

Cognitive Function, Gait Speed Decline, and Comorbidities: The Health, Aging and Body Composition Study

Hal H. Atkinson,¹ Caterina Rosano,² Eleanor M. Simonsick,³ Jeff D. Williamson,¹ Cralen Davis,⁴ Walter T. Ambrosius,⁴ Stephen R. Rapp,⁵ Matteo Cesari,⁶ Anne B. Newman,² Tamara B. Harris,³ Susan M. Rubin,⁷ Kristine Yaffe,⁸ Suzanne Satterfield,⁹ and Stephen B. Kritchevsky,¹
for the Health ABC study

¹Department of Internal Medicine, Section on Gerontology and Geriatric Medicine, Claude D. Pepper Older Americans Independence Center and Roena Kulynych Center for Memory and Cognition Research, Sticht Center on Aging, Wake Forest University School of Medicine, Winston-Salem, North Carolina.

²Department of Medicine, Division of Geriatrics, University of Pittsburgh Institute on Aging, Pennsylvania.

³Intramural Research Program, National Institute on Aging, Baltimore and Bethesda, Maryland.

⁴Division of Public Health Sciences and ⁵Department of Psychiatry and Behavioral Medicine, Wake Forest University School of Medicine, Winston-Salem, North Carolina.

⁶Department of Geriatrics and Aging Research, University of Florida, Gainesville. Departments of ⁷Epidemiology and Biostatistics and

⁸Psychiatry, Neurology and Epidemiology, University of California, San Francisco.

⁹Department of Preventive Medicine, University of Tennessee College of Medicine, Memphis.

Background. Emerging evidence indicates an association between cognitive function and physical performance in late life. This study examines the relationship between cognitive function and subsequent gait speed decline among high-functioning older adults.

Methods. Measures of global cognitive function (Modified Mini Mental State Examination [3MS]) and executive control function (ECF) (a clock drawing task [CLOX 1] and the 15-item Executive Interview [EXIT 15]) were obtained in the Health, Aging, and Body Composition Study in 1999–2000. Gait-speed (meters/second) was assessed over 20 meters at usual pace. Using a mixed model, we assessed the relationship between baseline cognitive function and gait-speed change over 3 years.

Results. Two thousand, three hundred forty-nine older adults (mean age 75.6 ± 2.9 years) completed the assessments. After adjustment for baseline gait speed, a 1-standard-deviation (*SD*) lower performance on each cognitive test was associated with greater gait-speed decline over 3 years: 0.016 m/s for the 3MS (*SD* = 8.1), 0.009 m/s for CLOX 1 (*SD* = 2.4), and 0.012 m/s for EXIT 15 (*SD* = 4.1) ($p < .0005$ for all). After adjustment for comorbidities, the effect size was attenuated for 3MS and CLOX 1, and the association for EXIT 15 was no longer significant. Depression score was most strongly associated with the EXIT 15 effect reduction.

Conclusion. Global and executive cognitive functions predict declines in gait speed. The association of ECF with gait speed decline is attenuated by comorbid conditions, particularly depression. Elucidation of the mechanisms underlying these associations may point to new pathways for the treatment of physical decline associated with diminished cognitive function.

STUDIES of the relationship between cognitive and physical function have focused primarily on cognitive function as a correlate of disability in performing tasks of daily living (1–4). Although these studies are important for characterizing the functional consequences of diminished cognitive function, they provide little insight into the mechanisms by which poor cognitive function leads to physical decrements. Additionally, this work has relied on self- or proxy reports, which may be less reliable in individuals with cognitive impairment (5). More recently, some studies have examined associations between cognitive performance and the performance of physical tasks, such as walking, standing balance, and strength assessment (6–15). Use of objective

performance tests: (a) enables detection of relationships between cognitive and physical performance earlier in the disablement process, and (b) can elucidate the potential effects of diminished cognitive function specifically on motor performance.

