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Physical activity and cognition in the Northern Manhattan Study

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Abstract

Background—To test the hypothesis that leisure time PA is associated with cognitive status.

Methods—We assessed cognition using the Mini-Mental Status Examination (MMSE) at enrollment, and using the modified Telephone Interview for Cognitive Status (TICS-m) administered annually since 2001 in the Northern Manhattan Study. Baseline measures of leisure-time PA were collected via in-person questionnaires. Total PA was categorized in three groups based on the metabolic equivalent (MET) score, a composite of total reported intensity and time. We used linear regression models to examine the association of PA with MMSE, and generalized estimating equations for change in TICS-m over time.

Results—There were 3298 stroke-free participants with MMSE data (mean MMSE 26.0±3.8) and 2279 with TICS-m scores available. Compared to no PA, those with the upper quartile of MET-score had greater baseline MMSE scores (adjusted $\beta=0.4, p=0.01$) but no association with change in TICS-m over time. There were interactions ($p<0.05$) between PA and both insurance and education; compared to no PA those in the upper quartile of MET-score had a greater MMSE score only among those with Medicaid/no insurance (adjusted $\beta =0.83, p=0.0005$) and those who did not complete high school (adjusted $\beta=0.68, p=0.001$).

Conclusions—Increased levels of physical activity were associated with better baseline MMSE, particularly among those with socioeconomic disadvantages, but not with cognitive decline.

Keywords

physical activity; cognition; dementia

Introduction

As the population continues to age, the public health impact of neuro-degenerative conditions that present with cognitive impairment or dementia will be particularly high¹.

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Several identified risk factors for cognitive impairment have shed light on the pathogenesis of the underlying causes, particularly on a genetic and molecular basis². Physical activity (PA) is one useful target for prevention since individuals at risk may modify their behavior with little potential for adverse events or need of medications, and the added benefit of protection against other diseases of aging.

Several investigators³⁻⁹, and a recent meta-analysis¹⁰, have documented a dose-response association between baseline measures of PA and subsequent cognitive performance or risk of dementia; prior studies have demonstrated a protective effect on only vascular dementia, or on Alzheimer disease alone^{11,12}. Not all groups however have documented an association between cognitive function and PA, particularly among older individuals^{6,13,14}. Randomized clinical trials of PA programs have shown conflicting results^{15,16,17}. A recent National Institutes of Health State of the Science Statement argued that there was probably a “decreased risk” of cognitive decline with PA, though the data available was “low quality”^{18,19}. A recent Cochrane database review indicated insufficient evidence to support the effect of PA on cognition in older people²⁰. Several unanswered questions remain. Few studies have used the same population to examine cognitive performance at baseline and changes over time. The populations studied have also varied, ranging from participants enrolled in middle adulthood to those over the age of 65; these studies have rarely enrolled participants with low socio-economic status or educational achievement, or with a large proportion of Hispanics. Furthermore few studies have examined whether the effect of PA could be modified by socio-demographics. We aimed to examine the independent association between measures of PA and cognitive performance at enrollment and over time, and examine whether baseline factors modified these associations. We hypothesized that total PA would be associated with higher Mini-Mental Status Examination (MMSE) performance at baseline, and a slower decline over repeated measures of the modified Telephone Interview Cognitive Scale (TICS-m).

Methods

Recruitment of the Cohort

NOMAS is a population-based prospective cohort study designed to evaluate the effects of medical, socio-economic, and other risk factors on the incidence of stroke and other vascular outcomes in a stroke-free race/ethnically diverse community cohort. Methods of participant recruitment, evaluation, and follow-up have been previously reported²¹. A total of 3298 participants were recruited between 1993 and 2001, and participants have been followed annually by telephone.

Standard Protocol Approvals, Registrations, and Patient Consents

The study was approved by the Institutional Review Boards at Columbia University Medical Center and the University of Miami Miller School of Medicine. All participants provided written informed consent.

Cohort Evaluation

Data regarding baseline status and risk factors were collected through interviews of participants. Race-ethnicity was determined by self-identification. Standardized questions were asked regarding the following conditions: hypertension, diabetes, hypercholesterolemia, cigarette smoking, and cardiac conditions. Depression was defined based on Hamilton Depression Rating Scale score >10 or a history of antidepressant use. Insurance status was defined as having no insurance or Medicaid versus having private insurance or Medicare²². Educational achievement was assessed via self-reported grade at

which school was completed and classified as completing high school versus not. We did not collect information regarding household income.

