1975). Functional independence was determined as measured by the Older Americans Resource Scale Instrumental Activities of Daily Living (IADL) and categorized as independent (IADL = 0) versus any loss of independence (IADL > 0). Also, the presence or absence of an apolipoprotein E 4 (APOE4) allele was established. Salting out method (PureGene commercial kit, Gentra Systems Inc., Minneapolis, MN) was used to extract DNA from blood samples and APOE genotypes determined by standard method (Gonzales McNeal et al., 2001). Baseline speed of walking was assessed in a timed 30-foot out-and-back walking test where participants were instructed to walk at their normal pace. The number of steps and time taken to walk the course (seconds) was recorded on three trials and the speed of walking reported as average number of steps per second (Kaye et al., 1994). Depression status was determined at baseline as well. Throughout the years of data collection, three different scales were used to assess depression status in the OBAS population: Geriatric Depression Scale (GDS), Cornell Depression Scale, or Center for Epidemiologic Studies Short Depression Scale (CES-D 10). In this study, participants are categorized simply as depressed or not depressed based on the established cutoff point (Gonzales McNeal et al., 2001; Stanford Patient Education Research Center, n.d.) of the scale(s) that was in use at the time a participant entered the study. Finally, participants' baseline results of a neuropsychological test battery were obtained. In this analysis, the World List Acquisition Delayed Recall test (Morris et al., 1989) was used to control for age-related cognitive decline and the influence that a possible preclinical dementia might have on the participants' reporting of exercise and leisure activities (Howieson et al., 1997; Marquis et al., 2002).

Statistical Analysis

Descriptive statistics were obtained on all variables to detect important trends in the data. Continuous variables, such as age, education, socioeconomic status, baseline MMSE score, and Delayed Recall test scores, were crudely compared between the cognitively impaired and cognitively intact participants using an independent sample *t* test. Categorical variables, such as sex and APOE allele 4 status, were compared using Pearson's chi-square test or Fisher's exact test.

Continuous variables exercise and walking were recoded into categorical variables (≤ or > 4 hours/week for exercise, quartile split for walking). Baseline characteristics were compared across different levels of participation in physical activity using chi-square test or one-way ANOVA.

In the preliminary analysis, unadjusted survival curves for the participants in the two groups of participation in exercise were estimated using the Kaplan-Meier method and the differences tested using the log-rank test (p value < .15 was considered significant). This analysis was also repeated on the four categories of the walking variable. In addition, the covariates were categorized in the most meaningful way (e.g., median, quartiles) and tested as potential risk factors using Kaplan-Meier method as well.

The relationship between participation in physical activities and the time until progression to cognitive decline was investigated more formally using Cox proportional hazards models. In Alzheimer's research, the risk of cognitive impairment is thought to be a function of age rather than years of follow-up (Gonzales McNeal et al., 2001), therefore in these analyses the event time is the age at onset, if observed, or the age of last observation, if cognitively intact.

First, the associations of each physical activity variable (walking, exercise) and each relevant covariate, such as age, socioeconomic statue, education, MMSE, gait, Delayed Recall test score, and so on, with cognitive decline were assessed in univariate Cox proportional hazards models. Variables with associations with a p value < .15 we retained for inclusion in a multivariable Cox model.

Next, significant variables from the Kaplan-Meier and univariate analyses were used to develop multivariable Cox proportional hazards models. Two models were developed, one for walking and one for exercise. Initially, each model included a physical variable of interest (i.e., walking or exercise) and important confounders age, sex, and education. Subsequently, interactions of the physical activity variable in question and the confounders were created for each model (numerical product of the value for the variable in question) and evaluated one at a time. Following, important covariates Delayed Recall test score, APOE4 status, IADL, and MMSE were included in the model, and only those significant at . 05 level retained. The interactions of included covariates with activity variable of interest were created and evaluated (p value < .05 was considered significant). Finally, the incidence rates of the cognitive decline were explored across different gender and physical activity groups.

Results

From the time the physical activity questions were incorporated into intake questionnaire in 1992, exercise and walking data were collected on 72 community-dwelling, cognitively intact men and women 85 years of age and older. Among these individuals, 6 participants (8.3%) were excluded because they had depression (n = 2) or had been followed for less than 1 year (n = 4). The final study population consisted of 66 individuals with the mean age of 88.5 years (SD = 2.74). A total of 7 participants did not respond to the physical activity questions but were otherwise eligible for the inclusion into study. Comparison of the nonresponders in our study sample revealed that nonresponders were older (mean age 94.7 vs. 88.5, p < .05) and had less education (12.14 vs. 14.46, p < .05) but did not differ on any other baseline characteristics, including socioeconomic status, sex, functional independence, cognitive function, and apolipoprotein E status. One nonresponder developed cognitive impairment.

