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Physical inactivity predicts slow gait speed in an elderly multi-ethnic cohort study: the Northern Manhattan Study (NOMAS)

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Abstract

Introduction—Gait speed is associated with multiple adverse outcomes of aging. We hypothesized that physical inactivity would be prospectively inversely associated with gait speed independently of white matter hyperintensity volume (WMHV) and silent brain infarcts (SBI) on MRI.

Methods—Participants in the Northern Manhattan Study MRI sub-study had physical activity assessed at enrolment. Gait speed was measured via a timed 5-meter walk a mean of 5 years after the MRI. Physical inactivity was defined as reporting no leisure-time physical activity. Multivariable logistic and quantile regression was performed to examine the associations between physical inactivity and future gait speed adjusted for confounders.

Results—Among 711 participants with MRI and gait speed measures (62% women, 71% Hispanic, mean age 74.1 ± 8.4), mean gait speed was 1.02 ± 0.26 m/s. Physical inactivity was associated with a greater odds of gait speed in the lowest quartile (<0.85 m/s, adjusted OR 1.90, 95% confidence interval 1.17–3.08), and in quantile regression with 0.06 m/s slower gait speed at the lowest 20 percentile ($p = 0.005$).

Conclusions—Physical inactivity is associated with slower gait speed independently of osteoarthritis, grip strength, and subclinical ischemic brain injury. Modifying sedentary behavior poses a target for interventions aimed at reducing decline in mobility.

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Conflict of interest statement

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Keywords

mobility; physical activity; MRI; elderly; subclinical stroke; gait speed

Introduction

Gait speed decline is commonly observed with aging and is strongly associated with loss of independence, incident cardiovascular disease events, and mortality.^{1–3} Physical inactivity is a risk factor for subclinical cerebrovascular disease, such as white matter hyperintensities (WMH) and silent brain infarcts (SBI), as well as for slower gait speed^{4–6} but it remains unclear to what extent slowing of gait is mediated by this cerebrovascular disease. Clinical trials have shown a robust effect from structured exercise programs when started in the elderly on preventing disability and falls.⁷ Several unanswered questions remain regarding how preventing inactivity may be protective against gait decline. Subclinical cerebrovascular disease in the elderly has also been associated with further gait impairment, falls, and lower scores on physical performance measures.^{1,8–11} Epidemiological research on the effects of physical inactivity, however, is complicated by an inherent circularity of proposed explanatory models: that is, physical inactivity contributes to subclinical cerebrovascular disease, and subclinical disease contributes to further physical inactivity. The mechanisms by which subclinical cerebrovascular injury leads to impaired mobility is unclear though a potential explanation is disruption of cortical to subcortical connectivity, leading to impairment in cerebral pathways underlying gait.^{8,12,13} Due to the high public health burden associated with mobility impairment, further research is required to identify modifiable risk factors across a range of different populations.

Several studies have examined the association between physical inactivity and slower gait speed, though fewer have examined whether this association is mediated by WMH and SBI. It is unclear if the impact of physical inactivity is the same across the range of gait speeds, such that the magnitude of effect of an intervention could be greater depending on a baseline gait speed. Limitations of prior studies also include low recruitment of elderly minority urban participants who may have more limited opportunities to engage in physical activity. Studies examining the association of neuro-imaging findings with gait speed are frequently cross-sectional, with gait speed and risk factors collected at the same time, with incomplete adjustment for important confounders such as arthritis and grip strength. In the present analysis, we examined in a prospective design among an ethnically diverse community whether physical inactivity was associated with later development of slower gait. We hypothesized that physical inactivity would be associated with slower gait speed and that the association would be partly explained by the presence of WMH and SBI.

Methods

Recruitment of the cohort

The Northern Manhattan Study (NOMAS) (n=3298) 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.¹⁴ A sub-study of 1290 stroke-free participants was recruited sequentially during annual follow-up for magnetic resonance imaging (MRI) and a neuropsychological examination (NPE) between 2003 and 2009. 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 was collected at enrolment into NOMAS regarding baseline demographics and risk factors were collected through interviews of participants by trained bilingual research assistants. Race-ethnicity was determined by self-identification. Standardized questions were asked regarding cardiovascular disease risk factors as previously described.¹⁵ Smoking and moderate alcohol use were defined based on prior publications.¹⁶ Insurance status was defined as having no insurance or Medicaid versus having private insurance/Medicare.

