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Executive Function, More Than Global Cognition, Predicts Functional Decline and Mortality in Elderly Women

Julene K. Johnson[1], **Li-Yung Lui**[5], and **Kristine Yaffe**[1,2,3,4]

1 *Department of Neurology, University of California, San Francisco*

2 *Department of Medicine, University of California, San Francisco*

3 *Department of Psychiatry, University of California, San Francisco*

4 *San Francisco VA Medical Center, California*

5 *Research Institute, California Pacific Medical Center, San Francisco*

Abstract

Background—Functional impairment in community-dwelling older adults is common and is associated with poor outcomes. Our goal was to compare the contribution of impairment in executive function or global cognitive function to predicting functional decline and mortality.

Methods—We studied 7717 elderly women enrolled in a prospective study (mean age 73.3 years) and identified women with poor baseline executive function (score > 1 standard deviation [*SD*] below the mean on the Trail Making Test B (Trails B; *n* = 957, 12.4%), poor global cognitive function (score > 1 *SD* below the mean on a modified Mini-Mental State Examination [mMMSE], *n* = 387, 5.0%), impairment in both (*n* = 249, 3.2%), or no impairment (*n* = 6124, 79.4%). We compared level of functional difficulty (Activities of Daily Living [ADLs] and Instrumental ADLs [IADLs]) at baseline and at 6-year follow-up and survival at follow-up. We also determined if the association was independent of age, education, depression, medical comorbidities, and baseline functional ability.

Results—At baseline, women with Trails B impairment only or impairment on both tests reported the highest proportion of ADL and IADL dependence compared to the other groups. At the 6-year follow-up after adjusting for age, education, medical comorbidities, depression, and baseline ADL or IADL, women with only Trails B impairment were 1.3 times more likely to develop an incident ADL dependence (adjusted odds ratio [OR] = 1.34; 95% confidence interval [CI], 1.07–1.69) and 1.5 times more likely to develop a worsening of ADL dependence (adjusted OR = 1.48; 95% CI, 1.16–1.89) when compared to women with no impairment on either test. In addition, women with only Trails B impairment had a 1.5-fold increased risk of mortality (adjusted hazard ratio [HR] = 1.48; 95% CI, 1.21–1.81). In contrast, women with impairment on only mMMSE were not at increased risk to develop incident ADL or IADL dependence, a worsening of ADL or IADL dependence, or mortality.

Conclusion—Compared to women with no impairment, women with executive function impairment had significantly worse ADL and IADL function cross-sectionally and over 6 years. Individuals with executive dysfunction also had increased risk of mortality. These results suggest that screening of executive function can help to identify women who are at risk for functional decline and decreased survival.

Address correspondence to Julene K. Johnson, PhD, UCSF Department of Neurology, Memory and Aging Center, 350 Parnassus, Suite 706, San Francisco, CA 94117. E-mail: jjohnson@memory.ucsf.edu

Functional dependence in community-dwelling older adults is common and is associated with lower quality of life (1), increased health care costs (2), and mortality (3,4). Established risk factors for functional impairment in community-dwelling elderly individuals include age, female gender, depression, medical comorbidities, physical activity, and social factors [see (5) for review]. In addition, several cross-sectional and prospective studies of nondemented elders report an association between low scores on global tests of cognitive function, such as the Mini-Mental State Examination (MMSE) and functional dependence (6–9). Longitudinal studies also suggest that low baseline scores on measures of global cognition predict the onset of new functional impairment (10,11) and an increase in functional dependence over time (9, 12,13).

