

Computer Activities, Physical Exercise, Aging, and Mild Cognitive Impairment: A Population-Based Study

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Abstract

Objective: To examine the association between computer use, physical exercise, aging, and mild cognitive impairment (MCI).

Patients and Methods: The Mayo Clinic Study of Aging is a population-based study of aging and MCI in Olmsted County, Minnesota. The study sample consists of a random sample of 926 nondemented individuals aged 70 to 93 years who completed self-reported questionnaires on physical exercise, computer use, and caloric intake within 1 year of the date of interview. The study was conducted from April 1, 2006, through November 30, 2008. An expert consensus panel classified each study participant as cognitively normal or having MCI on the basis of published criteria.

Results: Using a multivariable logistic regression model, we examined the impact of the presence during the study period of 2 lifestyle factors (physical exercise and computer use) after adjusting for a third lifestyle factor (caloric intake) on aging and MCI. We also adjusted for age, sex, education, medical comorbidity, and depression. The median daily caloric intake was significantly higher in participants with MCI than in controls (odds ratio, 1.04; 95% confidence interval, 1.02-1.06; $P=.001$). Participants who engaged in both moderate physical exercise and computer use had significantly decreased odds of having MCI (odds ratio [95% confidence interval], 0.36 [0.20-0.68]) compared with the reference group. In the interaction analyses, there was an additive interaction ($P=.012$) but not multiplicative interaction ($P=.780$).

Conclusion: In this population-based sample, the presence of both physical exercise and computer use as assessed via survey was associated with decreased odds of having MCI, after adjustment for caloric intake and traditional confounders.

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Mild cognitive impairment (MCI) is an intermediate stage between the cognitive changes of normal aging and dementia.^{1,2}

Persons with MCI constitute a high-risk group because they develop dementia at a rate of 10% to 15% per year as compared with 1% to 2% per year in the general population.³ Therefore, it is critical to identify potential protective factors against MCI.

Several lifestyle factors are associated with cognitive function. Physical exercise is independently associated with decreased risk of cognitive decline^{4,5} and dementia.⁶⁻¹¹ On the other hand, high caloric intake is associated with increased risk of dementia.¹² A few studies have also reported the independent association of physical exercise with decreased odds of having MCI.¹³⁻¹⁵ Engaging in computer use, playing games, reading books, participating in craft activities (eg, quilting, knitting), and watching less television (TV) are associated with decreased odds of having MCI.¹⁶ Therefore, we sought to examine the combined effects of physical exercise and computer activities on the odds of hav-

ing MCI, after accounting for caloric intake and traditional confounders.

PATIENTS AND METHODS

The details of the design and conduct of the Mayo Clinic Study of Aging were reported elsewhere.¹⁷ Briefly, it is an ongoing population-based study of normal aging and MCI in Olmsted County, Minnesota. We used a stratified random sampling scheme to recruit elderly persons aged 70 to 89 years on the prevalence date of October 1, 2004, from the target population of nearly 10,000 elderly individuals in Olmsted County. There were equal numbers of men and women in 2 age strata: 70 to 79 years old and 80 to 89 years old. During the first follow-up phase of the study, which took place from April 1, 2006, through November 30, 2008, we introduced a structured interview format to collect data on cognitive and physical activities. At the time of the interview, neither the study participant nor the research personnel knew the case-control status of a participant. The classification of a study participant



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as having MCI or not was determined after the collection of data on computer use, physical exercise, and caloric intake. The study was approved by the institutional review boards of Mayo Clinic and Olmsted Medical Center. The design for this study was a case-control study derived from the Mayo Clinic Study of Aging. The sample for this study consisted of persons aged 70 to 93 years ($N = 926$) who completed questionnaires that assessed cognitive activities including computer use, physical exercise, and caloric intake within 1 year of the date of interview. Of the 926 elderly persons, 109 (12%) were classified as having MCI and the remaining 817 (88%) were classified as cognitively normal.