Cross-sectional studies have found a variety of cognitive function measures to be associated with various aspects of physical performance (7–10,12). Whether the observed relationship between cognitive and physical functioning signifies a parallel decline process or a reciprocal relationship requires longitudinal investigation. Existing longitudinal studies (6,11,13–17) have been limited by sample size, available covariates, selectivity of study participants, and/or

reliance on global tests of cognitive function only. Executive control function (ECF) involves attention, inhibition of distracting stimuli, and planning and execution of tasks. Recent research suggests that ECF mediates the stability and velocity of gait in older adults when interference is introduced during walking (18–20). However, ECF may also be an important predictor of subsequent declines in simple physical performance measures through its role in maintaining attention to walking and inhibiting distracting stimuli in older adults aging with comorbid conditions.

To gain a more complete understanding of the relationship between specific cognitive domains including executive function and physical performance decline, the present study examines the relationship between global cognitive function and two measures of executive control and decline in usual gait speed over 3 years in participants in the Health, Aging and Body Composition (Health ABC) study.

METHODS

The Health ABC Study and Participants

The Health ABC study is a prospective observational study of older adults aimed at characterizing body composition and the nature and extent of its relationship to physical changes with age. The study population consists of 3075 well-functioning black and white community-dwelling older adults. Prospective participants were recruited from a sample of white Medicare beneficiaries selected at random and all age-eligible black residents in designated ZIP code areas in and around Memphis, Tennessee and Pittsburgh, Pennsylvania between March 1997 and July 1998. Eligible participants were 70–79 years old at enrollment and could not have any self-reported difficulty in walking one quarter mile, walking up 10 steps, or performing basic activities of daily living. Persons with a life-threatening cancer or plans to move out of the area within 3 years were excluded. The study protocol was approved by the Institutional Review Boards of the University of Tennessee, Memphis and the University of Pittsburgh, and each participant provided written informed consent for participation.

Because ECF testing first occurred at the third annual visit that took place in 1999–2000, this visit was considered the study baseline. A total of 2505 participants had a clinic visit in year 3. Of this group, 2349 completed all cognitive and gait speed tests in 1999–2000 and had at least one gait speed measurement over the subsequent 3-year period. Compared to included participants, excluded participants were older (76.1 ± 2.6 years vs 75.6 ± 2.9 years), more likely to be men (52% vs 44%), and more likely to be black (53% vs 37%). Additionally, excluded participants were less educated, had slower baseline gait speed, and had poorer scores on all three cognitive tests.

Cognitive Tests

At the 1999–2000 visit, global cognitive function was measured using the Modified Mini-Mental Status Examination (3MS) (21). ECF was assessed with a scored clock drawing task (CLOX 1) (22) and the 15-item Executive Interview (EXIT 15), a shortened version of the 25-item

Executive Interview (23) developed for the Health ABC study. The 3MS is an expanded version of the Mini-Mental State Examination (24), with additional items assessing verbal fluency, delayed recall, and abstract reasoning. Scores can range from 0 to 100 points; lower scores indicate poorer performance. In the CLOX 1 test, participants are given a blank sheet of paper and are instructed to “draw a clock that says 1:45” and “set the numbers and face of the clock so that a child can read them” (22). The task is then scored from 0 to 15; lower scores indicate poorer performance. The EXIT 15 assesses several ECFs such as inhibition of automatic responses and intrusions, word and design fluency, and sequencing tasks. The test is scored from 0 to 30; lower scores indicate better performance. We chose to include these two measures of ECF although they were significantly correlated in our sample ($r = .39$), because clock drawing tasks represent a single task that is easy to complete and are often included in clinical practice, whereas the EXIT 15 provides a more lengthy compendium of other ECF tasks.

Gait Speed Assessment

Gait speed was assessed over a 20-meter straight course set up in a corridor. Participants were instructed to begin walking at their usual pace from the starting point and to continue just past an orange cone indicating the end of the course. Timing began at the first footfall over the starting line and ended with the first footfall over the finishing line.