Although an association between global cognitive impairment and functional status has been established, few studies have evaluated the contribution of domain-specific cognitive impairment. Executive function is a cognitive ability that involves the planning and execution of goal-directed behaviors, abstract reasoning, and judgment (14). Because the ability to perform Instrumental Activities of Daily Living (IADL) requires these abilities, even mild executive dysfunction may impair function. Several studies suggest that executive and visuospatial functions are related to functional impairment in patients with dementia (15–18). However, fewer studies have explored cognitive predictors of functional impairment in nondemented elderly individuals. For example, several cross-sectional studies suggest that community-dwelling, elderly individuals with low scores on executive function tests have more functional impairment than do elders without executive impairment (7,19,20). However, it is difficult to establish the direction of the association given the cross-sectional nature of these studies. Thus, it is important to prospectively compare the relative contribution of global cognition and executive function to functional decline so that appropriate screening tools can be used for identifying at-risk individuals. In one of the few longitudinal studies, Wang and colleagues (12) found that low cognitive function, as measured by the Cognitive Abilities Screening Instrument (CASI), was a predictor of functional decline. Another study found that a change in a measure of executive function better predicted IADL decline than the MMSE did (21). These studies all suggest that poor global cognition may be associated with functional impairment. However, domain-specific cognitive impairment, specifically executive dysfunction, may be a stronger contributor than measures of global cognition.

The purpose of the current study was to investigate the relationship between baseline impairment on executive function or on global cognition and functional decline over 6 years. We hypothesized that poor baseline performance on a brief test of executive function would be associated with greater functional dependence at baseline and after 6 years when compared to the performance of individuals without executive impairment or to those with only global cognitive impairment. We also hypothesized that this association would be independent of age, education, depression, medical comorbidities, and baseline ADL or IADL function.

Methods

Participants

The Study of Osteoporotic Fractures (SOF) is a multicenter, prospective study of risk factors for osteoporotic fractures in 9704 community-dwelling women older than 65 years who were recruited from four metropolitan areas in the United States (Baltimore, Pittsburgh, Minneapolis, and Portland). Participants did not receive a dementia evaluation at baseline; however, all women were living independently and were able to provide consent. In addition to the collection of extensive physical data, participants also underwent repeated cognitive and functional evaluations. A brief cognitive evaluation (including a modified MMSE [mMMSE] and the Trail Making Test B [Trails B]) was administered at baseline, and functional evaluations were completed at baseline and at the 6-year follow-up visit. The analytic cohort

included the 7717 women who completed the cognitive and functional evaluations at baseline and the 6313 women who completed functional evaluations at the 6-year follow-up visit. Participants who were unavailable at the 6-year visit included 834 who were deceased, 397 who participated in the follow-up but did not complete the functional evaluation, 99 who withdrew from the study, and 74 who did not complete the year 6 visit but remained in the study. All participants provided written consent that was approved by the institutional review boards.

Cognitive Tests

Global cognitive function was assessed using the 26-point mMMSE, a commonly used screening test for dementia (22). The mMMSE was modified from the original 30-point MMSE by excluding several orientation items. A higher score indicated better performance. The Trails B (23) was used as a brief measure of executive function. This test requires participants to connect numbers and letters in alternating order and requires the ability to shift sets. The maximum amount of time to complete Trails B (300 seconds) was used, and higher scores indicated worse performance. We defined impairment on either test as a baseline score that fell > 1 standard deviation (*SD*) below the sample mean (< 23 for mMMSE and > 180 seconds for Trails B). The cutoff values for Trails B (24) and mMMSE (25,26) are similar to those in other studies.

Demographics and Health-Related Variables

We collected information on demographics, medical history, and depression. We assessed medical comorbidity including history of self-reported physician diagnosis of myocardial infarction, stroke, transient ischemic attack (TIA), hypertension, or diabetes. Symptoms of depression were assessed using the Geriatric Depression Scale (GDS, short form; range = 0–15) (27), with higher scores indicating a greater number of symptoms.

