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Cognitive Function is Associated with the Development of Mobility Impairments in Community-Dwelling Elders

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Abstract

Objective—To examine the association of cognitive function with the risk of incident mobility impairments and the rate of declining mobility in older adults.

Design—Prospective, observational cohort study.

Setting—Retirement communities across metropolitan Chicago.

Participants—1154 ambulatory elders from two longitudinal studies without baseline clinical dementia or history of stroke or Parkinson's disease.

Measurements—All participants underwent baseline cognitive testing and annual mobility exams. Mobility impairments were based on annual timed walking performance. A composite mobility measure which summarized gait and balance measures was used to examine the annual rate of mobility change.

Results—During follow-up of 4.5 years, 423 of 836 (50.6%) participants developed impaired mobility. In a proportional hazards model controlled for age, sex, education and race, each 1-unit higher level of baseline global cognition was associated with a reduction to about half in the risk of mobility impairments (HR=0.51, 95% CI 0.40, 0.66) and was similar to a participant being about 13 years younger at baseline. These results did not vary by sex or race and were unchanged in analyses controlling for BMI, physical activity, vascular diseases and risk factors. The level of cognition in 5 different cognitive abilities was also related to incident mobility impairment. Cognition showed similar associations with incident loss of the ability to ambulate. Linear mixed-effects models showed that global cognition at baseline was associated with the rate of declining mobility.

Conclusions—Among ambulatory elders, cognition is associated with incident mobility impairment and mobility decline.

Keywords

Aging; Cognition; Mobility Impairment; Loss of Ambulation

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INTRODUCTION

Mobility disability, impaired activities of daily living due to walking and balance difficulties, is common in older persons and associated with loss of independence, disability, and death.1, 2 The prevention of mobility disability requires identifying persons at risk prior to the occurrence of mobility disability. Recent work has underscored that mobility performance (i.e., gait speed) is associated with both the level and subsequent development of mobility disability. 3–5 precise transition from mobility impairment to functional disability 6 may vary in part because definitions of disability differ and in part because a variety of psychosocial and environmental factors, [i.e. assistive devices or environmental resources] may be employed to compensate for mobility impairments. 7 Thus, objective measures of mobility impairment can be used as a potential marker of incipient mobility disability. 3–5 Therefore the identification of risk factors that are associated with the development of mobility impairment, such as reduced walking speed, is a crucial first step in efforts to prevent the development of mobility disability in elders.

Mobility requires the production of coordinated rhythmic patterns of muscle activation and the postural control of the moving body.8, 9 Adaptation of these movements to meet motivational and environmental demands is supported by widely distributed neural systems necessary for the planning and monitoring of mobility performance.10–12 Thus cognitive abilities those are important for planning and monitoring performance such as attention and perceptual speed may play an important role in mobility.13–15 Lower levels of cognitive function, especially dementia, have been reported to be associated with both physical impairments and self-reported disability.16, 17 However, there are relatively few longitudinal studies which have examined the association of cognition and different cognitive abilities with the development of mobility impairments and the rate of declining mobility in elders without dementia or other common chronic conditions known to impair mobility.18–20

In this study, we tested the hypothesis that the level of baseline global cognition and five cognitive abilities were related to the development of mobility impairments. We used data from 1154 community-dwelling elders participating in two ongoing longitudinal studies of aging, who underwent detailed baseline evaluation of cognition and annual gait and balance testing. Gait speed is a widely used performance-based measure of mobility that is associated with functional status in older adults.21 Furthermore using gait speed performance to define mobility impairments offers a potential advantage for longitudinal studies of elders in which recall of self-reported mobility disability during follow-up may be suspect as persons develop impaired cognition. Therefore, in the current study, we examined whether global cognition and five cognitive subscales were related to incident mobility impairments based on gait speed as previously described. 22 In subsequent analyses, we examined whether cognitive function was also related to a) incident loss of the ability to ambulate and b) the rate of change in a continuous composite measure of mobility.