Covariates

In addition to clinic site and baseline gait speed, we considered as possible covariates demographic variables (age, race, sex, educational level, literacy level); health habits (smoking, exercise in the previous week); comorbid conditions, risk factors, and medications (visual impairment, depressive symptoms, body mass index [BMI], hypertension, diabetes, cardiovascular disease, cerebrovascular disease, peripheral arterial disease, and medications including anxiolytic/sleep aids, anti-Parkinson drugs, antidepressants, and cholinesterase inhibitors); and interim health events (falls and hospitalizations). All time-dependent variables were assessed at the 1999–2000 visit except ankle–arm index and height, which were measured 2 years previously at the 1997–1998 visit. Presence of comorbid conditions was obtained from participant reports from the 1997–1998 through 1999–2000 visits. Hospitalizations and falls over the 3-year period of this analysis were assessed by self- or proxy report at each follow-up.

Literacy was assessed using the Rapid Estimate of Adult Literacy in Medicine (REALM) (25). Exercise level was assessed by questionnaire, and the metabolic equivalents of each activity were assigned to calculate the total kilocalories per kilogram body weight expended in the previous week (26). Depressive symptom severity was assessed using the Centers for Epidemiologic Studies of Depression 10-item scale (CESD-10) (27). The ratio of the lower of two systolic blood pressures obtained in the ankle to the systolic blood pressure of the right arm was used to calculate ankle–arm index. BMI was determined from measured weight in

Table 1. Baseline Characteristics of the Participants by Global Cognitive Function Scores

Characteristic	Overall (N = 2349)	By 3MS Quartiles				p Value*
		< 87 (N = 554)	87–93 (N = 618)	93–96 (N = 453)	> 96 (N = 724)	
Age, y	75.6 ± 2.9	76.1 ± 2.9	75.6 ± 2.9	75.3 ± 2.8	75.2 ± 2.7	< .0001
Women	52.3%	47.8%	51.9%	51.7%	56.5%	.02
Black	37.3%	68.8%	41.6%	24.5%	17.5%	< .0001
< High school education	21.8%	54.0%	20.9%	10.8%	4.8%	< .0001
Literacy score (REALM)	60.2 ± 12.0	48.7 ± 18.8	62.2 ± 6.1	63.8 ± 4.7	65.0 ± 3.9	< .0001
3MS score	90.4 ± 8.1	78.7 ± 7.2	89.7 ± 1.7	94.1 ± 0.81	97.6 ± 1.3	< .0001
CLOX 1 score	10.7 ± 2.4	9.2 ± 2.6	10.6 ± 2.3	11.2 ± 2.0	11.6 ± 2.0	< .0001
EXIT 15 score	6.4 ± 4.1	10.6 ± 4.0	6.7 ± 3.2	5.3 ± 2.9	3.8 ± 2.6	< .0001
Baseline gait speed (m/s)	1.15 ± 0.22	1.05 ± 0.21	1.14 ± 0.21	1.19 ± 0.20	1.23 ± 0.21	< .0001
Current smoker	7.2%	12.5%	6.5%	5.1%	5.1%	< .0001
Exercise in previous week (kcal/kg/wk)	6.9 ± 17.5	5.0 ± 18.6	6.4 ± 16.1	7.4 ± 17.5	8.6 ± 17.8	.0021
Visual acuity ≤20/50	4.3%	6.2%	5.4%	2.9%	2.9%	.007
BMI, kg/m ²	27.2 ± 4.7	27.5 ± 5.3	27.7 ± 4.8	27.2 ± 4.6	26.7 ± 4.3	.0007
Depressive symptoms (CESD-10 score)	4.4 ± 4.0	5.6 ± 4.6	4.6 ± 4.0	3.9 ± 3.6	3.7 ± 3.7	< .0001
Hypertension	73.5%	77.3%	77.4%	71.1%	68.8%	.0004
Diabetes mellitus	21.6%	24.2%	24.3%	19.9%	15.1%	< .0001
Coronary heart disease	23.5%	24.0%	24.9%	24.9%	20.9%	.24
Congestive heart failure	2.9%	4.7%	2.6%	3.5%	1.5%	.008
Cerebrovascular disease	7.7%	7.9%	7.1%	8.6%	7.5%	.82
Peripheral arterial disease	4.6%	4.7%	4.5%	5.3%	4.0%	.78
Ankle–arm index < 0.9	12.7%	18.9%	12.1%	9.5%	10.7%	< .0001
Antidepressant use	7.8%	6.1%	9.1%	6.8%	8.6%	.20
Anti-parkinson medication use	0.9%	1.2%	0.9%	1.4%	0.4%	.34
Cholinesterase inhibitor use	0.6%	1.9%	0.3%	0.2%	0.1%	.0003
Anxiolytic/sleep aid use	5.8%	6.4%	6.4%	4.4%	5.7%	.52