Assessment of leisure time physical activity

Reported leisure time physical activity (LTPA) was measured using an in-person questionnaire adapted from the National Health Interview Survey of the National Center for Health Statistics,¹⁷ and collected a mean of 5.5 years before the MRI. The questionnaire captured the duration and frequency of LTPA performed for exercise for the two weeks prior to the interview. Participants who answered “no” to having performed any activity were coded as inactive. For each activity, duration of activity and the number of times engaged in this same activity was obtained. If the reported 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 population,¹⁸ and correlates with body-mass index (BMI) and reported activities of daily living. For analytical purposes we defined the primary exposure as physical inactivity, with any LTPA as the referent group.

NOMAS MRI-imaging

Imaging for subclinical cerebrovascular disease was performed at enrolment into the MRI substudy on a 1.5T MRI system (Philips Medical Systems, Best, Netherlands) at the Hatch Research Center. White matter hyperintensity volume (WHMV) was calculated as a proportion of total cranial volume to adjust for head size, and log-transformed to achieve a normal distribution for analysis. SBI was defined as a cavitation on the FLAIR sequence of at least 3mm in size, and distinct from a vessel due to the lack of signal void on T2 sequence, and without associated focal neurological complaints. The processing of MRI scans has been described previously.¹⁹

Physical performance measurements

A mean of five years after the MRI participants were invited to return for a follow-up NPE starting in 2008. Recruitment into the gait and balance sub-study is summarized in supplemental figure 1. Physical performance measures (gait speed, grip strength and balance testing) were added in 2011 in the NOMAS-MRI cohort and were performed on participants who were returning for a second NPE. Starting in 2013, participants who had already completed the second NPE prior to 2011 were invited back to complete these physical

performance testing. Gait speed was measured using a 5-meter straight space free of obstacles and participants were given three trials to walk at their “normal pace” between the markers without the use of an assist device unless they were at high risk of falling. The average of these three trials was used for the analyses. A hand dynamometer was used to measure grip and participants exerted maximum effort with the dominant hand in 3 trials, and the mean was used in these analyses.²⁰

Participants were also asked if they had been diagnosed by a physician with osteoarthritis. Participants did not complete gait speed testing in the cases that 1) it was felt by the study physician to be medically unsafe, 2) they did not have capacity to consent, or 3) there was not an adequate space for home-bound participants who were examined at home or nursing home. Assistive devices to prevent falls, however, were permitted to use.

Statistical analysis

Baseline characteristics by physical inactivity status were compared using Chi-squared tests for categorical variables and Wilcoxon rank sum test for continuous variables.

The primary exposure was physical inactivity as a categorical variable. Since the time between initial MRI and gait speed assessment varied by each individual, we adjusted for this time difference in analyses. The outcome of interest was the mean of three trials of gait speed. Gait speed was dichotomized at the lowest quartile versus all other and conditional logistic regression models were used in order to take into account for variation of time difference from MRI to gait speed assessment across individuals. We also analyzed the effects of physical inactivity on the entire distribution of gait speed using quantile regression (percentiles: 10, 20, 25, 50, 60, 75, 80, 90). The analyses with quantile regression allowed for sensitivity analysis that include participants who did not have gait speed measurement due to disability with a gait speed of 0 (worst possible outcome), and also for participants with missing gait speed for a variety of reasons that were thought to be independent of gait speed. In secondary analyses we repeated our multivariable analyses using gait speed as a continuous variable using linear regression. Model 1 was adjusted for age at gait assessment, sex, education, insurance status, and modifiable vascular risk factors (smoking, moderate alcohol consumption, cardiac disease, waist circumference, low density lipoprotein cholesterol, high density lipoprotein cholesterol, hypertension, and diabetes). Model 2 adjusted for variables in Model 1 plus MRI markers of cerebrovascular brain injury (subclinical brain infarct (SBI), white matter hyperintensity volume (WMHV)); model 3 included additional adjustment for grip strength and diagnosis of arthritis. Model 1 covariates were chosen based on a priori hypothesized confounders; models 2 and 3 covariates were chosen respectively to examine confounding by imaging markers and newly acquired geriatric measures. A p-value of < 0.05 was considered significant in all our analyses.

All analyses were conducted using SAS version 9.2 (SAS Institute, Cary, NC).