Definition of Cases and Controls

Each study participant underwent the following 3 face-to-face evaluations: (1) a complete neurologic examination conducted by a physician; (2) a risk factor ascertainment as well as administration of the Clinical Dementia Rating scale,¹⁸ both conducted by a research nurse or study coordinator; and (3) psychometric testing. We considered as cases all the participants who met the revised Mayo Clinic criteria for MCI: (1) cognitive concern expressed by a physician, informant, participant, or nurse; (2) cognitive impairment in one or more domains (executive function, memory, language, or visuospatial); (3) normal functional activities; and (4) not demented.^{2,19} Participants with normal cognition are controls for this study.¹⁷

Measurement of Physical Exercise

We have previously reported the details of measuring physical exercise in our cohort.¹⁵ Briefly, the frequency (eg, once per week, twice per week) and intensity (ie, mild, moderate, and vigorous) of physical exercise that occurred within 1 year of the date of the interview were measured by using validated self-administered questionnaires.²⁰⁻²² Light physical exercise was defined as participating in activities such as bowling, leisurely walking, stretching, slow dancing, and golfing with a golf cart. Moderate physical exercise was defined as participating in activities such as brisk walking, hiking, aerobics, strength training, golfing without a golf cart, swimming, tennis doubles, moderate use of exercise machines (eg, exercise bike), yoga, martial arts, and weight lifting. Vigorous physical exercise was defined as participating in activities such as jogging, backpacking, bicycling uphill, tennis singles, racquetball, intense or extended use of exercise machines, and skiing. For each category of intensity, further inquiry was made as to the frequency of exercise.

Measurement of Computer Activities and Other Mentally Stimulating Activities

We have previously reported the details of measuring mentally stimulating activities in our cohort.¹⁶ Mentally stimulating activities included reading, craft activities, computer activities, playing games, playing music, group activities (eg, book club), social activities (eg, going out to movies and theaters), artistic activities, and watching TV. We modified previously validated instruments to measure these activities.^{13,22,23} A study participant completed a self-administered questionnaire on cognitive activities, including computer use. The frequency of activities was reported on an ordinal scale (eg, once per week, twice per week). The survey was reviewed by a psychometrist or nurse for completeness and accuracy. The measurement of these cognitive activities was conducted along with a neurologic evaluation, neuropsychological assessment, and risk factor ascertainment.

Measurement of Caloric Intake

We assessed dietary intake via the modified Block 1994 revision of the Health Habits and History Questionnaire that included 128 items: 103 food items and 25 beverages.²⁴ Participants were asked to provide information on usual eating habits during the previous year. For each food item, respondents were asked to indicate (1) their usual portion size consumed (small, medium, large), with the medium serving provided as a specific amount; and (2) how often they had consumed each food (never or <1 per month, 1 to 3 per month, 1 per week, 2 to 4 per week, 5 to 6 per week, 1 per day, 2 to 3 per day, 4 to 5 per day, 6+ per day). The Food Processor SQL nutrition analysis software program (version 10.0.0; ESHA Research, Salem, OR) was used to calculate the total nutrient, food group, and energy (caloric) intake per day, under the supervision of a registered dietician.²⁵

Assessment of Potential Confounders

Traditional confounders, ie, age and sex, as well as other pertinent covariates such as education, depression, and medical comorbidity were defined as covariates in this study. We used the Charlson index to measure medical comorbidity and the Beck Depression Inventory, second edition, to assess depression.²⁶⁻²⁸

Statistical Analyses

We previously reported that physical exercise and cognitive activities are independently associated with prevalent MCI.^{16,29} Therefore, the current analysis primarily focused on examining the interaction between physical exercise and computer ac-

tivities. We classified participants according to their participation in moderate physical exercise (any vs none) and according to their participation in computer activities (any vs none). Caloric intake was measured as a continuous variable. We examined these measures of physical exercise and computer activities for their association with MCI after adjusting for caloric intake, age, sex, education, medical comorbidity, and depression using logistic regression models. In addition, we examined the interaction between physical exercise and computer activities on both additive and multiplicative scales. We computed odds ratios (ORs) and 95% confidence intervals (CIs). Statistical testing was performed at the conventional 2-tailed $\alpha = .05$. All analyses were performed using commercially available statistical software (SAS, version 8; SAS Institute, Cary, NC).