Measures of Functional Status and Decline

Functional status was assessed using a self-report questionnaire about ADLs and IADLs modified from the 1984 National Health Interview Survey Supplement on Aging (28). Two scores were derived: One documented difficulty on four items (0–4 point scale), and the other measured degree of difficulty on the four items (0–12 point scale). To assess ADLs, participants were asked whether they had difficulty performing the following activities independently: (1) walking two or three blocks outside on level ground, (2) dressing, (3) getting in and out of bed, and (4) bathing. Scores ranged from 0–4 reflecting no difficulty on any items (0 points) to difficulty on all four items (4 points). At baseline, “ADL difficulty” was defined as having difficulty on one or more of the four items. At follow-up, an “incident ADL difficulty” was defined as an increase in one or more points on the four items. Participants also rated their level of ADL difficulty for each of the four items on a scale from 0 to 3 (0 = no difficulty, 1 = some difficulty, 2 = much difficulty, and 3 = cannot do). Individual scores (0–3) were summed across each of the four items to yield a total score from 0 to 12, with higher scores reflecting a higher level of ADL difficulty. At follow-up, a “worsening of ADL difficulty” was defined as an increase in two or more points on the 12-point ADL difficulty level scale.

To assess IADLs, participants were asked whether they had difficulty (1) preparing meals, (2) doing heavy housework, (3) doing other chores, or (4) shopping for groceries or clothes. Scores again ranged from 0 to 4, reflecting no difficulty to difficulty on all four items. “IADL difficulty” was defined as having difficulty on one or more of the IADL items. At follow-up, an “incident IADL difficulty” was defined as an increase in one or more points. Participants also rated IADL difficulty level for each item (0 = no difficulty, 1 = some difficulty, 2 = much difficulty, and 3 = cannot do). Individual scores (0–3) were summed across each of the four items to yield a total score from 0 to 12, with higher scores reflecting a higher level of IADL

difficulty. At follow-up, a "worsening of IADL difficulty" was defined as an increase in two or more points on the 12-point IADL difficulty level scale.

Statistical Analyses

The participants were categorized into four groups based on the baseline cognitive scores (i.e., no impairment on mMMSE or Trails B, mMMSE impairment only, Trails B impairment only, or impairment on both mMMSE and Trails B). Baseline characteristics were compared across four groups ($n = 7717$) using analysis of variance for continuous variables and chi-square tests for dichotomous variables. We calculated the change in functional status over 6 years and determined the proportion of women in each group with ADL or IADL incident and worsening dependence ($n = 6313$). Logistics regression models were used to estimate the relationship between baseline cognitive function and a worsening or incident ADL and IADL difficulty at follow-up. In order to explore whether the association between cognition and function was confounded by variables known to influence functional status, we adjusted for age, education, depression, medical comorbidities, and baseline ADL or IADL function. We also used Cox proportional hazard models to estimate the relationship between baseline cognitive function and mortality at the 6-year follow-up ($n = 834$).

Results

At baseline, the 7717 women had a mean age of 73.3 years (*SD* 5.0 years, range 67–98 years) and 12.7 years of education (*SD* 2.8 years, range 1–19 years). The mean mMMSE was 24.8 points of 26 (*SD* 1.5, range 14–26). The mean Trails B score was 132 seconds (*SD* 59 seconds, range 39–300). At baseline, 79.4% ($n = 6124$) of the participants performed within the normal range (i.e., at or above 1 *SD* below the mean) on both the mMMSE and Trails B. Of the remaining participants, 12.4% ($n = 957$) were impaired on Trails B only, 5.0% ($n = 387$) on mMMSE only, and 3.2% ($n = 249$) were impaired on both the mMMSE and Trails B. These four cognitive groups were used in subsequent analyses.

Table 1 summarizes the baseline demographic and health-related variables for each of the four groups. There were significant group differences ($p < .05$) on all variables with the exception of the number of current smokers. Participants with impaired Trails B only and those with both tests impaired were older, had more medical comorbidities, and had higher depression scores. In contrast, participants with no impairment on either test were younger, better educated, and had the lowest proportion of medical comorbidities.