METHODS

Participants

Participants are from two ongoing studies of aging approved by the Institutional Review Board of Rush University Medical Center. Participants in the Memory and Aging Project (MAP) agree to annual clinical exams and donation of brain, spinal cord, muscle and nerve at the time of death. 23 To enrich minority representation in these analyses we included participants from the Minority Aging Research Study (MARS) which began in 2004 and whose participants agree to annual exams. The catchment area for MARS is within that of

the Memory and Aging Project. Both studies have a large common core of identical data collection and operational methods, which facilitates analyses of data from the combined cohorts.

To be included in these analyses participants had to be ambulatory without clinical dementia or a history of stroke or Parkinson's disease at baseline and needed valid cognitive and mobility assessment at baseline and at least one or more valid follow-up mobility assessments. Figure 1 shows that there were 1154 participants with valid follow-up data included in these analyses. Their baseline characteristics are given in Table 1. Participants were followed for a mean of 4.5 years of follow-up (MAP=4.9 [SD=2.39], MARS=3.4[SD=0.74])

Assessment of Cognitive Function and Clinical Diagnoses

Trained technicians administered 18 cognitive tests including: 23, 24 seven measures of episodic memory: immediate and delayed recall of story A from Logical Memory and of the East Boston Story and Word List Memory, Word List Recall, and Word List Recognition; two measures of semantic memory: a 15-item version of the Boston Naming Test, Verbal Fluency; three working memory tests: Digit Span Forward and Digit Span Backward and Digit Ordering; four measures of perceptual speed: Symbol Digit Modalities Test, Number Comparison, and two indices from a modified version of the Stroop Neuropsychological Screening Test; and two measures of visuospatial ability: a 15-item version of Judgment of Line Orientation and a 16-item version of Standard Progressive Matrices.

To construct the composite measure of global cognition and five cognitive abilities, raw scores on each of the individual tests were converted to z-scores using the baseline mean and standard deviation of the entire cohort, and then z-scores of all 18 tests were averaged. Similarly, summary scores for each of the 5 cognitive abilities were derived by converting raw scores on each of the individual tests and then averaging the z-scores from tests within a specific cognitive ability. Psychometric information including factor analytic support for the five cognitive abilities is contained in previous publications.23, 24 Participants were evaluated by an experienced physician who diagnosed dementia, stroke and Parkinson's disease based on published criteria as previously described.23

Assessment of Mobility Function and Mobility impairment

Mobility Function—We asked people to walk eight feet and turn 360° and measured the time and number of steps taken on each task. We asked people to stand on each leg for ten seconds. Scores ranged from 0–5. A score of 0 was given to those unable to perform the task. Results for everyone able to perform the tasks were divided into quintiles and scores ranged from 1–5. Each of these six performance measures (time and steps to walk eight feet and turn 360° [4 measures]) and the time to stand on both legs [2 measures]) were converted to z scores and averaged to yield a composite mobility measure.25

Mobility Impairments—Impaired mobility was present if 8 foot walk gait speed was ≤ 0.55m/s as previously described.22 In this prior study, receiver operating curves were constructed and it was determined that a cut-point of 0.55m/s was an effective cut-point for the current cohort at baseline in predicting self-report mobility disability using the Rosow-Breslau scale.22 We also examined a second more severe threshold for mobility impairment, the loss of the ability to ambulate 8 feet.22

Co-morbidities and Other Covariates

Demographic information including date of birth, sex, race and years of education were collected via participant interview. Body mass index was determined by dividing weight

represented in kilograms with the square of height represented in meters, as previously described. Physical activity was assessed using questions adapted from the 1985 National Health Interview Survey. Activities included walking for exercise, gardening or yard work and calisthenics. The number of activities performed was used in these analyses.25 We summarized 3 vascular risk factors and 4 vascular diseases as previously described (1).26