RESULTS

The demographic data are displayed in Table 1. The sample for this study comprised participants who completed the survey on all 3 lifestyle factors: physical exercise, cognitive activities, and caloric intake. The median daily caloric intake was significantly higher in the MCI group than in controls (OR [95% CI], 1.04 [1.02-1.06]; $P = .001$); thus, caloric intake was controlled for in all the analyses. In addition, we previously reported that moderate physical exercise is independently associated with decreased odds of having MCI (OR [95% CI], 0.64 [0.42-0.98]; $P = .04$) after adjusting for age, sex, education, medical comorbidity, caloric intake, and depression.¹⁵ Similarly, we also reported that engaging in computer use, playing games, reading books, craft activities, and watching less TV are associated with 30% to 50% reduced odds of having MCI.¹⁶ Of these cognitive activities, computer use had the lowest OR. Therefore, we sought to examine whether there is an interaction between physical exercise and computer activities after accounting for caloric intake and other covariates (age, sex, education, depres-

TABLE 1. Demographic Characteristics of Study Participants^a

Variable	Normal (n=817)	MCI (n=109)	P value
Male, No. (%)	416 (50.9)	62 (56.9)	.24
Age, y ^b	79 (75-84)	82 (77-86)	<.001
70-79	414 (50.7)	35 (32.1)	
80-93	403 (49.3)	74 (67.9)	
Education, y ^b	14 (12-16)	13 (12-16)	.018
>12	488 (59.7)	57 (52.3)	
BDI-II (total score) ^b	4 (1-7)	5 (2-10)	<.001
Charlson index ^b	2 (1-4)	3 (2-5)	.004
Total calories/d, kcal	—	—	.004 ^c
Median	1802.4	2099.6	
Q1, Q3	1363.4, 2369.6	1532.4, 2727.7	
BMI, kg/m ²			.34 ^c
Median	27.0	26.9	
Q1, Q3	24.3, 30.1	23.4, 29.6	

^aBDI-II = Beck Depression Inventory, second edition; BMI = body mass index; MCI = mild cognitive impairment; Q = quartile.

^bMedian (interquartile range).

^cWilcoxon rank sum test.

sion, and comorbid medical conditions). We performed analyses to evaluate interactions on both additive and multiplicative scales (Table 2). There was no significant multiplicative interaction ($P = .78$); however, there was an additive interaction between moderate physical exercise and computer use ($P = .01$). Compared with the reference group (ie, no moderate physical exercise and no computer use), moderate physical exercise alone showed a protective trend (OR [95% CI], 0.61 [0.36-1.04]; $P = .068$), as did computer use alone (OR [95% CI], 0.53 [0.27-1.02]; $P = .058$). Those participants who engaged in both moderate physical exercise and computer use had significantly decreased odds of having MCI (OR [95% CI], 0.36 [0.20-0.68]; $P = .001$) compared with the reference group.

TABLE 2. Interaction of Exercise and Computer Use^{a-d}

Characteristic	Cognitively normal	Prevalent MCI	OR (95% CI)	P value
No exercise and no computer use	164 (20.1)	41 (37.6)	1.00 (reference)	—
Exercise but no computer use	229 (28.0)	33 (30.3)	0.61 (0.36-1.04)	.068
Computer use but no exercise	130 (15.9)	15 (13.8)	0.53 (0.27-1.02)	.058
Both exercise and computer use	294 (36.0)	20 (18.3)	0.36 (0.20-0.68)	.001

^aCI = confidence interval; MCI = mild cognitive impairment; OR = odds ratio.

^bData are presented as No. (percentage) unless indicated otherwise.