Cognitive performance at baseline was measured using the MMSE in either English or a validated Spanish translation administered by trained bi-lingual research assistants.

Starting in 2001, a mean of 4.7 years after the initial MMSE, the TICS-m was administered to participants during annual telephone follow-up²³. The TICS-m was designed to assess cognitive performance across multiple domains and includes calculations, delayed 10 word recall, language, and attention. It was administered over the phone at each annual follow up and required 10 minutes on average to complete. Incomplete TICS-m tests were not used in statistical analysis as only the total score is valid.

Assessment of physical activity

Physical activity was measured using an in-person questionnaire adapted from the National Health Interview Survey of the National Center for Health Statistics at enrollment, when the mini-mental status examination was also obtained²⁴. This questionnaire records the duration and frequency of various leisure time / recreational activities for the two weeks prior to the interview. Participants were then asked if they engaged in any PA in the preceding two weeks, and those who answered “no” were coded as physically inactive. For each activity, the participant was asked the duration of activity, and the number of times they engaged in this same activity, and if this level of activity was typical of other weeks. If the duration of activity was less than 10 minutes, it was coded as “no activity”. This questionnaire has been previously reported as reliable and valid in this population²⁵, and correlates with body-mass index (BMI) and activities of daily living. Objective measures of physical fitness correlate well with PA questionnaires²⁶.

Questionnaires were correlated with validated compendia of PA that outline the intensity of multiple leisure time physical activities measured in metabolic equivalents (MET)²⁷. Total activity was summarized via the MET-score, whereby the MET for each individual activity is multiplied by the frequency per week and duration. Total energy expenditure was estimated by accounting for the participant's weight²¹.

Statistical Analysis

Baseline demographics by PA categories were compared using Chi-squared test for categorical variables and Kruskal-Wallis Test for continuous variables. We fitted (1) linear regression models with MMSE as the outcome to calculate parameter estimates (β) and 95% CIs, and (2) generalized estimating equations with identity link to calculate parameter estimates (β) and 95% CIs for change in TICS-m scores over time.

The MET-score was our primary exposure of interest and was categorized in three groups: 1) no PA (MET-score=0) as the reference (41%), 2) intermediate PA (MET-score \leq 14), and 3) high PA (MET-score > 14). In secondary analyses, physical activity was assessed as (1) any versus none, and (2) total energy expenditure in increments of 500 kcal-week.

Unadjusted and adjusted models were constructed with hypothesized confounders: demographics (age, sex, race-ethnicity, medical insurance and education) and vascular risk factors (dyslipidemia, current tobacco use, moderate alcohol use, hypertension, depression, and diabetes). We tested for interactions between PA and baseline socio-demographic factors (age, sex, race-ethnicity, education, medical insurance), and stratified models were carried out only when the p-value for the interaction term was < 0.05. Final models were checked for improvements of fit using the likelihood ratio test (LRT) or Wald test as appropriate. All analyses were conducted using SAS version 9.2 (Cary, NC).

Results

Description of the cohort

The entire NOMAS cohort (n = 3298) participants contributed data on PA and MMSE at enrollment. Demographics of the cohort are presented in table 1. The mean MMSE at baseline was 26 (median 27, interquartile range 24-29), with a lower value among those who did not complete high school (median 25, interquartile range 22-28) versus those who did (median 28, interquartile range 27-29), and those with Medicaid or no insurance (median 26, interquartile range 23-28) compared to their counterparts (median 28, interquartile range 26-29). The TICS-m was obtained annually on 2279 participants after a mean follow-up 4.7 years from baseline, and 1969 participants had at least two measures (median 4 measures; minimum 1 and maximum 9). Since we were primarily interested in the effect of PA on cognition in a community-based sample, we excluded 44 participants with stroke prior to the first TICS-m, as well as those with TICS-m administered after a stroke (n=60). The main reason for not obtaining TICS-m scores was death before the first TICS was administered (n=525). Participants who did not have a TICS-m study were more likely to be younger, women, and Hispanic compared to white; participants were also less likely to have been smokers or have diabetes or coronary artery disease compared to the rest of the cohort.