Statistical Analysis

Pearson correlations were used to examine the bivariate associations between global cognition and demographic variables and other covariates at baseline. Student's t-tests and nonparametric tests were used to compare the baseline characteristics of participants with and without mobility impairment (Table 1). We used a series of discrete-time Cox proportional odds models adjusted for age, sex, education to examine the association of global cognition with incident mobility impairment. Then, we added interaction terms to determine if this association varied by sex or race. Then we repeated the core model including a number of potential confounders which might affect the association of cognition and mobility impairment. We employed both linear and quadratic terms for BMI, since both high and low BMI may be associated with adverse health outcomes. Then we repeated the core model using five cognitive abilities instead of global cognition. Next we repeated these prior analyses with a complementary outcome, loss of the ability to ambulate. We then employed linear mixed-effect models to examine the association of global cognition and five cognitive subscales with the rate of change in a composite measure of mobility.27 The annual rate of change in cognition and mobility were assessed from separate linear mixed-effect models. Because it is more challenging to enroll and maintain Blacks in cohort studies, follow-up for Blacks in both MAP and MARS was shorter than for whites. The maximal number of follow-up visits was 6 in blacks versus 11 for whites. Therefore, we truncated follow-up in whites to 6, so that their longer follow-up would not have a disproportionate effect on our results. *A priori* level of statistical significance was 0.05. All models were validated graphically and analytically. Analyses were programmed in SAS®, Version 9.1.3 for LINUX (SAS Institute Inc., Cary, NC).28

RESULTS

Descriptive Properties of Global Cognition

There were 1154 participants included in these analyses and their baseline characteristics are included in Table 1. Global cognition scores at baseline ranged from −1.84 to 1.50 (mean 0.12; SD, 0.53) with higher scores indicating better function. Global cognition was related to age (r= −0.28 (df=1152); p<0.001), education (r= 0.37 (df=1152); p<.001), race (r=−0.09 (df=1152); p=0.003) and women had higher levels of cognition (t[1152] =2.57; p=0.010). Global cognition was related to physical activity (r =0.11(df=1152); p<0.001); vascular diseases (r =−0.10; p<0.001) and showed a trend for vascular risk factors (r =−.05 (df=1152); p=0.071).

Baseline Cognition and Risk of Mobility Impairment

This analysis was restricted to 836 participants without mobility impairment at baseline. Over a mean of 3.9 years of follow-up, 423 persons (50.6% of 836) developed mobility impairment. In the core proportional hazards model which controlled for age, sex, education and race, each 1-unit higher baseline level of global cognition was associated with a reduction to about half in the risk of mobility impairment during follow-up (HR=0.51, 95% CI 0.40, 0.66; Wald x^2 25.9, (DF=1), p<0.001). Another way of describing the association of cognition with mobility impairment is to compare its association with that of age and mobility impairment. Each 1- year younger age at baseline was associated with an additional 5% decreased risk of developing mobility impairment (HR=1.06, 95% CI 1.04, 1.07; Wald

x^2 42.3 [df=1], p<0.001). Thus by comparing the estimates, the association between a 1-unit higher level of global cognition at baseline with mobility impairment was similar to a participant being about 13 years younger at baseline (estimates for 1-unit global cognition/ estimate per 1 year younger at baseline, 0.671/0.052= 12.9 years).

In further analyses, the association of global cognition with incident mobility impairment did not vary by sex (Global Cognition × Sex, HR=1.05, 95% CI 0.65,1.71, Wald x^2 0.04 [df=1], p=0.840) or race (Global Cognition × Race, HR=0.98, 95% CI 0.57,1.68; Wald x^2 0.38 [df=1], p=0.535); and was unchanged in analyses that controlled for BMI, physical activity, vascular diseases and risk factors (results not shown).

Cognition is composed of dissociable systems which may be differentially associated with mobility. Therefore, we examined whether specific cognitive abilities were related to incident mobility impairment, we repeated the core model, described above, five times replacing global cognition with episodic memory, the hallmark of AD, and semantic memory, visuospatial abilities, perceptual speed and working memory. All five cognitive abilities showed similar associations with incident mobility impairment (Table 2).