Demographic and Baseline Characteristics

A total of 66 participants 85 years of age and older (39 women and 27 men) were followed for an average of 4.73 years (SD = 2.71). During this time period, 38 participants (23 women and 15 men) developed mild cognitive impairment, with mean onset age of 92.88 years (SD = 3.30).

When compared on range of baseline characteristic, participants who developed mild cognitive impairment had lower score on Delayed Recall test and had higher percentage of individuals with apolipoprotein E allele 4. Although in the normal range, their average baseline MMSE score was lower as well. The impaired and intact participants did not differ on any other baseline characteristics, including age, education, socioeconomic status, sex, and functional independence (Table 1).

Physical Activity

Exercise—In all, 12 men and 11 women reported more than 4 hours of exercise per week. The reported median for the whole study population was 3 hours, but women reported exercising fewer hours than men (median men 3.75, median women 2.50). Those who exercised more than 4 hours per week were significantly more educated. More active exercisers were male, younger, and had higher socioeconomic status, but differences were not significant (Table 2).

Estimated crude Kaplan-Meier survival curves for the two groups of exercisers (≤ 4 hours/week and > 4 hours/week) were significantly different (log-rank test *p* value .04). Also, in univariate Cox proportional hazard analysis, exercising 4 or more hours per week was associated with cognitive decline (HR 0.48, 95% CI 0.23 to 0.10).

In the final proportional hazards model that adjusted for age, sex, and education and included significant covariates APOE allele 4 status and Delayed Recall Test, the association of exercise and cognitive impairment was modified by gender. Women who exercised more than 4 hours per week had 88% decrease in rate of cognitive impairment compared to women who exercised 4 hours or less (95% CI 0.03, 0.41) (Table 3). The association was not significant in men. Active women had about 5 times smaller incidence rate of cognitive impairment compared to less active women (87 cases of mild cognitive impairment [MCI] / 1,000 person-years [p-y] vs. 415 MCI cases / 1,000 p-y) and 2 times smaller incidence rate compared to more active men (87 MCI cases / 1,000 p-y vs. 175 MCI cases / 1,000 p-y) (Table 3).

Walking—Participants reported walking median of 6 blocks per day. Women reported walking fewer blocks than men (median for men 10.3, median for women 5). In both univariate and multivariable analysis, walking was not significantly associated with cognitive impairment, either in its continuous or categorical form.

Discussion

This prospective study demonstrated a strong association between higher participation in exercise with a decreased risk of cognitive impairment in optimally healthy women older than 85 years of age. In women who exercised more than 4 hours per week, the risk of cognitive impairment was reduced by 88% (95% CI 0.03 to 0.41) compared to those less active. The association remained after adjustment for age and education. This study did not demonstrate a significant association between higher participation in exercise with decreased risk of cognitive impairment in men. However, although not significant, the risk in men was also reduced, suggesting that our sample size was not big enough to detect the difference in this group. We did not find a significant association between walking and risk of cognitive impairment in this analysis (HR = 0.97, 95% CI 0.93, 1.02).

Our finding that exercise was associated with reduced risk of cognitive decline in the oldest old was consistent with previous studies conducted in the younger old population (Laurin et al., 2001; Weuve et al., 2004; Yaffe et al., 2001). However, unlike our study, prior research in the young old population that evaluated walking separately from exercise also found a reduction in risk associated with walking (Weuve et al., 2004; Yaffe et al., 2001). In one study of women 65 years of age and older (Yaffe et al., 2001), participants were asked to report how many city blocks they walk each day for exercise or as a part of their normal routine. They found a significant association between walking and risk of cognitive decline even when the analysis was limited only to women older than 70 years of age without comorbidities (e.g., stroke, myocardial infraction, Parkinson's disease, diabetes, and hypertension) (comparing to risk in the lowest quartile of walking, OR second quartile 0.83,