Association of physical activity and MMSE using linear regression

PA was associated with the MMSE at enrollment (LRT with 2 df, p=0.007). In analyses adjusting for age, sex, race-ethnicity, insurance, and education (Model 1), and further adjusting for vascular disease risk factors (Model 2), those engaging in intermediate and high total PA had higher MMSE scores than those who were physically inactive (Table 2). Total activity in kcal/week was only associated with MMSE in univariate analyses.

We found evidence that the effect of PA on MMSE differed by socio-demographics: health insurance status (LRT with 2 df, p interaction =0.03), and educational achievement (LRT with 2 df, p interaction = 0.02). Compared to those who were inactive, those in the high PA group had higher MMSE scores if they had Medicaid or no insurance (adjusted β = 0.83, standard error 0.24, p=0.0005) or if they did not complete high school (adjusted β = 0.68, standard error 0.21, p=0.001). We found no associations among those with Medicare / private insurance and among those who completed high school.

Association of physical activity and TICS-m

The results of GEE models examining the association of PA with TICS-m over time are outlined in table 3. In summary we found that PA was associated with TICS-m at the first measurement, but not with changes over time. In univariate analyses one year of aging was associated with a 0.01 decline in TICS-m per year (p <0.0001). Compared to those who were inactive, those with high PA had a trend towards greater TICS-m on the first assessment (adjusted β = 0.55 points, p=0.06). We did not find an association between PA and change in TICS-m performance over time (Chi-squared with 2 df, p=0.83). We found no interaction with insurance status, educational attainment, or baseline MMSE.

Discussion

In our study we found that more leisure time PA was independently associated with better cognitive performance in a cross-sectional manner, but not over time. In further analyses we found that the associations between leisure time PA and performance on the MMSE were apparent only among those of lower socio-economic status: i.e. those who did not complete high school, or who had Medicaid or no insurance. Physical activity remains an attractive target for preventing cognitive decline because it is relatively low risk, does not require

medications or medical follow up, and can be inexpensive. The mechanisms by which PA may influence the MMSE are several, and can be categorized by vascular dependent and independent effects. Physical activity modulates the effect and levels of stroke risk factors such as hypertension and diabetes²⁸, thereby potentially reducing the burden of subclinical cerebrovascular disease. Physical activity may also lower the risk of subclinical cerebrovascular disease independent of its effects on modifiable stroke risk factors²². An extensive literature has demonstrated the protective effects of PA on the brain, including neurogenesis, angiogenesis, hippocampal size and levels of brain derived neurotrophic factor²⁹, and neuronal connectivity³⁰. We did not find an association with cognitive scores over time, counter to other studies¹⁷. Our results may differ for several reasons. We used the TICS-m as a global cognitive screening measure which may lack sensitivity for subtle changes in domains that have been previously associated with PA, such as cognitive speed and executive function. Further, we do not have information on prevalent or incident dementia in this sample, though the prevalence of dementia was less than 5% in a sub-sample who underwent a full neuropsychological battery. The mean age of our participants was 71.5 years, which is younger than most dementia studies, and our average of four years of follow-up may not have been long enough to detect an association. Close to one third of the sample died or had an incident cardiovascular event, the latter potentially a competing factor in cognitive decline. In our study we did not collect information on PA in earlier adulthood, which could be more protective³¹. Further, our data are observational and differed from randomized clinical trials of healthy participants, or those with mild cognitive impairment¹⁵ or Alzheimer disease^{32,33}. Interestingly trials of PA in patients with Alzheimer's disease have mostly shown improvements in functional impairment and depression but not necessarily cognition³⁴. Lastly, it is possible that the influence of PA on cognition in later life is relatively weak, particularly in the face of other non-modifiable risk factors such as age or genetics.

An additional novel finding in our study was that PA was associated with better performance on the MMSE only among those who have Medicaid/no insurance, and those who did not complete high school, while there were no associations among their counterparts. We did not collect information on household income, but believe that these two measures could be a proxy for socio-economic status. It may be that higher MMSE scores among those with better socio-economic status and more education mitigate the effect of leisure time PA. Possibly only those at higher risk due to other factors would benefit from life-style interventions such as exercise. We may have been unable to detect an effect of PA in the upper ranges of the MMSE due to ceiling effects or lack of power.