Baseline Cognition and the Loss of the Ability to Ambulate

To examine further the robustness of the associations of global cognition with mobility impairment, we examined its association with a complementary outcome, the loss of the ability to ambulate. During follow-up, 238 persons (20.6% of 1154) became unable to ambulate. In a proportional hazards model which controlled for age, sex, education and race, each 1-unit higher level of baseline global cognition was associated with a risk reduction of about 40% for developing mobility impairment during follow-up (Table 2). For comparison with age, each 1 year less of age at baseline was associated with an additional 5% decreased risk of loss of the ability to ambulate (Age, HR=1.06, 95% CI 1.03, 1.08; Wald x^2 0.04 [df=1], p=0.840)). Thus, a 1-unit higher level of cognition at baseline had a similar association with loss of the ability to ambulate as a participant being 17 years younger at baseline. (Estimate for 1-unit global cognition baseline /estimate for 1 year younger at baseline, 0.936/0.055= 17.0 years) In further analyses, the association of global cognition with loss of the ability to ambulate did not vary by sex or race and was unchanged even after controlling for BMI, physical activity and vascular diseases and risk factors (results not shown).

Finally, we examined whether specific cognitive abilities were related to incident loss of the ability to ambulate. We repeated the core model five times replacing global cognition with five cognitive abilities including episodic memory, semantic memory, visuospatial abilities, perceptual speed and working memory. All five cognitive abilities showed similar associations with loss of the ability to ambulate (Table 2).

Baseline Cognition and the Rate of Change in Mobility

To ensure that those participants who were nearing the threshold for our cut-point for mobility impairment did not account for our results, we examined whether global cognition was related to the rate of change in mobility function. We used a mixed-effects model to test the association of global cognition with the annual rate of mobility decline, adjusting for age, sex, education and race. In these models, the terms for time indicate the mean annual rate of change in composite mobility in the cohort. On average, the rate of change of mobility (Time) declined by more than 0.10 unit/year (Table 3). Global cognition was associated with both baseline level of mobility (Global cognition, Table 3) and the rate of change in mobility (Global cognition × Time, Table 3). The effect of a 1-unit higher baseline level of global cognition on the rate of mobility decline can be estimated by adding the

coefficient for the interaction of global cognition with Time to the coefficient for Time alone (global cognition × Time × 0.054 + Time × − 0.123 = − 0.069, Table 3). This shows that a 1-unit higher level of global cognition at baseline is associated with a more than 40% slower rate of mobility decline.

To examine whether specific cognitive abilities were related to mobility decline, we repeated the previous model replacing global cognition with each of the five cognitive abilities. All 5 cognitive abilities were associated with baseline level of mobility and 4 were associated with the rate of change of mobility (Table 3). As described above, comparing the coefficients for the interaction of these cognitive abilities with Time to Time alone showed that a 1- unit increase in these cognitive abilities at baseline was associated with an average 23% slower rate of mobility decline [episodic memory (30.0%); perceptual speed (24.7%), semantic memory (24.4%) and working memory (11.4%)].

Rate of Change of Both Cognition and Mobility

To determine if both the annual rates of change in cognition and mobility were related, we calculated their rates of change using separate mixed-effect models and computed their correlations. Declining global cognition and each of the 5 cognitive abilities were all associated with declining mobility; Spearman correlations ranged from 0.25 – 0.34. Figure 2 illustrates the association of the rate of change of global cognition and declining mobility for a 25% random sample of the participants included in this study.

DISCUSSION

In this cohort of 1154 ambulatory community-dwelling elders without dementia, history of stroke or Parkinson's disease, baseline global cognition was associated with incident mobility impairment. This association did not vary by sex or race and persisted even after adjustment for body composition, physical activity, chronic vascular diseases and vascular risk factors. Five different cognitive abilities including episodic memory, semantic memory, visuospatial abilities, perceptual speed and working memory were also related to incident mobility impairment. In subsequent analyses, similar associations were observed with respect to global cognition and five cognitive subscales and severe mobility impairment i.e. loss of the ability to ambulate. Lower levels of global cognition and 4 of 5 cognitive abilities at baseline were related to a more rapid decline in a continuous measure of mobility function. Finally, the rate of change of global cognition and 5 cognitive abilities were related to the rate of mobility decline. These findings suggest that there may be common pathophysiological processes contributing to both cognitive and mobility decline in the elderly. However, the current cohort study cannot exclude the possibility that lower levels of cognition cause mobility impairments.