At the 6-year follow-up, 6313 women had available functional data. When comparing baseline characteristics of the follow-up sample ($n = 7717$) and those without follow-up ($n = 1404$), the follow-up sample was slightly younger (72.8 vs 75.6 years), had slightly higher education (12.8 vs 12.4 years), and had fewer medical comorbidities: history of myocardial infarction (5.8% vs 12.4%), stroke/TIA (2.2% vs 5.1%), hypertension (35.9% vs 44.4%), and diabetes (5.5% vs 10.6%) (all $p < .001$). Participants with follow-up data also reported lower proportions of baseline ADL difficulty (22.3%) when compared to participants without follow-up data (36.8%) ($p < .0001$). Similarly, the follow-up sample reported lower proportions of baseline IADL difficulty (32.2%) when compared to participants without follow-up data (47.9%) ($p < .0001$). The women in the follow-up sample also had significantly higher baseline mMMSE (24.9 vs 24.5, $p < .0001$) and Trails B scores (125.5 vs 163.6, $p < .0001$). Of the 99 participants who withdrew from the study, the majority were from the "Both Impaired" ($n = 62$) and "Trails B Only Impaired" ($n = 29$) groups.

Baseline Prevalent Functional Difficulty

At baseline, 1926 of all participants reported difficulty on one or more of the four ADL items. The relative rates of baseline ADL difficulty within each of the four cognitive groups were 22.4% (No Impairment), 28.2% (mMMSE Only Impaired), 36.3% (Trails B Only Impaired), and 38.6% (Both Impaired). Thus, women with impairment on Trails B only and on both tests reported the highest proportion of baseline ADL difficulty compared to women with no impairment or mMMSE only impairment.

In terms of baseline IADL difficulty, 2704 women reported difficulty on one or more of the four IADL items. Relative rates of IADL difficulty within each of the four groups were 32.4% (No Impairment), 33.1% (mMMSE Only Impaired), 48.5% (Trails B Only Impaired), and 50.6% (Both Impaired). When comparing the four groups, women with impairment on Trails B only and on both tests reported the highest proportion of IADL difficulty.

Incident Functional Difficulty at Follow-Up

At the 6-year follow-up, 1272 (20%) of the women reported incident difficulty on one or more of the four ADLs. Table 2 summarizes the likelihood of developing incident ADL or IADL difficulty (increase in 1 or more points on the 0–4 point scale) over 6 years. Compared to women with no impairment on either test, women with impairment on Trails B only and on both tests were approximately 2 times more likely to develop incident ADL difficulty (Trails B Only Impaired odds ratio [OR] = 1.87; 95% confidence interval [CI], 1.56–2.26 and Both Impaired OR = 2.09; 95% CI, 1.47–2.96). The unadjusted OR was significantly higher for participants with Trails B impairment only when compared with the OR for mMMSE impairment only ($p < .05$). When adjusting for age, education, medical comorbidities, GDS, and baseline ADL, the magnitude of the association diminished. After adjustment, the Trails B Only Impaired and Both Impaired groups were 1.3 times more likely to develop incident ADL impairment (Trails B Only Impaired adjusted OR = 1.34; 95% CI, 1.07–1.69 and Both Impaired adjusted OR = 1.27;95% CI, 0.84–1.93), although the both impaired group result did not reach statistical significance. Adjusting for age was a primary factor that weakened the OR values, particularly in the Both Impaired group. In contrast, the participants with mMMSE only impairment were not likely to develop incident ADL difficulty (adjusted OR = 1.06; 95% CI, 0.77–1.47).

In terms of IADLs, 1653 participants (26%) reported incident difficulty on one or more of the four IADL items after 6 years. The women with impairment on Trails B only or on both tests were between 1.5 and 1.9 times more likely to develop incident IADL difficulty (Trails B Only Impaired OR = 1.51; 95% CI, 1.26–1.80 and Both Impaired OR = 1.87; 95% CI, 1.33–2.61) (Table 2). In contrast, participants with mMMSE only impairment were not at an increased risk to develop incident IADL difficulty (OR = 1.13; 95% CI, 0.88–1.45). After adjusting for age, education, GDS, medical comorbidities, and baseline ADL, none of the groups were more likely to develop incident IADL impairment. However, the trend for participants in the Trails B Only Impaired group to have increased risk for IADL difficulty remained (OR = 1.11; 95% CI, 0.90–1.39) but did not reach statistical significance.