Results

Description of the cohort

Among the NOMAS MRI cohort ($n = 1290$), 803 participants underwent physical performance measures as of November 2015, with 729 having gait speed measurements obtained. Participants who underwent physical performance measures were 6.2 years younger ($p < 0.0001$), had lower mean WMHV (0.55 cc versus 0.84 cc, $p < 0.0001$), and a lower prevalence of silent brain infarcts (11.8% versus 20.3%, $p < 0.0001$) than those who did not. Other differences are outlined in supplemental table 1. The primary reasons for not having gait speed (not mutually exclusive): 52 home visits of which 38 could not be performed due to home environment restrictions, 25 due to physical disability and 11 due to other technical reasons; the final sample was 711 after excluding those with prior stroke ($n = 18$). Physical inactivity was slightly more common in those who did not have gait speed tested versus those who did (52% versus 45%, $p=0.3$). The mean time from the MRI to gait speed measure was 6.8 years (± 2.5). At the time of gait speed measurement, the mean age was 74 ± 8 years, with 442 (62%) women and 505 (71%) Hispanics. Baseline demographics of the sample are outlined in table 1. The mean gait speed in the sample was 1.02 ± 0.26 m/s.

Association of physical inactivity with gait speed dichotomized at the lowest quartile

Table 2 outlines the results of the association of physical inactivity with gait speed < 0.85 m/s (25th percentile) vs. > 0.85 m/s. Compared to any LTPA, physical inactivity was associated with a greater odds of slow gait speed (adjusted OR 1.90, 95% CI 1.17–3.08) in models further adjusted for MRI markers, arthritis and sarcopenia. The magnitude of association of physical inactivity with slow gait speed was similar in magnitude to that of arthritis. Subclinical cerebrovascular disease was not independently associated with gait speed < 0.85 m/s. We carried out subgroup analyses by race-ethnicity and found a statistically significant association among the Hispanics (OR 1.96, 95% CI 1.13–3.40), with similar results for non-Hispanic blacks (OR 2.66, 95% CI 0.76–9.28), but no association in non-Hispanic whites (OR 0.77, 95% CI 0.13–4.48). We did not, however find evidence of statistically significant effect modification.

Association of physical inactivity with gait speed using quantile regression

We examined whether the association of physical inactivity with gait speed was constant over the range of measured gait speed (online figure 2). Using multi-variable quantile regression (table 3) we noted that physical inactivity was associated with 0.06 m/s slower gait speed at the lowest 20 percentile ($p = 0.005$). In analyses including those with missing gait speeds due to disability or other technical reasons (total $n = 781$), physical inactivity was associated with a 0.08 m/s slower gait speed in the lowest 20th and 0.05 m/s slower gait speed in 75th percentile ($p=0.008$). In additional analyses using linear regression (supplemental table 1) we found that physical inactivity was associated with a slower gait speed (beta -0.04 , p -value 0.03), while WMHV was not (beta -0.02 , p -value 0.06).

Discussion

In this study examining predictors of gait speed in an elderly cohort, we found that physical inactivity was significantly associated with slower gait speed, with the effect being independent of potential confounders such as arthritis or grip strength. Our study is one of the few to comprehensively assess confounders such as grip strength or arthritis and to include a large proportion of urban dwellers and Hispanics. Gait speed is an important public health outcome that has been strongly associated with aging related outcomes such as frailty, falls, fractures, stroke, and mortality.²¹ We did not, however, find an association of markers of SCVD as seen on an MRI with gait speed, or that these markers attenuated the effect of physical inactivity. Quantile regression suggested that the association of physical inactivity with gait speed might not be linear. When the effect of physical inactivity is combined with other treatable risk factors for slow gait speed, such as diabetes, the overall effect approached a clinically significant difference used in prior studies (0.08–0.1 m/s).²¹ Physical inactivity was also significantly associated with a nearly two-fold increased odds of having slow gait speed (< 0.85 meters/second), a velocity similar to that associated with falls and mortality in other cohorts.²¹ The results of our study are in keeping with prior cohorts with some notable differences, including our population having a higher proportion of cardiovascular disease risk factors including hypertension (66%) and diabetes (18%) and an overall low socio-economic status (50% Medicaid or no insurance). One of the first and largest studies to examine the association of cardiovascular disease risk factors, SCVD, and gait speed was the Cardiovascular Health Study.²² The findings on physical inactivity and SCVD with gait speed were similar to our study, with notable differences being a low proportion of Hispanics and lack of adjustment for osteoarthritis. In the Leukoariosis and Disability study (LADIS) (n = 639, mean age 74) the association of SCVD with gait speed was examined cross-sectionally and prospectively in a predominantly European population with similar findings to ours.¹³ Unlike LADIS however we found no association of silent infarcts with gait speed. Investigators in the Tasmanian Study of Cognition and Gait (n = 395) also found a cross-sectional association of SBI and cardiovascular disease risk factors, with gait speed.²³ Interestingly we found that the difference in gait speed between two physical inactivity groups was the greatest at the 20th percentile indicating that increasing physical activity in those who walk more slowly may have the largest impact. These findings were in keeping with a recent sub-analysis of the LIFE study, which included approximately 75% non-Hispanic whites, where the greatest gain in gait speed in the intervention occurred among those most physically impaired at baseline.²⁴ Further research is required to determine if this represents whether there is a ceiling effect in those least impaired or a greater capacity to improve in those who walk most slowly.²⁴ The mechanisms by which physical inactivity leads to slower gait speed are multi-factorial, potentially involving complex relationships among motor and sensory processes in the brain.²⁵ Though at least a partial effect via SCVD is likely we did not find that adjusting for SCVD influenced the association of physical inactivity with gait speed, arguing against partial mediation. On the one hand, physical inactivity may be a result of medical or physical comorbidities that may also influence gait mechanics and speed.²⁶ In our study, however, we accounted for medical comorbidities which could affect both gait and ability to exercise such as heart disease, osteoarthritis, and adiposity,²⁷ and the associations in adjusted models remained. Similarly,