^cAdjusted for age, sex, education, depression, medical comorbidity, and caloric intake.

^dP value for additive interaction, .012.

DISCUSSION

In this population-based, case-control study, we observed that having engaged in both moderate physical exercise and computer use in late life (within 1 year of date of interview) was associated with decreased odds of having MCI. The synergistic interaction between the 2 activities occurred on an additive scale but not on multiplicative, after adjustment for caloric intake and other confounders (age, sex, education, depression, and medical comorbidity). This additive interaction suggests that the observed combined presence of moderate physical exercise and computer use was greater than the expected sum of their independent effects. Additive interaction can occur in the absence of multiplicative interaction. Moreover, additive interaction is also considered to be more applicable to biologic events.³⁰

Previous studies have examined the independent associations of either physical exercise or mentally stimulating activities with MCI,^{13,15,16} but to our knowledge, no study has specifically examined the presence of simultaneous engagement in physical exercise and computer activities on the outcome of MCI, after accounting for caloric intake.²⁹ On the other hand, several studies have examined the association between combined physical and mental activities and dementia, although the studies did not show an added benefit from having engaged in physical and cognitive activities.^{10,11,31} Other studies have examined the interaction between physical activity and diet, not an interaction with computer use; for example, a prospective cohort study in New York observed a synergistic interaction between physical activity and adherence to Mediterranean-type diet in reducing risk of Alzheimer disease.^{32,33}

Our study has focused primarily on aging and MCI, not dementia; therefore, we compared our findings with a New York study that had an outcome of MCI, that is, a prospective cohort study that examined the association of baseline participation in physical and cognitive activities with the outcome of incident amnesic MCI. The investigators observed that a 1-point increase on a composite cognitive measure was associated with decreased risk of amnesic MCI, but no such decrease was observed for physical activity. However, they did not specifically examine an interaction between physical activity and computer use. In this respect, our study is different from theirs.¹³

There are various strengths to our study. First, we examined the impact of the presence of 2 lifestyle factors (physical exercise and computer use) after adjusting for a third factor (caloric intake) on aging and MCI. Second, we used a large sample in a population-based setting. Third, we measured MCI using a comprehensive face-to-face evaluation including 3 well-established components: clin-

ical evaluation by a behavioral neurologist or neuropsychiatrist, neuropsychological assessment, and cognitive measures from the participant and a proxy ascertained by nurses.

The study should be interpreted in the context of the following limitations. The assessment of computer activities was very limited. We only asked how many times per week a person engaged in computer activities. We did not ask for the duration of the computer use. Any future study that investigates computer use should assess both duration and frequency because excessive sedentary lifestyle may additionally predispose a person to health problems.³⁴ Another limitation of our study is recall bias, which is an unavoidable drawback of any survey-based study.³⁰ However, one potentially reassuring factor is that, in the past, we conducted analyses in which 80 study participants from the same cohort completed the survey in 2 successive years. We observed that there was no significant difference between participants with MCI and normal participants in recalling midlife activities on the 2 successive surveys.¹⁵ Finally, the case-control design limits our ability to determine causal associations, since one cannot tell the direction of causality in a case-control study.

This study did not investigate mechanisms of action. However, on the basis of the existing literature we can speculate about the following possible explanations. The combined presence of having participated in both physical exercise and computer use may be a marker of a healthy and disciplined lifestyle.¹⁵ On the other hand, it is possible that the combined activities may have direct beneficial effect on the brain. Physical exercise may target a particular circuit in the brain (eg, increasing the production of brain-derived neurotrophic factor in the hippocampus),³⁵ whereas cognitively stimulating activity (eg, computer use) may enhance functional connections contributing to cognitive reserve.³⁶⁻³⁸