Worsening of Functional Difficulty at Follow-up

Table 3 summarizes the likelihood of developing a worsening of ADL difficulty level (0–12 point scale) for each group at the 6-year follow-up. Participants who had either impairment on Trails B only or on both tests were between 2.4 and 2.8 times more likely to develop a worsening of ADL difficulty (Trails B Only Impaired OR = 2.37; 95% CI, 1.94–2.89 and Both Impaired OR = 2.80; 95% CI, 1.95–4.03). The unadjusted OR for the Trails B Only Impaired group was significantly higher than the OR for the mMMSE Only Impaired group ($p < .05$). When adjusting for age, education, GDS, medical comorbidities, and baseline ADL difficulty level,

the magnitude of the association diminished, and the association remained significant for only Trails B impairment (adjusted OR = 1.48; 95% CI, 1.16–1.89). The trend for the Both Impaired group remained but did not reach statistical significance (adjusted OR = 1.31; 95% CI, 0.84–2.04). In contrast, participants with impaired mMMSE alone were not more likely to develop a worsening of ADL difficulty after 6 years (adjusted OR = 1.10; 95% CI, 0.77–1.58).

In terms of IADL difficulty level at follow-up, participants with impairment on Trails B only or on both tests were 1.8 and 2.4 times more likely to develop a worsening of IADL difficulty (Trails B Only Impaired OR = 1.80; 95% CI, 1.50–2.16 and Both Impaired OR = 2.44; 95% CI, 1.74–3.41) (Table 3). The unadjusted OR for the Trails B Only Impaired group was significantly greater than the OR for the mMMSE only impairment ($p < .05$). This association did not remain statistically significant after adjustment for age, education, GDS, medical comorbidities, and baseline IADL difficulty level. However, the trend remained for the Trails B Only Impaired (adjusted OR = 1.2; 95% CI, 0.98–1.54) and Both Impaired groups (adjusted OR = 1.22; 95% CI, 0.81–1.83).

Survival at Follow-Up

At the 6-year follow-up, 834 (10.8%) of the women were deceased. Compared to women with no impairment on either test, the women with Trails B only impaired or both tests impaired had between 2.4- and 2.8-fold increased risks of mortality after 6 years (Trails B Only Impaired hazard ratio [HR] = 2.42; 95% CI, 2.05–2.84 and Both Impaired HR = 2.81; 95% CI, 2.15–3.66) (Table 4). In contrast, the women with mMMSE only impairment did not have an increased risk for mortality. After adjusting for age, education, medical comorbidities, and GDS, this association remained statistically significant. Women with Trails B only impaired and both tests impaired had an approximately 1.5 times greater risk of mortality (Trails B Only Impaired HR= 1.48; 95% CI, 1.21–1.81 and Both Impaired HR= 1.39; 95% CI, 1.00–1.04) than did women with no impairment. Thus, women who scored lower on Trails B at baseline (with or without a low mMMSE score) were at increased risk for mortality after 6 years.

Discussion

In this large sample of community-dwelling older women, baseline scores on a brief measure of executive function (Trails B) and a combination of impairment on Trails B and a test of global cognitive function (mMMSE) were associated with ADL and IADL difficulty both cross-sectionally and longitudinally. The cross-sectional results suggest that individuals with poor executive function, either with or without impaired scores on the mMMSE, were more likely to have prevalent functional difficulty when compared to women with no cognitive impairment. This finding is supported by prior studies that also found a strong cross-sectional relationship between executive function and functional dependence (7,19,20,29).

In addition, the participants with Trails B impairment at baseline were more likely to develop incident as well as worsening of functional difficulty level, especially ADL difficulty, after 6 years, suggesting that a low score on an executive function test is also a risk for future functional decline. This association remained after adjusting for age, education, medical comorbidities, depression, and baseline functional difficulty level. This finding is important to demonstrate because other studies suggest that age, education, and medical comorbidities influence functional status (30,31). Finally, women with low scores on Trails B, either with or without mMMSE impairment, also had an increased risk of mortality after 6 years, suggesting that low scores on a brief test of executive function are associated with poor outcomes on multiple measures.