95% CI 0.65 to 1.06; OR third quartile 0.49, 95% CI 0.38 to 0.64; OR highest quartile 0.58, 95% CI 0.44 to 0.75). Similarly, another recent study reported an association between walking and cognitive impairment independent of vigorous exercise (Weuve et al., 2004). In this study, women 70 years of age and older who reported participation in vigorous exercise were excluded from the analysis of walking in an attempt to separate the effect of walking from that of exercise. In women walking an equivalent of at least 1.5 hours/week at an easy pace, mean global cognitive scores were 0.06 to 0.07 units higher compared with walking less than 40 minutes/week (p value ≤ .003). Compared to our study population, the women in both studies reporting an association between walking and cognitive health were significantly younger (≥ 70 years vs. OBAS age ≥ 85). It is likely that intensity of walking decreases with increasing age (Centers for Disease Control and Prevention, 2005a), thus perhaps even the normal walking reported by the young old participants in the Yaffe et al. (2001) and Weuve et al. (2004) studies is more vigorous than the walking reported by the oldest old OBAS participants. This could imply that walking for pleasure and walking for exercise have different impact on cognitive aging in oldest old. Possibly, it is the vigorousness of the activity that protects against cognitive decline via vascular mechanism in this age group (Podewils et al., 2005; Yaffe et al., 2001). Self-reported walking in OBAS was not significantly correlated with either exercise (Pearson's correlation coefficient = −. 01, p value = .97) or light exercise (Pearson's correlation coefficient = .06, p value = .65). The question on walking in the OBAS intake questionnaire did not specify the type of walking that should be reported (e.g., leisurely vs. walking for exercise). Also, the question did not ask about the level of walking intensity. It is possible that there was more error in categorization of walking in our variable compared to these other studies, hence limiting our ability to objectively assess the association of walking and cognitive decline in the oldest old. However, all of the other published studies have also relied on self-reported activity.

Several limitations should be considered in this study. The frequency of participation in walking and exercise that was reported in the questionnaires was not objectively measured or verified with friends or relatives. We attempted to statistically validate the self-reported information. Both exercise and walking variables were additionally analyzed excluding any unusually high observations, but results did not differ from those in the original analysis (data not shown but available on request). In addition, we examined correlation of self-reported exercise with the speed of walking (objective measure of physical fitness in older adults), following the idea that better physical fitness should be reflected in the level of participation in physical activity. Self-reported exercise was significantly but minimally correlated with speed of walking (r = .26, p value = .04), but self-reported walking was not (r = .12, p value = .35). In this case, any error in self-reported physical activity would result in nondifferential misclassification, or error in the classification of exposure that is independent of the classification of the outcome (Hennekens & Buring, 1987). In the case of binary exposures (e.g., high vs. low exercise), this would have biased results toward the null. It is also important to consider the possible influence of differential misclassification of physical activity, or error in the classification of exposure that is not independent of the classification of the outcome (Hennekens & Buring, 1987). If for example respondents with lower cognitive function were less able to report physical activity accurately and also more likely to experience a decline in activity during the study period, this would introduce differential misclassification, although the direction of the bias would be unknown. In this prospective study, all participants were cognitively intact at the time they provided information on participation in physical activities, as measured by Mini Mental State Examination and Clinical Dementia Rating Scale, making differential misclassification of this kind unlikely.

Unmeasured confounding could have influenced our effect estimate. However, we had extensive demographic, social, health, psychoneurological, and genetic information that

allowed us to control for the most important confounders at baseline. In addition, the exclusion criteria for this study were carefully designed, keeping a variety of other potential influences in mind (e.g., living arrangements/place of residence). We did not have information to statistically evaluate some of the less frequently included confounders, such as body mass index (BMI). On the other hand, BMI would most likely be a negative confounder of this association (Podewils et al., 2005; Yaffe et al., 2001), and if controlled for it would only increase the strength of the observed association.

The analysis was based on 66 older adults 85 years of age and older. This was a small sample size, and findings should be validated in a larger study. However, the availability of participants in this age group who are in optimal health and willing to participate in research is generally scarce (Howieson et al., 1993), making any opportunity to study this population invaluable.

The overall health of this cohort is above the average, and it consists of predominately White older adults (only 3 non-White participants). The racial composition of the study population in this analysis closely resembles the racial composition of the Portland metropolitan area, where 88% of the population older than 60 years of age is White (Multnomah County Aging and Disability Services, 2005). Regardless, caution should be exercised with respect to generalizability of the study findings to oldest old of average (or less) health and non-White race.