Mobility is a complex behavior that involves dissociable neural systems which control gait initiation, planning and execution and the adaptation of these movements to meet motivational and environmental demands.[29–32] These complex interactions underscore why a variety of psychosocial and environmental factors and resources may be employed to compensate for mobility impairments and prevent the clinical transition to disability. Cognitive abilities are crucial for ongoing planning, decision-making and monitoring of movements necessary for successful locomotion.[31, 33] Cross-sectional clinical studies have shown that level of cognition is related to mobility disability and mobility function.[16, 17, 20] However, there are few longitudinal studies assessing the temporal relationship between cognition and declining mobility function in elders,[18–20] and the association of specific cognitive abilities with mobility remains unclear. Thus the current study fills an important gap by showing that there is a temporal relationship between low levels of a wide range of cognitive abilities and the subsequent development of mobility impairments. Furthermore, in

contrast to prior longitudinal studies which have only studied the association of cognition with gait speed,19, 20 the current study provides evidence that a wide range of cognitive abilities are associated with the rate of decline in a composite measure of mobility based on several gait and balance performance measures.

Some prior studies have suggested that executive cognitive function may be preferentially related to mobility.19, 20 A novel feature of the current study is the availability of a detailed battery of 18 cognitive tests summarized either as global cognition or grouped into five different constituent cognitive abilities. There has been increasing use of composite measures in aging research since these measures have metric properties which reduce random error, minimize floor and ceiling effects, and tend to be normally distributed making them well suited for longitudinal analyses. These advantages may account in part for the stronger association between global cognition with mobility decline as compared to the other cognitive abilities constructed from fewer tests (Table 2).34 All five cognitive abilities were related to incident mobility impairment and loss of the ability to ambulate and 4 of 5 abilities (except visuospatial abilities) were associated with the rate of declining mobility. These results provide some support for the association of executive cognitive abilities and declining mobility, as perceptual speed is a well-recognized component of executive function; further, semantic and working memory, which support executive function, also were associated with mobility impairments. However, episodic memory, the hallmark and often the earliest sign of Alzheimer's disease, was also related to declining mobility, as well as mobility impairments. In contrast visuospatial ability was related to incident mobility impairment but not declining mobility. This lack of association may derive from the fact that our cognitive measures for this domain may not be as sensitive as the other cognitive abilities or that these abilities are involved in more complex visuospatial transformations which may not be employed during the mobility performances examined in the current study. Overall, these findings suggest a more generalized association between cognition and mobility in old age.

The present study suggests that a lower level of cognitive function is associated with incident mobility impairments and declining mobility, but the biology of this association remains unclear. Although cognitive function may represent a true risk factor for mobility impairments, causal inferences from this cohort study are limited. While environmental enrichment studies in animals suggest improved motor function, we are unaware of extant human intervention studies showing that cognitive enrichment improves mobility. Our results showing that the rate of cognitive decline was correlated with declining mobility suggests that both cognitive and mobility decline in old age may share a common eitopathogenesis. Recent work in this cohort suggests that several other genetic and experiential risk factors for cognitive decline are also associated with motor decline.35, 36 Furthermore, risk factors for cardiovascular disease (e.g., diabetes) and common vascular diseases (e.g., congestive heart failure, brain infarcts) have been related to both declining mobility and cognition. However, in the current study, controlling for vascular diseases and risk factors had little effect on the association of cognition and mobility. Recent work37 raises the possibility that subclinical neuropathologic changes of AD in cortical and subcortical motor regions may account, in part, for progressive decline in motor function in elders. Finally, AD pathology in cognitive systems which are now recognized to play an important role in mobility may contribute to declining cognition and mobility.38 The results from the current study have important translational implications and suggest that interventions to improve cognition may decrease the development of mobility impairments and thereby reduce the burden of mobility disability in elders.