Notes: *p values were determined by chi-square test for binary variables and analysis of variance for continuous variables for differences among groups.

3MS = Modified Mini-Mental State Examination; REALM = Rapid Estimate of Adult Literacy in Medicine; CESD-10 = Centers for Epidemiologic Studies of Depression 10-item scale; BMI = body mass index; CLOX 1 = scored clock drawing task; EXIT 15 = the 15-item Executive Interview; SD = standard deviation.

kilograms divided by measured height in meters squared. Medications of interest were classified according to the Iowa Drug Information System (IDIS) (28) codes as follows: anxiolytics/sleep aids (codes 28240202–28240276 or 28240834), anti-Parkinson drugs (codes 12080802–12080806 or 28280002–28280013), antidepressants (codes 28160415, 28160434, 28160458, 28160486, or 28160500–28160711) and cholinesterase inhibitors (28200039).

Statistical Analysis

All results are reported as mean ± standard deviation unless otherwise stated. For descriptive statistics according to quartiles of global cognition, we used a chi-square test for binary variables and analysis of variance for continuous variables to compare groups. To assess the relationship between cognitive function and gait speed decline, we first examined gait speed decline according to quartiles of baseline cognitive function for each test, adjusted for baseline gait speed, age, race, and clinic site. Separate mixed-effects models (SAS Proc Mixed) were used to assess the relationship between each independent cognitive variable (3MS, CLOX 1, and EXIT 15) at baseline and gait speed decline over the following 3 years. All models included clinic site as a random effect and baseline gait speed as a fixed effect. A model was also fit controlling for demographics, health habits, comorbid conditions, risk factors, and interim health events. After this analysis, further reduced models were fit in a series of four models. The first included site and base-

line gait speed. The second added age, race, education, sex, and the REALM score. The third added exercise level, BMI, visual acuity ≤20/50, interim hospitalizations, interim falls, CESD-10 score, and medications. The fourth added smoking status, hypertension, diabetes, cerebrovascular disease, coronary artery disease, and peripheral arterial disease. This was done to assess which covariates diminished the relationship between cognition and gait speed decline. A backward elimination procedure from the full model was also performed to determine the impact of each variable in reducing the association of ECF with gait speed decline. All analyses were performed using SAS software (version 8.2; SAS Institute, Cary, NC).

RESULTS

The study population characteristics by quartiles of global cognitive function (measured by the 3MS) are presented in Table 1. Cognitive test scores and gait speed indicate this cohort to be generally high functioning. Average gait speed declined by 0.05 m/s over the 3-year follow-up period. On average, 25.7% of participants reported at least one fall, and 14.6% reported at least one hospitalization during each year of the follow-up period. Participants in the lower quartiles of 3MS scores were slightly older and more likely to be men, black, less educated, and have lower literacy. Additionally, participants in the lower quartiles of 3MS scored worse on the other cognitive tests, and had higher depressive