Our study has important strengths, including an urban population with a large proportion of Hispanics and individuals with Medicaid or no insurance, who have been underrepresented in previous studies. We were able to examine the effects with both cross-sectional and longitudinal analyses to help investigate the concept of cognitive reserve³⁵. Our study also has some important weaknesses, however. We did not have available direct measures of physical fitness or activity such as actigraphy³⁶. Actigraphy, however, only measures activity when the participant wears the device, and habitual activity may not be captured. In our study we did not collect TICS-m until 2001 and it was not measured in all of the cohort mostly due to early deaths. Cardio-vascular disease was the main cause of death in our cohort, for which PA would be a protective factor. The missing TICS-m could lead to a non-differential loss to follow up, thereby biasing our results towards the null³⁷. Overall in our cohort the TICS-m declined over time, and we have noted previously a deleterious effect of renal function on the TICS-m over time³⁸; any independent effect of PA is likely to be clinically small if we are underpowered. We followed participants for a limited number of years, and it is possible that over a longer period of time there could be a protective effect of PA. One prior study showed a strong effect of PA when assessed in middle age suggesting

that by the time participants reach the average age in our study the underlying pathologic process leading to cognitive decline may already be underway without overt clinical signs. It is important to note that PA has protective effects against multiple other conditions associated with aging, including stroke and MI^{21,39}, and our findings should not discourage individuals from performing even light intensity activities. As with any epidemiological study it is not possible to establish causation and residual confounding may be present. Further studies will be required to clarify these causal pathways.

In our study we found that PA was associated with baseline cognitive status particularly in lower socioeconomic older adults, but not significantly associated with a decline in cognitive performance. This however should not dissuade older patients from exercising, but it highlights the importance of continuing to search for modifiable risk factors for cognitive decline.

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References

1. Middleton LE, Yaffe K. Promising strategies for the prevention of dementia. *Arch Neurol.* Oct; 2009 66(10):1210–1215. [PubMed: 19822776]
2. Cummings JL, Cole G. Alzheimer disease. *JAMA.* May 8; 2002 287(18):2335–2338. [PubMed: 11988038]
3. Etgen T, Sander D, Huntgeburth U, Poppert H, Forstl H, Bickel H. Physical activity and incident cognitive impairment in elderly persons: the INVADE study. *Arch Intern Med.* Jan 25; 2010 170(2): 186–193. [PubMed: 20101014]
4. 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.* Jan 17; 2006 144(2):73–81. [PubMed: 16418406]
5. Middleton LE, Manini TM, Simonsick EM, et al. Activity energy expenditure and incident cognitive impairment in older adults. *Arch Intern Med.* Jul 25; 2011 171(14):1251–1257. [PubMed: 21771893]
6. Rovio S, Kareholt I, Helkala EL, et al. Leisure-time physical activity at midlife and the risk of dementia and Alzheimer's disease. *Lancet Neurol.* Nov; 2005 4(11):705–711. [PubMed: 16239176]
7. Scarmeas N, Luchsinger JA, Schupf N, et al. Physical activity, diet, and risk of Alzheimer disease. *JAMA.* Aug 12; 2009 302(6):627–637. [PubMed: 19671904]
8. Vercambre MN, Grodstein F, Manson JE, Stampfer MJ, Kang JH. Physical activity and cognition in women with vascular conditions. *Arch Intern Med.* Jul 25; 2011 171(14):1244–1250. [PubMed: 21771894]
9. Verghese J, Lipton RB, Katz MJ, et al. Leisure activities and the risk of dementia in the elderly. *N Engl J Med.* Jun 19; 2003 348(25):2508–2516. [PubMed: 12815136]
10. Sofi F, Valecchi D, Bacci D, et al. Physical activity and risk of cognitive decline: a meta-analysis of prospective studies. *J Intern Med.* Jan; 2011 269(1):107–117. [PubMed: 20831630]
11. Ravaglia G, Forti P, Lucicesare A, et al. Physical activity and dementia risk in the elderly: findings from a prospective Italian study. *Neurology.* May 6; 2008 70(19 Pt 2):1786–1794. [PubMed: 18094335]