The current study has some limitations. Although we adjusted for vascular risk factors and diseases, there is a possibility that other subclinical diseases may also contribute to incident

mobility impairment and mobility decline. Finally, our results are based on selected cohorts that may differ in important ways from the general population, which underscores the need to replicate these findings in other cohorts. However, confidence in these findings is enhanced by several factors. Participants included a large number of community-dwelling elders initially free of dementia, history of stroke or Parkinson's disease. Detailed cognitive testing allowed for composite measures of global cognition and five cognitive abilities, and annual testing with little missing data allowed for complementary analyses of both incident mobility impairments and mobility decline.

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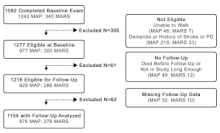

Figure 1. Participants Included in These Analyses

The total number of participants who were enrolled and had completed baseline exam at the time of these analyses in the Memory and Aging Project (MAP) and Minority Aging Research Study (MARS) is shown. Also shown are the numbers of those participants who were excluded from these analyses because they did not meet the inclusion criteria or were missing the requisite data.

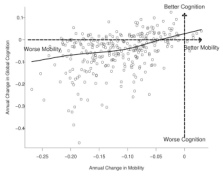

Figure 2.

A scatterplot of the person-specific annual rate of change of both mobility and global cognition during the course of the study for a 25% random sample of the participants included in these analyses. To portray the association between the rate of change in mobility and global cognition, we used a locally weighted regression smooth function that is based on weighted locally linear fits, thereby reducing the influence of outliers on the regression line.

Table 1

Baseline Characteristics of Participants With and Without Mobility Impairment *

Variable	Impaired Mobility (N=318)	No Mobility Impairment (N=836)	Significance ** (t- , x^2- or Fisher's Exact -test)
Age	80.6 (7.31)	76.9 (7.21)	t [1152] = −7.66, p<0.001
Sex (male)	57 (17.9%)	257 (30.7%)	x^2 = 19.1, p<.001
Education (years)	13.8 (3.30)	15.1 (3.22)	t [1152] = −5.94, p<0.001
Black participants	76 (23.9 %)	255 (30.5 %)	x^2 = 3.31,p=0.069
White non-Hispanic participants	220 (69.2 %)	559 (66.9%)	x^2 = 0.56.p=0.454
BMI (kg/m^2)	28.9 (6.72)	27.4 (5.01)	t[449] = −3.50, p<0.001
Physical Activity (sum of activities)	1.1 (0.81)	1.3 (0.86)	t[1152] = −3.67, p<0.001
Mobility (composite)	−0.64 (0.51)	0.42 (0.55)	t(1152) = 29.9, p<.001
Timed 8 feet walk (s)	5.9 (2.75)	3.3 (0.60)	t[329] = −16.90, p<0.001
Number of steps	8.1 (2.08)	5.8 (1.09)	t[384] = −18.81, p<0.001
Time to turn (s)	7.4 (4.96)	4.6 (1.56)	t[339] = −9.61, p<0.001
Number of steps to turn	10.7(4.90)	8.1 (2.48)	t[378] = −8.90, p<0.001
Leg Stand (s)	4.1 (2.83)	6.1 (3.20)	t[346] = 9.04, p<0.001
Toe Stand (s)	5.5 (3.50)	7.4 (3.27)	t[1003] = 7.17, p<0.001
Global Cognition (composite)	−0.08(0.56)	0.20(0.49)	t[515]=8, p<0.001
Episodic Memory (composite)	−0.04 (0.70)	0.19 (0.62)	t[519] = 5.29, p<0.001
Word List Recall (30 items)	16.3 (4.14)	17.7 (4.08)	t[1151] = 5.08, p<0.001
Word List Delay (10 items)	4.7 (2.29)	5.5 (2.31)	t[1149] = 5.25, p<0.001
Word List Recognition (10 items)	9.4 (1.37)	9.6 (1.07)	t[471] = 2.39, p=0.017
Immediate Story Recall (12 items)	9.2 (2.0)	9.6 (1.8)	t[1150] = 4.62, p<0.001
Delayed Story Recall (12 items)	8.7 (2.41)	9.1 (2.13)	t[1151] = 4.56, p<0.001
Logical Memory Ia (25)	9.9 (4.38)	11.2 (4.06)	t[1151] = 3.23, p=0.001
Logical Memory IIa (25)	8.1 (4.42)	9.4 (4.24)	t[1147] = 2.88, p=0.004
Semantic Memory (composite)	−0.06 (0.75)	0.23 (0.68)	t[526] = 6.10, p<0.001
Boston Naming (15 items)	13.4 (1.60)	14.0 (1.28)	t[480] = 5.75, p<0.001
Verbal Fluency (items in 2 1' trials)	31.9 (8.68)	34.4 (8.50)	t[500] = 5.08, p<0.001
Working Memory (composite)	−0.10 (0.73)	0.17 (0.71)	t[1152] = −5.76, p<0.001
Digit Span Forward (12 items)	7.9 (2.01)	8.6 (1.99)	t[1152] = 5.28, p<0.001
Digit Span Backward (10 items)	5.5 (5.75)	6.3 (2.00)	t[1151] = 3.87, p<0.001
Digit Ordering (9 items)	6.7 (1.69)	7.2 (1.54)	t[1152] = 4.22, p<0.001
Perceptual Speed (composite)	−0.15 (0.80)	0.23 (0.74)	t[1143] = 7.65, p<0.001
Symbol Digit (items in 90s)	32.9 (10.7)	39.2 (10.2)	t[1137] = 9.18, p<0.001
Number Comparison (pairs in 90s)	22.6 (7.43)	24.9 (7.17)	t[1138] = 4.70, p<0.001
Stroop Color Naming (items in 30s)	16.2 (7.87)	19.0 (7.32)	t[976] = 5.23, p<0.001
Stroop Word Naming (items in 30s)	47.4 (14.92)	51.4 (13.0)	t[427] = 3.82, p<0.001