physical inactivity may lead to the development of more rapid muscle loss with aging which could then affect gait mechanics,²⁰ and is an important component in frailty which is also associated with slower gait speed.²⁸ We adjusted for grip strength, however, and the parameter estimates did not appreciably change. Though in prior studies there was a weak association of gait speed with cardio-respiratory fitness,²⁹ it is not per se a measure of exercise capacity like the 6-minute walk test.³⁰ Our study was not designed to fully address the mechanistic pathways by which physical inactivity may lead to slower speed, but it adds to the literature on several treatable conditions that may prevent decline.

Our study has several important strengths, including the benefit of the risk factor having been obtained before the outcome, and information on confounders such as arthritis. The benefit of temporality supports that physical inactivity led to slower gait speed. There have been few studies in the past that have explored an elderly urban-dwelling population with a race-ethnically diverse composition and with a large burden of vascular disease risk factors, including close to 65% hypertensives and 15% diabetics. Our findings add to the literature on predictors of slow gait speed in populations living in cities with diverse backgrounds with low levels of engagement in LTPA, though we cannot comment further on Hispanics as they frequently did not self-identify with another race-ethnicity when asked to do so. Identifying treatable conditions that do not require pharmacological therapy, such as physical inactivity, in an aging population such as ours is an important step leading that could be used to better design prevention trials. Our study does have several limitations that should be noted. We did not capture important confounders such as pain. We collected gait speed and an MRI only once; documenting a change in gait speed due to progressive SCVD would support a potential causal pathway.³¹ We found only a weak and non-significant association of WMHV with slower gait speed making it unlikely to have been the explanation for the association of LTPA with gait speed. Further we did not collect more advanced MRI measures which in recent studies are more predictive of gait speed compared to overall volumes.^{32–34} While the absolute magnitude of the gait speed may differ between examination in the artificial environment of the clinic and a more natural environment, we doubt that the associations of the explanatory variables, such as physical inactivity and subclinical disease, differ substantially based on location of measurement. It may be helpful in future studies to explore differences between natural and exam room gait tests. Our sample size was smaller compared to other studies, such as the Cardiovascular Health Study,²² and though this may have limited our ability to detect more subtle effects the magnitude of those effects would likely be too small to be clinically significant. This study included only one measure of physical activity and other cardiovascular disease risk factors, and changes over time would help rule out reverse causality with slower gait speed leading to more physical inactivity. We expect however that the proportion who are inactive will increase in the age group of our participants such that we are likely underestimating the effect size on gait speed. Lastly the gait and balance sub-study participants were selected from participants in the NOMAS MRI cohort who were healthy enough to return for the assessment raising the concern for selection bias. On the other hand we did not find appreciable differences in baseline risk factors between the two samples, and we had a high proportion of participants over the age of 80 with slow gait speeds. In summary, our study identified physical inactivity as a potentially modifiable predictor of slower gait speed.

Strategies aimed at preventing physical inactivity in the elderly hold the potential for preventing disability in the geriatric age group and have important implications on preventing loss of mobility.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Baseline demographics of the Northern Manhattan gait and balance sub-study.