12. Abbott RD, White LR, Ross GW, Masaki KH, Curb JD, Petrovitch H. Walking and dementia in physically capable elderly men. *JAMA*. Sep 22; 2004 292(12):1447–1453. [PubMed: 15383515]
13. Podewils LJ, Guallar E, Kuller LH, et al. Physical activity, APOE genotype, and dementia risk: findings from the Cardiovascular Health Cognition Study. *Am J Epidemiol*. Apr 1; 2005 161(7): 639–651. [PubMed: 15781953]
14. Burns JM, Cronk BB, Anderson HS, et al. Cardiorespiratory fitness and brain atrophy in early Alzheimer disease. *Neurology*. Jul 15; 2008 71(3):210–216. [PubMed: 18625967]
15. Baker LD, Frank LL, Foster-Schubert K, et al. Effects of aerobic exercise on mild cognitive impairment: a controlled trial. *Arch Neurol*. Jan; 2010 67(1):71–79. [PubMed: 20065132]
16. Kramer AF, Hahn S, Cohen NJ, et al. Ageing, fitness and neurocognitive function. *Nature*. Jul 29; 1999 400(6743):418–419. [PubMed: 10440369]
17. 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*. Sep 3; 2008 300(9):1027–1037. [PubMed: 18768414]
18. Plassman BL, Williams JW Jr, Burke JR, Holsinger T, Benjamin S. Systematic review: factors associated with risk for and possible prevention of cognitive decline in later life. *Ann Intern Med*. Aug 3; 2010 153(3):182–193. [PubMed: 20547887]
19. Daviglus ML, Bell CC, Berrettini W, et al. NIH State-of-the-Science Conference Statement: Preventing Alzheimer's Disease and Cognitive Decline. *NIH Consens State Sci Statements*. Apr 28.2010 27(4)
20. Angevaren M, Aufdemkampe G, Verhaar HJ, Aleman A, Vanhees L. Physical activity and enhanced fitness to improve cognitive function in older people without known cognitive impairment. *Cochrane Database Syst Rev*. 2008; (2):CD005381.
21. Willey JZ, Moon YP, Paik MC, Boden-Albala B, Sacco RL, Elkind MS. Physical activity and risk of ischemic stroke in the Northern Manhattan Study. *Neurology*. Nov 24; 2009 73(21):1774–1779. [PubMed: 19933979]
22. Willey JZ, Moon YP, Paik MC, et al. Lower prevalence of silent brain infarcts in the physically active: the Northern Manhattan Study. *Neurology*. Jun 14; 2011 76(24):2112–2118. [PubMed: 21653889]
23. de Jager CA, Budge MM, Clarke R. Utility of TICS-M for the assessment of cognitive function in older adults. *International journal of geriatric psychiatry*. Apr; 2003 18(4):318–324. [PubMed: 12673608]
24. Moss AJ, Parsons VL. Current estimates from the National Health Interview Survey. United States, 1985. *Vital and health statistics*. Sep; 1986(160):i–iv. 1–182.
25. Sacco RL, Gan R, Boden-Albala B, et al. Leisure-time physical activity and ischemic stroke risk: the Northern Manhattan Stroke Study. *Stroke*. Feb; 1998 29(2):380–387. [PubMed: 9472878]
26. Siconolfi SF, Lasater TM, Snow RC, Carleton RA. Self-reported physical activity compared with maximal oxygen uptake. *Am J Epidemiol*. Jul; 1985 122(1):101–105. [PubMed: 4014188]
27. Ainsworth BE, Haskell WL, Whitt MC, et al. Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exerc*. Sep; 2000 32(9 Suppl):S498–504. [PubMed: 10993420]
28. Thompson PD, Buchner D, Pina IL, et al. Exercise and physical activity in the prevention and treatment of atherosclerotic cardiovascular disease: a statement from the Council on Clinical Cardiology (Subcommittee on Exercise, Rehabilitation, and Prevention) and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity). *Circulation*. Jun 24; 2003 107(24):3109–3116. [PubMed: 12821592]
29. Erickson KI, Voss MW, Prakash RS, et al. Exercise training increases size of hippocampus and improves memory. *Proc Natl Acad Sci U S A*. Feb 15; 2011 108(7):3017–3022. [PubMed: 21282661]
30. Cotman CW, Berchtold NC, Christie LA. Exercise builds brain health: key roles of growth factor cascades and inflammation. *Trends Neurosci*. Sep; 2007 30(9):464–472. [PubMed: 17765329]
31. Middleton LE, Barnes DE, Lui LY, Yaffe K. Physical activity over the life course and its association with cognitive performance and impairment in old age. *J Am Geriatr Soc*. Jul; 2010 58(7):1322–1326. [PubMed: 20609030]