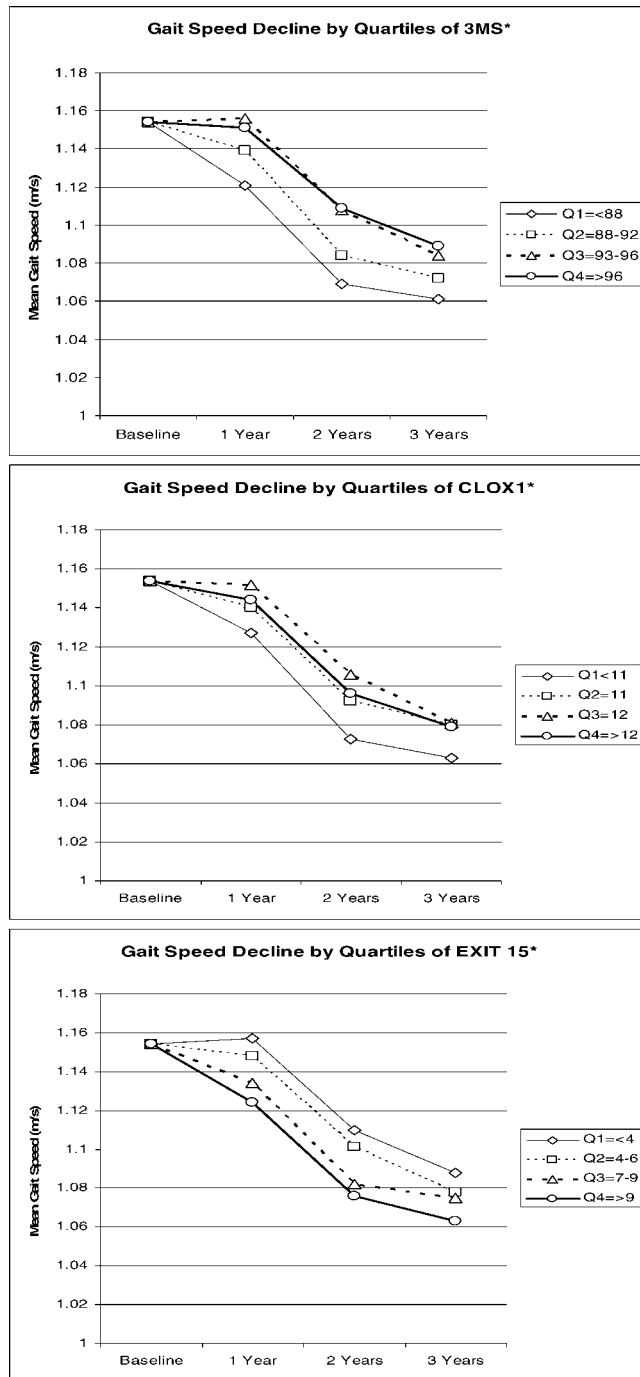


Figure 1. Quartiles of cognitive tests and 3-year gait speed decline. These figures are based on least squares means calculated for each of the cognitive variables using mixed-effects modeling with gait speed decline over 3 years as the outcome variable. The models were adjusted for baseline gait speed, age, race, gender, and clinic site. Follow-up differences between mean gait speeds were not statistically significantly different among quartiles. Lower quartiles indicate poorer cognitive performance on Modified Mini-Mental State Examination (3MS) and the scored clock drawing task (CLOX 1), and lower quartiles indicate higher cognitive performance on the 15-item Executive Interview (EXIT 15).

symptoms, slightly higher BMI values, and slower baseline gait speeds. They also had a higher prevalence of current smoking, diabetes mellitus, hypertension, congestive heart failure, low ankle–arm index, lower visual acuity, and use of cholinesterase inhibitors.

Figure 1 portrays the relationship between cognitive function and mean gait speed decline over the follow-up period after direct adjustment for baseline gait speed, age, race, and sex. Although not statistically significant, a separation of the trajectory of decline for 3MS is seen between the upper and lower quartiles of cognitive performance, with lower baseline cognitive performance associated with steeper trajectories of decline. Similar relationships were found for CLOX 1 and EXIT 15 (also not statistically significant).

The relationship between cognition and gait speed decline over 3 years is presented in Table 2. For 1-standard-deviation poorer performance on the 3MS (8.1 points), 0.016 m/s greater decline in gait speed was observed over the follow-up period. Although the effect was slightly diminished in the full model, the association of 3MS with gait speed decline remained significant. CLOX 1 and EXIT 15 scores were also significantly associated with gait speed decline. However, the association of EXIT 15 was diminished and no longer significant in the full model.

