OXFORD
UNIVERSITY PRESS

Archives of Clinical Neuropsychology 34 (2019) 814–824

Archives of CLINICAL NEUROPSYCHOLOGY

The Association between the Montreal Cognitive Assessment and Functional Activity Questionnaire in the Systolic Blood Pressure Intervention Trial (SPRINT)

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Editorial Decision 7 November 2018; Accepted 16 November 2018

Abstract

Objective: To examine the association of global cognitive function assessed via the Montreal Cognitive Assessment (MoCA) and deficiencies in instrumental activities of daily living (IADL) on the Functional Activity Questionnaire (FAQ) in hypertensive older adults in the Systolic Blood Pressure Intervention Trial (SPRINT).
Methods: In cross-sectional analysis, 9,296 SPRINT participants completed the MoCA at baseline. The FAQ was obtained from 2,705 informants for SPRINT participants scoring <21 or <22 on the MoCA, depending on education. FAQ severity ranged from no dysfunction (Score = 0) to moderate/severe dysfunction (Score = 5+).
Results: Participants who triggered FAQ administration were older, less educated, and more likely to be Black or Hispanic ($p < 0.001$). Sixty-one percent (n = 1,661) of participants' informants reported no functional difficulties in IADLs. An informant report, however, of any difficulty on the FAQ was associated with lower MoCA scores after controlling for age, sex, race/ethnicity, and education ($p < 0.05$). Partial proportional odds regression indicates that participants scoring lower on the MoCA (in the 10th to <25th, fifth to <10th, and <fifth percentiles) had higher adjusted odds of their informant indicating dysfunction on the FAQ, relative to participants scoring at or above the 25th percentile on the MoCA ($p < 0.001$).
Conclusions: While lower global cognitive function was strongly associated with IADL deficits on FAQ, informants indicated no functional difficulties for the majority of SPRINT participants, despite low MoCA scores. These findings can help with designing future studies which aim to detect mild cognitive impairment and/or dementia in large, community-dwelling populations.

Keywords: Mild cognitive impairment; Dementia; Cardiovascular disease, Assessment, Clinical trials

Introduction

Dementia is a leading cause of loss of autonomy, loss of independence in performing instrumental activities of daily living (IADL), and placement into nursing homes and assisted living facilities in aging populations (Alzheimer's Association, 2017;

doi:10.1093/arclin/acy094 Advance Access publication on 5 December 2018

Centers for Disease Control and Prevention [CDC], 2013; National Institute on Aging, 2013). Dementia affects approximately 5.5 million persons in the United States, a number expected to double by 2040, with an estimated cost of $259 billion (Alzheimer's Association). Both dementia and its prodrome, mild cognitive impairment (MCI), are highly prevalent among older adults. For example, in adults over the age of 80, the prevalence of MCI approaches 40–50%, with the prevalence of dementia being approximately 15–20% (Petersen, 2000). MCI represents a transitional state between normal cognition and the disabling effects of dementia, most commonly Alzheimer's Disease (Petersen, 2000). Moreover, there is increasing evidence that both subtle functional impairments (e.g., deficits with IADL), and gait dysfunction are associated with MCI; additionally, they have been shown to increase rates of progression from MCI to dementia, and may precede a dementia diagnosis by 10 to 12 years (Farias et al., 2006; Fauth et al., 2013; Peres et al., 2008). Current evidence suggest that slower gait and gait instability are linked to impaired cognitive ability (Montero-Odasso, Verghese, Beauchet, & Hausdorff, 2012; Nasreddine et al., 2005). Given that executive function and working memory are components required for walking, gait abnormalities in the presence of impaired cognition can increase the risk for falls, disability, and mortality, and they may contribute to disabling forms of dementia (Montero-Odasso et al., 2012). This study examines patterns of functional impairment and its relationship with Neuropsychological test in the Systolic Blood Pressure Intervention Trial (SPRINT) (Ambrosius et al., 2014).