In summary, this prospective study demonstrates significant association of higher participation in exercise and reduced risk of cognitive decline in a cohort of successful aging oldest old. This work adds to the existing body of knowledge of successful aging by showing that protective effect of exercise continues even at the very old age and in optimally healthy older adults. The important implication of these findings is that it is never too late to gain benefits from exercise, even when other health indicators are good. This study did not find an association of walking and risk of cognitive decline, possibly providing support for the hypothesis that it is the vigorousness of exercise that protects against cognitive decline via vascular mechanism in this age group. However, more precise measures of activity in this age group are needed to evaluate the influence of different physical activities on cognitive health in the oldest old. Finally, this study identified less active women, two thirds of the population older than 85 years of age (Gonzales McNeal et al., 2001), as the group of oldest old at the highest risk of cognitive impairment, recognizing the need for research and prevention strategies that would specifically target this population.

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Table 1

Baseline Characteristics of Participants Who Remained Cognitively Intact and Those Who Developed Cognitive Impairment, the Oldest Old Oregon Brain Aging Study (OBAS),[a] 1992–2004

	Cognitively Impaired (*N* = 38)		Cognitively Intact (*N* = 28)		*p* Value
		SD		*SD*	
Mean evaluation age (years)	88.35	2.56	88.74	3.03	.57[b]
Mean education (years)	14.13	2.64	14.89	2.69	.26[b]
Mean socioeconomic status	46.05	12.10	49.36	12.15	.28[b]
Mean baseline MMSE score	27.50	1.47	28.43	1.35	.01[b]
Mean Delayed Recall Test score	4.95	2.17	6.29	2.09	.01[b]
IADL limitation (%)					.45[c]
Yes (*N* = 8)[d]	16		7		
No (*N* = 58)[e]	84		93		
Sex (%)					.78[f]
Female (*N* = 39)	60		57		
Male (*N* = 27)	40		43		
APOE ∈ 4 (%)					.002[f]
Yes (*N* = 8)	29		0		
No (*N* = 58)	71		100		

Note: MMSE = Mini Mental State Examination; IADL = Instrumental Activities of Daily Living; APOE = apolipoprotein E 4 allele.

[a] Evaluation age ≥ 85.

[b] Two *t* test.

[c] Fisher's Exact test.

[d] Mean = 1.

[e] Mean = 0.

[f] Chi-square test.

Table 2

Baseline Characteristics of Low and High Exercisers, the Oldest Old Oregon Brain Aging Study (OBAS),[a] 1992–2004

	Low Exercise (≤ 4 Hours/Week) *N* = 41		**High Exercise (> 4 Hours/Week) *N* = 23**		***p* Value**
Covariate		***SD***		***SD***	
Mean age (years)	88.86	2.85	87.97	2.57	.22[b]
Mean education (years)	13.85	2.20	15.52	3.20	.02[b]
Mean socioeconomic status	45.93	12.04	50.04	12.67	.20[b]
Mean MMSE score	27.66	1.54	28.30	1.22	.07[b]
IADL limitation (%)					
Yes (*N* = 8)[d]	20		0		.04[c]
No (*N* = 56)[e]	80		100		
Sex (%)					
Female (*N* = 37)	63		48		.23[f]
Male (*N* = 27)	37		52		
APOE ∈ 4 (%)					
Yes (*N* = 11)	15		22		.47[f]
No (*N* = 53)	85		78		

Note: MMSE = Mini Mental State Examination; IADL = Instrumental Activities of Daily Living. APOE = apolipoprotein E 4 allele.

[a] Evaluation age ≥ 85.

[b] Two *t* test.

[c] Fisher's Exact test.

[d] Mean = 1.

[e] Mean = 0.

[f] Chi-square test.

Table 3

Results of the Multivariable Model[a] for Association Between Exercise and Cognitive Impairment in the Optimally Healthy Oldest Old Oregon Brain Aging Study Participants (OBAS),[b] 1992–2004

Variable	Incidence Rate (*N* Cases/ 1,000 Person-Years)	Hazard Ratio	95% Confidence Interval
Women			
Exercise			
> 4 hours/week	87	.12	0.03, 0.41
≤ 4 hours/week	415		
Men			
Exercise			
> 4 hours/week	175	.91	0.25, 3.40
≤ 4 hours/week	250		

[a] Multivariable model adjusted for age, education, apolipoprotein allele 4 status, and cognitive function (Delayed Recall Test).

[b] Evaluation age ≥ 85.