Variable	Impaired Mobility (N=318)	No Mobility Impairment (N=836)	Significance ** (t- , x^2- or Fisher's Exact -test)
Visuospatial Abilities (composite)	−0.13 (0.81)	0.18 (0.77)	t[1142] = 6.15, p<0.001
Line Orientation (15 items)	8.9 (3.15)	10.0 (3.13)	t[1142] = 5.55, p<0.001
Progressive Matrices (16 items)	9.5 (2.30)	10.1 (2.11)	t[1138] = 4.39, p<0.001
Vascular Diseases (sum)	0.3 (0.47)	0.2 (0.43)	t[473] = −3.70, p<0.001
Myocardial Infarction	43 (13.5%)	70 (8.4%)	x^2 = 6.88, p=0.009
Congestive Heart Failure	14 (5.2%)	25 (3.5%)	x^2 = 1.51, p=0.218
Claudication	34 (10.7%)	40 (4.8%)	x^2 = 13.39, p<0.001
Vascular Risk Factors (sum)	1.1 (1.21)	1.1(1.15)	t[1152] = −1.11, p=0.266
Smoking	123 (38.7%)	359 (42.9%)	x^2 = 1.72, p=0.190
Diabetes	47 (14.8%)	117 (14.0%)	x^2 = 0.12, p=0.733
Hypertension	215 (67.6%)	485 (58.0%)	x^2 = 8.89, p=0.003

* The cohort was divided based on presence or absence of mobility disability at baseline (gait speed ≤ 0.55m/s). Mean (SD) or percentage is shown for each measure.

** Significance was based on Student t-tests (with Satterthwaite-adjusted degrees of freedom as appropriate), Mann-Whitney test or Chi-Square tests (df=1).

BMI: Body mass index: weight in kilograms divided by the square of height in meters. **Physical Activity**: Self-reported frequency of participation in 3 physical activities; a higher score indicates more frequent participation. **Mobility**: Composite measure of mobility based on mean z score of Steps and time to walk 8 feet, Time and steps to turn 360°, Time to stand on leg and toes. **Global Cognition**: Composite measure of cognition based on mean z score of 18 cognitive tests. **Cognitive Subscales**: 18 cognitive tests were summarized into five cognitive subscales: episodic memory, semantic memory, working memory, perceptual speed, and visuospatial abilities. **Vascular Risk Factors** Number of 3 risk factors (smoking, diabetes, and hypertension), self-reported. **Vascular Diseases** Number of 3 vascular diseases (of myocardial infarction, congestive heart failure and claudication), self-reported.