A growing body of literature indicates that functional impairment is an essential criterion for the diagnosis of MCI (Albert et al., 1999; Di Carlo et al., 2000; Farias et al., 2006; Tabert et al., 2002; Teng, Becker, Woo, Cummings, & Lu, 2010; Wadley et al., 2007), despite general guidelines suggesting that activities of daily living should be intact (Petersen, 2004). For example, several studies have found that adults with cognitive impairment report more difficulty with IADLs, including greater difficulty with managing finances, performing household tasks, and performing health-related self-care (e.g., medication administration), with these deficits being strong predictors of incident dementia (Burton, Strauss, Bunce, Hunter, & Hultsch, 2009; Czaja et al., 2017; Defranceso et al., 2010; Farias et al., 2017). However, distinguishing MCI and its subtypes (e.g., amnestic or non-amnestic) based on decrements to function is a challenge due to the variety of IADL performance assessment tools (Albert et al., 2011; Kaur, Belchior, Gelinas, & Bier, 2016). There are both objective and subjective tools, and responses can be obtained either from an informant or via self-report. Consequently, these tools have yielded conflicting results when validated in populations with MCI (Albert et al., 2011; Kaur et al., 2016). Additionally, most of the studies utilizing the FAQ have been conducted in heavily selected, but extremely well-characterized cohorts with varying compositions of normal MCI and AD cases (Burton et al., 2009; Farias et al., 2017; Kaur et al., 2016). There have been fewer large-scale studies of community-dwelling, ambulatory older adults using general cognitive screening instruments.

Early detection of functional difficulties in individuals with possible MCI is increasingly important. Several studies have examined agreement between patient and informant reports of functional and cognitive status (Brown, Devanand, Liu, & Caccappolo, 2011; Farias et al., 2006; Peres et al., 2008). Informant ratings generally reveal greater loss of everyday functional abilities and cognitive impairment than self-ratings of everyday functional abilities and cognitive impairment (Brown et al., 2011; Farias et al., 2006, 2017; Kaur et al., 2016; Teng et al., 2010). Among numerous questionnaire-based measures of functional limitation, the FAQ is a widely used, validated measure of IADL that is sensitive to early cognitive impairment in amnestic MCI (Brown et al., 2011; Kaur et al., 2016). In addition, FAQ scores have been shown to correlate with performance on many commonly used neuropsychological tests (Albert et al., 2011; Perneczky et al., 2006; Teng et al., 2010). Previous studies have examined patterns of impairments based on the FAQ in MCI, but they have tended to be based on the Mini-Mental State Examination (MMSE) rather than the MoCA (Teng et al., 2010), which was designed to be more sensitive to MCI and is being increasingly used in research and clinical practice (Farias et al., 2017; Nasreddine et al., 2005; Teng et al., 2010). However, because it is a newer instrument, there are relatively little current data on its relationships to other assessment scales used in cognitive and behavioral studies (Burton et al., 2009; Nasreddine et al., 2005).

SPRINT was designed to determine whether treating to a lower systolic blood pressure (SBP) target of <120 mm Hg compared to <140 mm Hg (using BP goal set forth by 2014 U.S. Hypertension Guideline, [James et al., 2014]) would reduce the incidence of cardiovascular morbidity and mortality (Ambrosius et al., 2014; SPRINT Research Group, 2012). Moreover, a secondary outcome for SPRINT was whether intensive blood pressure control would produce a slower rate of cognitive decline, and thus reducing the incidence of all-cause dementia. Here, we use baseline (cross-sectional) data from SPRINT to describe the pattern of informant-reported impairment on the FAQ for participants in SPRINT and exploring how performance on the MoCA correlates with functional impairment as indicated by the FAQ. Furthermore, we examine how functional impairment correlates with an objective measure of physical function (gait speed) in a subgroup of participants 75 years and older at the time of randomization