Our results also suggested that the participants with Trails B impairment were at greater risk for changes in ADL than IADL dependence. This is a curious observation because most studies

link executive dysfunction with IADL dependence. In our study, the ADLs included walking several blocks, dressing, getting in and out of bed, and bathing. Thus, the ADLs assessed in the current study may require a higher level of functioning than other ADLs assessed (such as toileting) and depend on executive function. A recent study suggests that dependence in bathing, which requires multiple steps, is associated with risk for nursing home placement in a community-dwelling sample (32) and, thereby, may require some higher cognitive functions. It is also important to keep in mind that few studies assess both ADLs and IADLs and executive function in the same study, and several combine ADL and IADL scores. In one study, Wang and colleagues (12) assessed both ADLs and IADLs but did not comment extensively about the differential effects. Most models of functional dependence [e.g., (33)] predict that IADLs are more strongly associated with tests of higher cognitive function than ADLs. Future studies should directly compare the impact of global cognition and domain-specific cognition on ADLs and IADLs independently.

Executive functioning is a cognitive skill that involves the planning, initiation, and execution of goal-directed behaviors, mental flexibility, and problem solving (34–36). Because the ability to perform ADL and IADLs, such as paying bills, dressing, preparing meals, and shopping, involves many of these skills, it is possible that even mild executive dysfunction could impact functional ability. Trails B, the measure of executive function in the current study, requires mental flexibility, set-shifting, and attention, which are needed for many ADLs, IADLs, and other daily functions (7,19). It is important to note that using Trails B alone without the Trails A condition, which controls for the motor component, is not an optimal measure of executive function; however, several studies, particularly older epidemiological studies, administer only Trails B [e.g., (37–39)]. Carlson and colleagues (20) found that Trails B, but not Trails A, accounted for a significant proportion of the variance in IADL performance in a sample of community-dwelling older adults. Future studies should use more comprehensive measures of executive function.

Measures of executive function may be a more sensitive marker than global measures of cognition of functional difficulty (7,40). In our study, Trails B was also a stronger predictor than the mMMSE of functional decline over time. This is not surprising because measures of global cognition test a wide range of skills in a superficial manner and do not adequately test executive function. It is also plausible that executive function is more sensitive than other cognitive domains. For example, Carlson and colleagues (20) found that a factor score derived from four tests of executive function was more strongly associated with IADLs than with learning and memory performance in community-dwelling women. Another study with 27 community-dwelling elders found that executive measures were better predictors of functional status than memory, language, visuospatial, or psychomotor function (19). Intact executive function, in particular, appears to be important for performing ADLs and IADLs. Our findings are also supported by a recent study (21) that found that a decline in executive function, as measured by the Executive Interview (EXIT25), over time was related to a decline in functional status over 3 years in nondemented elderly persons. This study also found that the MMSE was not associated with a change in IADLs over time.

The presence of executive dysfunction despite a normal score on the MMSE may represent a continuum of normal aging or possibly a preclinical stage of dementia. The prefrontal cortex is particularly vulnerable to the effects of aging. Older individuals perform worse than younger individuals on tests of executive function (41), and brain imaging studies document a preferential decrease in pre-frontal cortex volume with age (42,43). Dysexecutive-like behaviors, such as difficulty with planning, impulsivity, and lapses of attention, have been described in normal, older adult populations (44–46). However, some individuals may show preferential damage to the prefrontal cortex and develop executive dysfunction (47). Grigsby and colleagues (29) found that 9% of community-dwelling elders older than 60 years had

impairment on the Behavioral Dyscontrol Scale despite normal performance on the MMSE, which is similar to the proportion of individuals with an isolated impairment on the Trails B test in the current study. An isolated impairment in executive function has also been documented in vascular cognitive impairment (48) and in preclinical stages of frontotemporal dementia (49) and Parkinson's disease (50). Thus, differentiating between normal, age-related changes and declines that hallmark a pre-clinical disease stage is important.