Table 2

Baseline Cognition, Incident Mobility Impairment and Loss of Ambulation*

Baseline Cognitive Measure	Mobility Impairment HR (95% CI) WALD X^2(DF=1), p-value	Loss of Ambulation HR (95% CI) WALD X^2(DF=1), p-value
Global Cognition	0.51(0.40, 0.66) 25.9, (DF=1), p<0.001	0.39 (0.29, 0.52) 40.5; (DF=1), p<0.001
Episodic Memory	0.79 (0.66, 0.95) 6.3, (DF=1), p=0.012	0.62 (0.50, 0.76) 22.0, (DF=1), p<0.001
Semantic Memory	0.66 (0.55, 0.78) 22.1, (DF=1), p<0.001	0.61 (0.50, 0.75) 21.8, (DF=1), p<0.001
Perceptual Speed	0.67 (0.58, 0.79) 24.3, (DF=1), p<0.001	0.58 (0.48, 0.69) 35.5, (DF=1), p<0.001
Working Memory	0.80 (0.68, 0.94) 7.5, (DF=1), p=0.006	0.72 (0.59,0.89) 9.7, (DF=1), p=0.002
Visuospatial Abilities	0.80 (0.68, 0.93) 8.4, (DF=1), p=0.004	0.76 (0.62,0.92) 8.0, (DF=1), p=0.005

*Based on a series of discrete-time proportional hazards models for time to incident mobility impairment and incident loss of the ability to ambulate. Results show the effect of a 1- unit higher level for each cognitive measure at baseline. All models also included terms to adjust for age, sex, education, and race (estimates not shown).

Table 3

Baseline Cognition and the Annual Rate of Change in Mobility *

Baseline Cognitive Measure	Model Terms	coefficient (S.E., P Value)
Global Cognition	Time	−0.123 (0.006, p<0.001)
	Global Cognition	0.295 (0.037, p<0.001)
	Global Cognition × Time	0.054 (0.010, p<0.001)
Episodic Memory	Time	−0.119 (0.006, p<0.001)
	Episodic Memory	0.105 (0.029, p<0.001)
	Episodic Memory × Time	0.036 (0.008, p<0.001)
Semantic Memory	Time	−0.119 (0.006, p<0.001)
	Semantic Memory	0.172 (0.027, p<0.001)
	Semantic Memory × Time	0.029 (0.007, p<0.001)
Perceptual Speed	Time	−0.118 (0.006, p<0.001)
	Perceptual Speed	0.186 (0.025, p<0.001)
	Perceptual Speed × Time	0.028 (0.007, p<0.001)
Working Memory	Time	−0.114 (0.006, p<0.001)
	Working Memory	0.133 (0.025, p<0.001)
	Working Memory × Time	0.013 (0.007, p=0.054)
Visuospatial Abilities	Time	−0.113 (0.006, p<0.001)
	Visuospatial Abilities	0.164 (0.024, p<0.001)
	Visuospatial Abilities × Time	0.008 (0.007, p=0.271)

* Estimated from a linear mixed-effect model with composite mobility as the outcome; including a term for composite mobility decline, Time (in years since baseline). Each of the 6 models included a term for a different baseline cognitive measure and its interactions with the rate of change in composite mobility (Time). Significance was based on a t-statistic from the mixed-effect model. The degrees of freedom for the slope terms including the annual rate of change in Mobility (Time) and the interaction of global cognition with the annual rate of change in mobility (Global Cognition × Time) have 4470 of freedom and the intercept term (Global Cognition) has 1148 degree of freedom. Similarly with respect to the other 5 cognitive abilities, slope terms have at least 4430 degrees of freedom and all intercept terms have at least 1138 degree of freedom. Each of the 6 models was also adjusted for age, sex, education, and race and their interactions with Time (data not shown). Results show the effect of a 1-unit higher level of baseline cognitive ability.