32. Graessel E, Stemmer R, Eichenseer B, et al. Non-pharmacological, multicomponent group therapy in patients with degenerative dementia: a 12-month randomized, controlled trial. *BMC Med.* 2011; 9:129. [PubMed: 22133165]
33. Ahlskog JE, Geda YE, Graff-Radford NR, Petersen RC. Physical exercise as a preventive or disease-modifying treatment of dementia and brain aging. *Mayo Clin Proc.* Sep; 2011 86(9):876–884. [PubMed: 21878600]
34. Teri L, Gibbons LE, McCurry SM, et al. Exercise plus behavioral management in patients with Alzheimer disease: a randomized controlled trial. *JAMA.* Oct 15; 2003 290(15):2015–2022. [PubMed: 14559955]
35. Stern Y. Cognitive reserve in ageing and Alzheimer's disease. *Lancet Neurol.* Nov; 2012 11(11): 1006–1012. [PubMed: 23079557]
36. Buchman AS, Boyle PA, Yu L, Shah RC, Wilson RS, Bennett DA. Total daily physical activity and the risk of AD and cognitive decline in older adults. *Neurology.* Apr 24; 2012 78(17):1323–1329. [PubMed: 22517108]
37. Greenland S. Response and follow-up bias in cohort studies. *Am J Epidemiol.* Sep; 1977 106(3): 184–187. [PubMed: 900117]
38. Khatri M, Nickolas T, Moon YP, et al. CKD associates with cognitive decline. *J Am Soc Nephrol.* Nov; 2009 20(11):2427–2432. [PubMed: 19729443]
39. Sacco RL, Khatri M, Rundek T, et al. Improving global vascular risk prediction with behavioral and anthropometric factors. The multiethnic NOMAS (Northern Manhattan Cohort Study). *J Am Coll Cardiol.* Dec 8; 2009 54(24):2303–2311. [PubMed: 19958966]

Table 1

Baseline demographics of the Northern Manhattan Study (n = 3298).

Socio-demographic characteristics		Whole cohort (n = 3298). Mean +/- SD or n (%)	Physically inactive (n = 1347). Mean +/- SD or n (%)	Intermediate MET-score (n = 1178). Mean +/- SD or n (%)	High MET- score (n = 773). Mean +/- SD or n (%)	p-value for difference[§]
Age, years		69.2 (10.3)	69.3 (10.3)	69.3 (10.3)	69.0 (10.4)	0.9
Women		2071 (62.8%)	898 (66.7%)	755 (64.1%)	418 (54.1%)	<0.0001
Race-Ethnicity	Hispanic	1726 (52.3%)	836 (62.1%)	578 (49.1%)	312 (40.4%)	<0.0001
	Non-Hispanic Black	803 (24.4%)	269 (20.0%)	319 (27.1%)	215 (27.8%)	
	Non-Hispanic White	690 (20.9%)	212 (15.7%)	257 (21.8%)	221 (28.6%)	
Less than high school education		1786 (54.2%)	842 (62.6%)	614 (52.1%)	330 (42.7%)	<0.0001
Medicaid or no insurance		1435 (43.8%)	688 (51.3%)	476 (40.7%)	271 (35.4%)	<0.0001
Medical Co-morbidities						
Tobacco use	Never used	1548 (47.0%)	625 (46.4%)	610 (51.8%)	313 (40.5%)	<0.0001
	Former smoker	1179 (35.8%)	476 (35.4%)	390 (33.1%)	313 (40.5%)	
	Current user	569 (17.2%)	245 (18.2%)	178 (15.1%)	146 (18.9%)	
Alcohol use	Moderate use	1086 (32.9%)	371 (27.5%)	386 (32.8%)	329 (42.6%)	<0.0001
Hypertension		2429 (73.7%)	1018 (75.6%)	866 (73.5%)	545 (70.5%)	0.04
Diabetes mellitus ^{††}		716 (21.8%)	325 (24.2%)	261 (22.2%)	130 (16.8%)	0.0003
High-density lipoprotein cholesterol		46.8 (14.6)	45.6 (14.1)	47.0 (14.9)	48.4 (14.8)	<0.0001
Any cardiac disease		792 (24.0%)	329 (24.4%)	275 (23.3%)	188 (24.3%)	0.8
Depression		336 (10.2%)	169 (12.6%)	107 (9.1%)	60 (7.8%)	0.0006
Taking cholesterol lowering medications		411 (12.4%)	179 (13.3%)	132 (11.2%)	100 (12.9%)	0.3
Mini-mental status examination score at baseline		26.0 (3.8)	25.4 (4.2)	26.2 (3.5)	26.7 (3.2)	<0.0001