Cognitive impairment in older adults is a well-known predictor of mortality in both demented and nondemented populations, even after controlling for demographic and baseline characteristics. Although it is well-documented that moderate to severe cognitive impairment is associated with mortality, fewer studies evaluate the effect of subtle cognitive impairment on mortality. Several studies document a relationship between the MMSE (or other tests of general cognition) and mortality in nondemented samples (51–53); however, other studies have not found this relationship (3). Although few studies evaluate cognitive tests from multiple cognitive domains, earlier studies found that low performance on verbal fluency and episodic memory tasks are significant predictors of mortality (54). Fried and colleagues (3) found that the Digit Symbol Substitution task (which requires visuomotor coordination), but not the MMSE, predicted mortality after 5 years. In our study, low scores on Trails B were also associated with an increased risk of mortality.

There are several limitations of this study. First, the use of self-report functional questionnaires, and not performance-based measures, may underestimate functional dependence in elderly individuals (6). In addition, tests from multiple cognitive domains were not available to compare the contribution to functional dependence. The use of Trails B (without using Trails A as a control) is also not ideal. Future studies should use more comprehensive measures of executive function. Although several studies suggest that executive function is a good predictor of functional decline, few studies compare multiple cognitive domains (19,20) or use a comprehensive selection of executive function tests. Another weakness of this study is the absence of a comprehensive dementia evaluation. It is possible that women with mild cognitive impairment or possibly mild dementia were included in the sample. Although we can infer that the community-dwelling individuals were not severely demented, a comprehensive dementia evaluation is the only way to confirm the absence of dementia. A dementia evaluation was not possible due to the large sample size. Another limitation was the fact that the follow-up sample was 18% smaller than the original sample. The participants who completed the 6-year follow-up visit reported significantly less baseline difficulty on both ADL and IADL scales, and the longitudinal results are likely an underestimate of functional decline. Finally, the study population was composed of only women who were primarily Caucasian, making it difficult to generalize to men or other ethnic groups.

Summary

Executive dysfunction is a predictor of functional difficulty in community-dwelling elderly women both cross-sectionally and longitudinally. The findings from this study add to other studies suggesting that executive function is more strongly associated with functional difficulty than measures of global cognition. This study is unique in that it provides strong support that executive function is a predictor of future functional difficulty and decline over time. This result emphasizes the importance of screening for executive impairment, in addition to measures of global cognition, in elderly individuals. Future studies should also better investigate the clinical outcome of individuals who have executive impairment and preserved global cognition.

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Table 1

Baseline Characteristics by Cognitive Impairment Group

Characteristics	No Impairment (*N* = 6124)	mMMSE Only Impaired (*N* = 387)	Trails B Only Impaired (*N* = 957)	Both Impaired (*N* = 249)	*p* Value*
Age, y	72.6 ± 4.5	73.7 ± 4.9	76.4 ± 5.8	77.9 ± 5.6	< .001
Education, y	13.0 ± 2.7	11.4 ± 2.9	11.8 ± 2.8	10.4 ± 3.0	< .001
% Current smoking	7.6	6.5	9.0	6.4	.30
% History of:					
Myocardial infarction	6.0	7.5	11.2	13.2	< .001
Stroke/TIA	2.1	2.3	6.4	5.2	< .001
Hypertension	35.7	39.0	46.9	42.6	< .001
Diabetes	5.7	6.2	10.3	8.9	< .001
Geriatric Depression Scale	1.5 ± 2.0	1.8 ± 2.2	2.4 ± 2.5	3.1 ± 3.1	< .001
mMMSE score (max. 26)	25.± 6 0.9	21.3 ± 1.1	24.7 ± 1.0	20.8 ± 1.4	< .001
Trails B, s	110 ± 31	131 ± 30	243 ± 41	258 ± 40	< .001
% of ADL impairment, ≥1 item	22.4	28.2	36.3	38.6	< .001
% of IADL impairment, ≥1 item	32.4	33.1	48.5	50.6	< .001

Notes: Values are presented as mean ± standard deviation %.