		All participants with gait speed measurements ^a (n = 711) ^b	Physically inactive (n = 318) ^a	Performing any Leisure-time physical activity (n = 382) ^a
Age		74.1 (8.4)	73.6 (8.2)	74.7 (8.4)
Women		442 (62.2)	200 (62.9)	233 (70.0)
Race-ethnicity	Hispanic	505 (71.0)	255 (80.2)	239 (62.6)
	Non-Hispanic black	105 (14.8)	38 (11.9)	67 (17.5)
	Non-Hispanic white	89 (12.5)	23 (7.2)	66 (17.3)
Medicaid or no insurance ^c		359 (50.5)	174 (54.7)	175 (45.8)
Did not complete high school ^c		391 (55.0)	212 (66.7)	173 (45.3)
Moderate alcohol use ^d		299 (42.1)	123 (38.7)	171 (44.8)
Current tobacco user		111 (15.6)	57 (17.9)	52 (13.6)
Former tobacco user		260 (36.6)	110 (34.6)	147 (38.5)
Cardiac disease ^e		80 (11.3)	41 (13.6)	38 (10.3)
Diabetes		125 (17.6)	62 (19.5)	60 (15.7)
Hypertension		472 (66.4)	217 (68.2)	247 (64.7)
Waist (inches)		37.7 (4.7)	37.9 (4.7)	37.5 (4.9)
Low-density lipoprotein cholesterol (mg/dl)		116.6 (35.4)	117.7 (36.7)	115.9 (34.3)
High-density lipoprotein cholesterol (mg/dl)		52.7 (16.5)	50.8 (15.3)	54.2 (17.3)
Mean white matter hyperintensity volume		0.55 (0.71)	0.54 (0.73)	0.56 (0.71)
Silent brain infarcts		80 (11.8)	41 (13.6)	38 (10.3)
Mean grip strength (Newtons)		44.9 (19.9)	44.4 (19.4)	45.3 (20.4)
Arthritis		391 (55.0)	170 (53.5)	213 (55.8)

^a Mean ($\pm$ standard deviation) or n (% proportion)^b physical activity status was not collected for 11 subjects.^c $p < 0.05$ for testing difference of proportions between physical inactivity vs. physical activity^d Defined as current drinking of >1 serving/month and 2 servings/day^e Defined as coronary heart disease or prior myocardial infarction

Table 2

Association of physical inactivity with gait speed 0.85 meters per second in the Northern Manhattan gait and balance sub-study

	Model 1 [*]	Model 2 [*]	Model 3 [*]
Physical inactivity	1.56 (1.01–2.41)	1.59 (1.02–2.50)	1.90 (1.17–3.08)
White matter hyperintensity volume ^a		1.06 (0.84–1.35)	1.08 (0.84–1.38)
Silent brain infarcts		1.39 (0.72–2.71)	1.42 (0.70–2.92)
Arthritis			1.81 (1.10–2.98)
Grip strength (per standard deviation increase)			0.23 (0.15–0.36)

^alog-white matter hyperintensity volume per standard deviation increase

^{*}Odds ratio, 95% confidence interval

Model 1 was adjusted for age at MRI, sex, education, insurance status, and modifiable vascular risk factors (smoking, moderate alcohol consumption, cardiac disease, waist circumference, low density lipoprotein cholesterol, high density lipoprotein cholesterol, hypertension, diabetes).

Model 2 adjusted for variables in Model 1 plus MRI markers (subclinical brain infarct, white matter hyperintensity volume)

Model 3 included additional adjustment for grip strength and diagnosis of arthritis.

Boldface indicates statistical significance (p < 0.05)

Table 3

Association of physical inactivity with gait speed in the NOMAS gait and balance cohort using quantile regression.

Percentile	Gait speed measured (n = 711)		Gait speed measured and participants with disability (n = 736)		Gait speed measured and participants with missing gait speed (n = 781) ^a	
	Parameter estimate ^b	p-value	Parameter estimate ^b	p-value	Parameter estimate ^b	p-value
10	-0.04	0.2	-0.01	0.8	-0.06	0.2
20	-0.06	0.005	-0.06	0.03	-0.08	0.01
25	-0.05	0.03	-0.05	0.05	-0.08	0.002
50	-0.01	0.5	-0.01	0.6	-0.02	0.4
60	-0.02	0.2	-0.02	0.3	-0.02	0.2
75	-0.05	0.009	-0.04	0.07	-0.05	0.008
80	-0.04	0.1	-0.04	0.07	-0.04	0.02
90	-0.005	0.9	0.002	0.9	-0.02	0.9

^a sensitivity analyses including those with missing gait speed due to disability or other technical reasons

^b this estimate indicates the difference in gait speed at specific percentiles between two physical activity groups.

Boldface indicates statistical significance (p < 0.05)