Four models were fit to determine the relative contribution of each set of variables to the reduction in the association of EXIT 15 with gait speed decline. These results are presented in Figure 2. An overall reduction in effect size of 66% was observed from the reduced to the full model. As Figure 2 demonstrates, addition of demographics to the reduced model resulted in a 20% reduction in the effect size. Addition of health habits, interim events, comorbidities, and medications resulted in 30% further reduction in the effect size, and addition of vascular factors accounted for the final 16% of the reduction in effect size in the full model. The backward elimination procedure identified the CESD-10 score as the only single variable the removal of which returned the association of EXIT 15 and gait speed decline to a significant level, accounting for 17% of the 66% total reduction in the effect in the full model. Given this finding, we tested for an interaction between CESD-10 and cognitive test score for each of the three original models; we found no statistically significant interaction term at an α of 0.10.

Because of concern that the performance of participants with clearly abnormal cognitive function (e.g., those with probable dementia) might be responsible for these findings, we repeated these analyses in individuals with a 3MS score of ≥ 80 ($n = 2106$); these associations remained.

DISCUSSION

In an initially high-functioning cohort of community-dwelling older adults, small but statistically significant incremental declines in gait speed were observed in association with poorer global cognitive function and poorer performance on two tests of ECF. After adjustment for covariates, there was a reduction of the association for all three cognitive measures, with the greatest reduction observed for measures of executive function.

Table 2. Calculated Contribution of Cognitive Function to Change in Gait Speed Over 3 Years

Test (<i>SD</i>)	Reduced Model		Full Model	
	Δ Gait Speed (<i>SD</i>) (m/s)	<i>p</i> Value	Δ Gait Speed (<i>SD</i>) (m/s)	<i>p</i> Value
3 MS (8.1)	-0.016 (.003)	< .0001	-0.012 (.004)	.001
CLOX 1(2.4)	-0.009 (.002)	.0004	-0.007 (.003)	.011
EXIT 15 (4.1)	-0.012 (.003)	< .0001	-0.004 (.003)	.18

Note: Results are based on separate reduced and full mixed models for each cognitive test. Per 1-standard-deviation (*SD*) lower performance in cognitive function, the expected change in gait speed is shown. Reduced model adjusted for the Health, Aging and Body Composition study (Health ABC) site and baseline gait speed. Full model adjusted for age, gender, education, Rapid Estimate of Adult Literacy in Medicine (REALM) score, smoking status, physical activity in the previous week, body mass index, visual acuity $\leq 20/50$, Centers for Epidemiologic Studies of Depression 10-item scale (CESD-10) score, cardiovascular disease, cerebrovascular disease, diabetes, medication use (antidepressants, anti-parkinson medications, cholinesterase inhibitors, or anxiolytics/sleep aids), interim falls, and interim hospitalizations.

The present study adds to the growing body of longitudinal studies examining the relationship of cognition and physical performance in older adults (6,11,13–15), suggesting a role for cognitive function in preventing a decline in motor task performance over time. We offer a few explanations for the apparent influence of cognitive function on gait speed decline. First, maintenance of an efficient gait may require specific cognitive capacities. Memory, visuospatial skills, cognitive processing speed, and ECFs (such as sustaining attention and inhibiting distraction) may be differentially important to the planning, initiating, and maintaining of walking. A recent small study using functional magnetic resonance imaging indicated greater cognitive monitoring of movements in old adults versus young adults (29), possibly due to sensory declines. Secondly, cognition may be associated with physical performance decline through common pathologies affecting both higher order cognitive functions and physical performance, such as vascular or degenerative lesions.