Methods

Study Overview and Participants

SPRINT was a multisite, randomized controlled trial that examined whether an intensive treatment strategy to reduce SBP to a lower target of <120 mmHg than recommended by the 2014 Hypertension Guideline (SBP of <140 mmHg) reduced the incidence of cardiovascular disease (CVD) (Ambrosius et al., 2014; SPRINT Research Group, 2012). The design and primary cardiovascular results have been previously described (Ambrosius, et al., 2014; SPRINT Research Group, 2012). Briefly, SPRINT enrolled 9,361 participants without a history of diabetes, stroke, or dementia from across the US and Puerto Rico from November 10 2010 to March 13 2013 (SPRINT Research Group, 2012). At the time of randomization, all participants received a brief cognitive screening battery including the MoCA, the Logical memory subtest of the Wechsler Memory Scale-IV, and the Digit Symbol Coding test.

At baseline, the FAQ was administered conditionally, dependent on the participants' MoCA score. For participants with <12 years of education, the threshold for administering the FAQ was <21, and it was <22 for participants with ≥12 years of education. The FAQ was administered to an identified contact or proxy of the participant, either locally at the SPRINT clinical site or centrally via telephone by the coordinating center at Wake Forest School of Medicine (Winston-Salem, NC). Central administration of FAQs was utilized in 65% (67 of 102) of SPRINT clinics. Clinics were instructed to administer the FAQ within 30 days of the screening battery assessment; however, data was accepted up to six months following the baseline screening battery assessment.

Prior to administering any neuropsychological tests, all research staff were trained centrally by the SPRINT Coordinating Center using a standardized protocol and were required to complete a certification process to become a cognitive examiner in SPRINT (SPRINT Research Group, 2012). In addition, periodic quality assurance was performed on cognitive examiners to ensure the examiner demonstrated competency and continual standardized administration. Institutional Review Board approval was obtained from all clinical sites and all participants provided informed consent, including consent to audio recording of cognitive testing.

Study Measures

Cognitive screening battery. The SPRINT cognitive screening battery included three instruments, the MoCA, Logical Memory, and Digit Symbol Coding Test (Nasreddine et al. 2005; Wechsler, 2008). The MoCA was selected because of its sensitivity (>85%) to detect cognitive impairment and dementia and for its brevity as a rapid screening instrument of global cognitive function (completion time of approximately 10 minutes) (Farias et al., 2017; Teng et al., 2010). The MoCA has items assessing attention and concentration, executive function, naming, memory, language, visuoconstructional skills, conceptual thinking, calculations, and orientation. Scores on the MoCA range from 0 to 30, with lower scores indicating worse global cognitive functioning. The MoCA was administered, depending on a subject's language of choice, in English or Spanish. Certification of all cognitive examiners (English or Spanish) was required prior to administering the MoCA.

The Logical memory, a subtest of the Wechsler Memory Scale-IV (WAIS-IV) (Pearson, 2008) measures episodic verbal memory and is a sensitive predictor of amnestic MCI and Alzheimer's disease. For Logical Memory I, participants are read a short story aloud that consists of 14 bits of information and immediately asked to verbally recall as many details as possible about the story. The same story is repeated aloud and a second oral recall is tested. In Logical Memory II, after a delay of approximately 15 minutes, participants are asked to orally recall as much information from the story as possible, without the story being reread aloud. Both the Logical Memory I and II total score is a composite of bits of information recalled. Raw scores for Logical Memory I and II ranged from 0 to 28 and 0 to 14, respectively (Pearson, 2008).

The Digit Symbol Coding test, a sub-test of the WAIS-IV (Pearson, 2008), measures psychomotor speed and working memory. The test consists of eight rows containing a total of 144 small blank squares, each of which is paired with a randomly assigned number from 1 to 9. Above these rows is a printed key that pairs each number with a different symbol. The participant is asked to fill in the blank spaces with the symbol that is paired to the number as quickly as possible for 2 minutes.