*Moderate alcohol use = 2 servings of alcohol per day

† Hypertension = Systolic blood pressure \geq 140 mm Hg or diastolic blood pressure \geq 90 mm Hg based on the average of two blood pressure measurements, a physician diagnosis of hypertension, or a patient's self-report of a history of hypertension or anti-hypertensive use.†† Diabetes mellitus was defined as fasting blood glucose \geq 126 mg/dl, the patient's self-report of diabetes mellitus, or insulin and/or hypoglycemic agent use.

§ Chi-squared test for categorical variables and Kruskal-Wallis Test for continuous variables

Table 2

Association between measures of physical activity and mini-mental status examination (MMSE) score in the Northern Manhattan Study.

	Unadjusted analysis, β (standard error, p-value)	Model 1 [*] , β (standard error, p-value)	Model 2 ^{**} , β (standard error, p-value)
MET-score (high vs. no PA)	1.37 (0.17, < 0.0001)	0.52 (0.15, 0.0006)	0.40 (0.15, 0.01)
MET-score (intermediate vs. no PA)	0.84 (0.15, < 0.0001)	0.40 (0.13, 0.003)	0.36 (0.13, 0.007)
Total Intensity of Physical activity (per 500 kcal/week)	0.07 (0.01, < 0.0001)	0.01 (0.01, 0.2)	0.005 (0.01, 0.6)
Any physical activity versus none	1.05 (0.13, < 0.0001)	0.44 (0.19, 0.0002)	0.38 (0.12, 0.002)

* Model 1: adjusted for age, race-ethnicity, sex, insurance (Medicaid/none versus others), and completing high school education

** Model 2: further adjusted for high-density lipoprotein cholesterol, current tobacco use, moderate alcohol use, hypertension, current cholesterol lowering medications, depression, and diabetes

Table 3

Association between measures of physical activity and telephone interview of cognition scale (TICS-m) over time in the Northern Manhattan Study.

	Unadjusted analysis, β (standard error, p-value)	Model 1 [*] , β (standard error, p-value)	Model 2 ^{**} , β (standard error, p-value)
MET-score (high vs. no PA)	-0.03/year (0.05, 0.6)	-0.03/year (0.05, 0.6)	-0.03/year (0.05, 0.5)
MET-score (intermediate vs. no PA)	-0.02/year (0.05, 0.6)	-0.02/year (0.05, 0.7)	-0.02/year (0.05, 0.7)
Total Intensity of Physical activity (per 500 kcal/week)	-0.002/year (0.003, 0.6)	-0.001/year (0.003, 0.7)	-0.001/year (0.003, 0.8)
Any physical activity versus none	-0.02/year (0.04, 0.6)	-0.03/year (0.04, 0.6)	-0.02/year (0.04, 0.6)

* Model 1: adjusted for age, race-ethnicity, sex, insurance (Medicaid/none versus others), and completing high school education

** Model 2: further adjusted for high-density lipoprotein cholesterol, current tobacco use, moderate alcohol use, hypertension, current cholesterol lowering medications, depression, and diabetes