CONCLUSION

We observed an additive interaction between the presence of both physical exercise and computer activities in this population-based case-control study among elderly persons in Olmsted County, Minnesota. Using our study participants, we will be able to design a prospective cohort study that permits comparison of the rates at which MCI develops in a cohort that uses computers and exercises vs a cohort that does neither. Finally, confirmation in other prospective studies will add to the generalizability of our findings. The aging of the baby boomers is projected to lead to dramatic increases in the prevalence and incidence of dementia; hence, experts have recently called for interventional studies that examine the combined effects of physical exer-

cise, mentally stimulating activities, and diet on cognitive outcomes. Frequent computer use is becoming increasingly common among all age groups; hence, it is important to examine how it is related to aging and dementia. Our observational study further adds to this line of discussion

Abbreviations and Acronyms: CDR = Clinical Dementia Rating; CI = confidence interval; MCI = mild cognitive impairment; OR = odds ratio

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REFERENCES

- Petersen RC, Smith GE, Waring SC, Ivnik RJ, Tangalos EG, Kokmen E. Mild cognitive impairment: clinical characterization and outcome. *Arch Neurol*. 1999;56(3):303-308.
- Winblad B, Palmer K, Kivipelto M, et al. Mild cognitive impairment—beyond controversies, towards a consensus: report of the International Working Group on Mild Cognitive Impairment. *J Intern Med*. 2004;256(3):240-246.
- Petersen RC, Stevens JC, Ganguli M, Tangalos EG, Cummings JL, DeKosky ST. Practice parameter: early detection of dementia: mild cognitive impairment (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2001;56(9):1133-1142.
- Lytle ME, Vander Bilt J, Pandav RS, Dodge HH, Ganguli M. Exercise level and cognitive decline: the MoVIES project. *Alzheimer Dis Assoc Disord*. 2004;18(2):57-64.
- Middleton LE, Mitnitski A, Fallah N, Kirkland SA, Rockwood K. Changes in cognition and mortality in relation to exercise in late life: a population based study. *PLoS One*. 2008;3(9):e3124.
- Laurin D, Verreault R, Lindsay J, MacPherson K, Rockwood K. Physical activity and risk of cognitive impairment and dementia in elderly persons. *Arch Neurol*. 2001;58(3):498-504.
- Yaffe K, Barnes D, Nevitt M, Lui LY, Covinsky K. A prospective study of physical activity and cognitive decline in elderly women: women who walk. *Arch Intern Med*. 2001;161(14):1703-1708.
- Abbott RD, White LR, Ross GW, Masaki KH, Curb JD, Petrovitch H. Walking and dementia in physically capable elderly men. *JAMA*. 2004;292(12):1447-1453.
- Larson EB, Wang L, Bowen JD, et al. Exercise is associated with reduced risk for incident dementia among persons 65 years of age and older. *Ann Intern Med*. 2006;144(2):73-81.
- Verghese J, Lipton RB, Katz MJ, et al. Leisure activities and the risk of dementia in the elderly. *N Engl J Med*. 2003;348(25):2508-2516.
- Wilson RS, Bennett DA, Bienias JL, et al. Cognitive activity and incident AD in a population-based sample of older persons. *Neurology*. 2002;59(12):1910-1914.
- Luchsinger JA, Tang MX, Shea S, Mayeux R. Caloric intake and the risk of Alzheimer disease. *Arch Neurol*. 2002;59(8):1258-1263.
- Verghese J, LeValley A, Derby C, et al. Leisure activities and the risk of amnesic mild cognitive impairment in the elderly. *Neurology*. 2006;66(6):821-827.
- Lautenschlager NT, Cox KL, Flicker L, et al. Effect of physical activity on cognitive function in older adults at risk for Alzheimer disease: a randomized trial. *JAMA*. 2008;300(9):1027-1037.
- Geda YE, Roberts RO, Knopman DS, et al. Physical exercise, aging, and mild cognitive impairment: a population-based study. *Arch Neurol*. 2010;67(1):80-86.
- Geda YE, Topazian HM, Lewis RA, et al. Engaging in cognitive activities, aging, and mild cognitive impairment: a population-based study. *J Neuropsychiatry Clin Neurosci*. 2011;23(2):149-154.
- Roberts RO, Geda YE, Knopman DS, et al. The Mayo Clinic Study of Aging: design and sampling, participation, baseline measures and sample characteristics. *Neuroepidemiology*. 2008;30(1):58-69.
- Morris JC. The Clinical Dementia Rating (CDR): current version and scoring rules. *Neurology*. 1993;43(11):2412-2414.
- Petersen RC. Mild cognitive impairment as a diagnostic entity. *J Intern Med*. 2004;256(3):183-194.
- Folsom AR, Caspersen CJ, Taylor HL, et al. Leisure time physical activity and its relationship to coronary risk factors in a population-based sample; the Minnesota Heart Survey. *Am J Epidemiol*. 1985;121(4):570-579.
- Wilson RS, Beckett LA, Bennett DA, Albert MS, Evans DA. Change in cognitive function in older persons from a community population: relation to age and Alzheimer disease. *Arch Neurol*. 1999;56(10):1274-1279.
- Wilson RS, Bennett DA, Beckett LA, et al. Cognitive activity in older persons from a geographically defined population. *J Gerontol B Psychol Sci Soc Sci*. 1999;54(3):P155-P160.
- Friedland RP, Fritsch T, Smyth KA, et al. Patients with Alzheimer's disease have reduced activities in midlife compared with healthy control-group members. *Proc Natl Acad Sci U S A*. 2001;98(6):3440-3445.
- Block G, Coyle LM, Hartman AM, Scoppa SM. Revision of dietary analysis software for the Health Habits and History Questionnaire. *Am J Epidemiol*. 1994;139(12):1190-1196.
- Roberts RO, Geda YE, Cerhan JR, et al. Vegetables, unsaturated fats, moderate alcohol intake, and mild cognitive impairment. *Dement Geriatr Cogn Disord*. 2010;29(5):413-423.
- Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373-383.

27. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry*. 1961; 4:561-571.
28. Beck AT, Steer RA, Ball R, Ranieri W. Comparison of Beck Depression Inventories -IA and -II in psychiatric outpatients. *J Pers Assess*. 1996;67(3):588-597.
29. Geda YE, Roberts RO, Knopman DS, et al. Physical exercise, cognitive activity, caloric intake, and mild cognitive impairment: The Mayo Clinic Study of Aging. *Neurology*. 2010;74(9, suppl 2):A488.
30. Szklo M, Nieto FJ. *Epidemiology: Beyond the Basics*. Gaithersburg, MD: Aspen Publishers, Inc; 2000.
31. Sturman MT, Morris MC, Mendes de Leon CF, Bienias JL, Wilson RS, Evans DA. Physical activity, cognitive activity, and cognitive decline in a biracial community population. *Arch Neurol*. 2005;62(11):1750-1754.
32. Scarmeas N, Luchsinger JA, Schupf N, et al. Physical activity, diet, and risk of Alzheimer disease. *JAMA*. 2009;302(6):627-637.
33. Scarmeas N, Stern Y, Mayeux R, Manly JJ, Schupf N, Luchsinger JA. Mediterranean diet and mild cognitive impairment. *Arch Neurol*. 2009;66(2):216-225.
34. US Department of Health and Human Services. *Physical activity and health: a report of the Surgeon General*. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, 1996.
35. Churchill JD, Galvez R, Colcombe S, Swain RA, Kramer AF, Greenough WT. Exercise, experience and the aging brain. *Neurobiol Aging*. 2002;23(5):941-955.
36. Fratiglioni L, Wang HX. Brain reserve hypothesis in dementia. *J Alzheimers Dis*. 2007;12(1):11-22.
37. Fratiglioni L, Paillard-Borg S, Winblad B. An active and socially integrated lifestyle in late life might protect against dementia. *Lancet Neurol*. 2004;3(6):343-353.
38. Middleton LE, Yaffe K. Promising strategies for the prevention of dementia. *Arch Neurol*. 2009;66(10):1210-1215.