The significant reduction in the association between the EXIT 15 and gait speed decline following adjustment for covariates was unexpected. The association between CLOX 1 and gait speed decline was also attenuated, but not to the same extent. It is possible that the EXIT 15 measures a broader range of executive functions that are more sensitive to comorbidity. It is likely that multiple, potentially modifiable factors are related to both cognitive and physical function. For example, previous studies have specifically shown relationships between vascular risk and both cognitive and physical function in older adults (30,31). Including depressive symptoms had the greatest impact on reducing the association between EXIT 15 performance and gait speed decline in our model. Previous studies have found an independent association between depressive symptoms and both physical performance declines (32,33) and cognitive decline and impairment (34–36). Fatigue, a common symptom of depression, may affect gait and cognitive performance, and executive control might also be differentially affected because it may require more effort than other cognitive functions, although our data do not allow us to test this hypothesis. Another study provides evidence of an interaction between the Mini-Mental State Examination (24) and the 20-item CESD on subsequent physical performance (11). It is also possible that lower executive function, depressive symptoms, and slower gait may be linked by underlying subcortical vascular disease (31); however, we

were unable to address this possibility directly without brain imaging.

This study has several strengths, including a large community-representative study population, longitudinal design, the examination of both global cognitive function and ECF, use of a well-established objective measure of lower extremity physical performance that predicts functional limitations (37,38), and availability of important covariates. There are also several limitations. First, because participants in Health ABC are high functioning, our findings cannot be generalized to more frail populations. Second, the high mean scores on cognitive testing reflect a ceiling effect, which might account for the small magnitude of changes in gait speed that were observed. Although the assessments in Health ABC are detailed, this study is also limited by a lack of physical assessments for parkinsonism. Additionally, the 3MS, CLOX 1, and EXIT 15 all include test components that require good motor function (e.g., drawing pentagons or completing hand

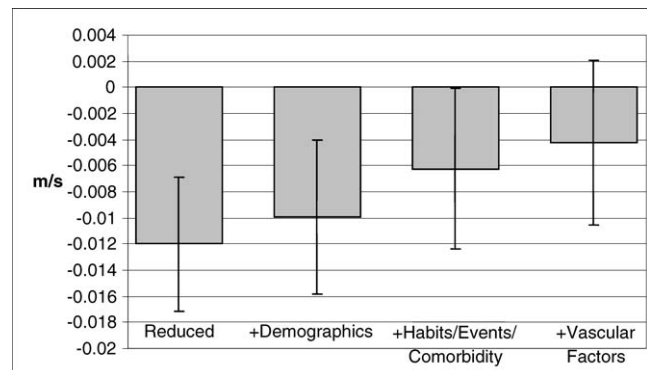


Figure 2. Nested models showing reduction of the 15-item Executive Interview (EXIT 15) effect on gait speed decline. In each model, per standard deviation lower performance on EXIT 15, the expected change in gait speed is shown. Reduced Model: site, baseline gait speed; Demographics added: + age, race, gender, education, Rapid Estimate of Adult Literacy in Medicine (REALM) literacy score; Health Habits/Events/Comorbidities added: + exercise in the previous week, body mass index, interim hospitalizations, interim falls, visual acuity $\leq 20/50$, Centers for Epidemiologic Studies of Depression 10-item scale (CESD-10) score, and medication use (antidepressants, anti-Parkinson medications, cholinesterase inhibitors, or anxiolytics/sleep aids); Vascular Factors added (Full Model): + smoking status, hypertension, diabetes mellitus, cerebrovascular disease, coronary artery disease, and peripheral arterial disease. Error bars indicate 95% confidence intervals.

movement sequences), which may blur the distinction between the two realms of function studied. Nonetheless, many of the tasks on the 3MS and EXIT 15 involve no motor skills, and none of the motor tasks involve the lower extremities.

Summary

This study provides further evidence that cognitive function is associated with subsequent decline in physical performance in late life. Future research should focus on which aspects of cognitive function are most associated with physical decline and clarification of the mechanisms underlying the association. Further investigation of the complex relationships between cognitive function, physical performance decline, and comorbidities may point to new pathways for the treatment of physical decline associated with diminished cognitive function.

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CORRESPONDENCE

Address correspondence to Hal H. Atkinson, MD, Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157. E-mail: hatkinso@wfubmc.edu

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