* *p* Values were from analysis of variance (ANOVA) for continuous variables and chi-square for dichotomous variables.

mMMSE =modified MMSE; TIA =transient ischemic attack; Trails B =Trail Making Test B; ADL =Activities of Daily Living; IADL =Instrumental Activities of Daily Living.

Table 2

Odds Ratio and 95% Confidence Interval of Incident Functional Difficulty (Increase in 1 or More Points on the 0–4 Scale) at 6-Year Follow-Up

Model	No Impairment	mMMSE Only Impaired	Trails B Only Impaired	Both Impaired
ADLs				
Unadjusted	1.0	1.22 (0.93, 1.61)	1.87 (1.56, 2.26)	2.09 (1.47, 2.96)
Age adjusted	1.0	1.14 (0.86, 1.50)	1.52 (1.25, 1.84)	1.50 (1.04, 2.15)
Adjusted for age, education, comorbidities, GDS, baseline ADL	1.0	1.06 (0.77, 1.47)	1.34 (1.07, 1.69)	1.27 (0.84, 1.93)
IADLs				
Unadjusted	1.0	1.13 (0.88, 1.45)	1.51 (1.26, 1.80)	1.87 (1.33, 2.61)
Age adjusted	1.0	1.05 (0.81, 1.35)	1.21 (1.00, 1.45)	1.32 (0.93, 1.86)
Adjusted for age, education, comorbidities, GDS, baseline ADL	1.0	1.02 (0.76, 1.37)	1.11 (0.90, 1.39)	0.95 (0.63, 1.42)

Note: mMMSE=modified Mini-Mental State Examination; Trails B =Trail Making Test B; ADLs =Activities of Daily Living; IADLs =Instrumental Activities of Daily Living; GDS = Geriatric Depression Scale.

Table 3

Odds Ratios and 95% Confidence Intervals of Developing a Worsening of Functional Difficulty (an Increase in 2 or More Points on the 0–12 Scale) at 6-Year Follow-Up

Model	No Impairment	mMMSE Only Impaired	Trails B Only Impaired	Both Impaired
ADL				
Unadjusted	1.0	1.25 (0.92, 1.71)	2.37 (1.94, 2.89)	2.80 (1.95, 4.03)
Age adjusted	1.0	1.14 (0.83, 1.56)	1.82 (1.48, 2.24)	1.84 (1.26, 2.69)
Adjusted for age, education, comorbidities, GDS, baseline ADL	1.0	1.10 (0.77, 1.58)	1.48 (1.16, 1.89)	1.31 (0.84, 2.04)
IADL				
Unadjusted	1.0	1.22 (0.93, 1.58)	1.80 (1.50, 2.16)	2.44 (1.74, 3.41)
Age adjusted	1.0	1.11 (0.85, 1.46)	1.39 (1.15, 1.68)	1.63 (1.15, 2.31)
Adjusted for age, education, comorbidities, GDS, baseline ADL	1.0	1.09 (0.80, 1.49)	1.23 (0.98, 1.54)	1.22 (0.81, 1.83)

Note: mMMSE = modified Mini-Mental State Examination; Trails B = Trail Making Test B; ADL = Activities of Daily Living; GDS = Geriatric Depression Scale; IADL = Instrumental Activities of Daily Living.

Table 4

Hazard Ratios and 95% Confidence Intervals of Mortality at 6-Year Follow-Up

Model	No Impairment	mMMSE Only Impaired	Trails B Only Impaired	Both Impaired
Unadjusted	1.0	0.95 (0.67, 1.34)	2.42 (2.05, 2.84)	2.81 (2.15, 3.66)
Age adjusted	1.0	0.85 (0.60, 1.21)	1.75 (1.47, 2.08)	1.81 (1.37, 2.38)
Adjusted for age, education, comorbidities, GDS	1.0	0.80 (0.54, 1.19)	1.48 (1.21, 1.81)	1.39 (1.00, 1.94)

Note: mMMSE = modified Mini-Mental State Examination; Trails B = Trail Making Test B; GDS = Geriatric Depression Scale.