Functional Activity Questionnaire (FAQ)

The Functional Activity Questionnaire (FAQ) is comprised of 10 questions inquiring about the difficulty observed (0 = normal, 1 = has difficulty but does by self, 2 = requires assistance, 3 = dependent) with various IADLs (e.g., writing checks,

paying bills, shopping, driving) within the past four weeks (Pfeffer, Kurosaki, Harrah, Chance & Filos, 1982). Scores can range from 0 to 30. Functional impairment was further summarized by total number of deficits (sum of items with score>0, ranging from 0 to 10) and average severity per deficit (total severity divided by total number of deficits).

Other Measures

At the baseline visit, participants completed questionnaires ascertaining health behaviors. We categorized smoking status as current, former, or never smokers and alcohol consumption (typical drinks/per week) as non-drinker, light drinker, moderate drinker, or heavy drinker. In participants 75 years or older at baseline, gait speed was measured by a timed 4-meter walk test performed twice at the participant's usual pace from a standing start. The use of an assistive device was permitted to walk short distances, if typically used by the participant. Gait speed was classified as 0.8 m/s or greater (normal walker), less than 0.8 m/s (slow walker) and the faster of the two gait speeds (measured in meters/second [m/s]) was used in the analysis.

Statistical Analysis

For our primary analyzes, we analyzed FAQ severity as an ordinal outcome using partial proportional odds (PO) models. FAQ severity was categorized as no dysfunction (Score = 0), mild dysfunction (Score = 1 to 4), or moderate to severe dysfunction (Score = 5+). Our primary predictor of interest was MoCA score, which we categorized into percentile groups (<fifth percentile, fifth to $<10^{th}$ percentile, 10^{th} to $<25^{th}$ percentile, and 25^{th} percentile or greater) based on normative data for the MoCA from the Irish Longitudinal Study of Ageing (TILDA) (Kenny et al., 2013). Because SPRINT represents a more ethnically diverse population than TILDA, we subtracted two points from the normative percentiles when applying them to Black and Hispanic participants in SPRINT. In the PO models, we included adjustments for the following covariates: age, gender, race/ethnicity (White, Black, Hispanic, Other), education (<12 years, 12 years, or >12 years of education), Body Mass Index, smoking status, alcohol consumption, participation in vigorous physical activity, chronic kidney disease (eGFR < 60 ml/min/1.73 m^2 based on the CKD-EPI equation), history of cardiovascular disease, and history of stroke (self-reported). We estimated the partial PO models using the *VGAM* package for R Statistical Computing Environment (Yee, 2010) with age modeled using linear tail-restricted cubic splines with five knots. For each covariate, we investigated the PO assumption using graphical techniques based on score residuals and partial residuals (Harrell et al., 1998). Based on this evaluation, we assumed non-proportional odds for age, sex, alcohol consumption, chronic kidney disease, having more than 12 years of education, and being in the other race/ethnicity category. We also considered additional models for FAQ severity, including gait speed as a predictor, which was only measured in participants 75 years and older in SPRINT. For these analyzes, we categorized gait speed as <0.8 m/s (slow walkers), >0.8 to <1.0 m/s (normal walkers), and ≥1.0 m/s (fast walkers).

We also examined the association between functional impairment on individual FAQ items (normal versus any difficulty) and test scores on the MoCA, Logical Memory, and Digit Symbol Coding. Because neuropsychological test scores tend to exhibit skewed distributions with floor and/or ceiling effects, we used quantile (median) regression, estimated using the *quantreg* package for the R Statistical Computing Environment. For these models, we included age, sex, race/ethnicity, and education as covariates.

Results

Study Participants

Table 1 summarizes the baseline characteristics of SPRINT participants who did and did not prompt FAQ administration based on their MoCA score. At baseline, 2,971 participants (mean age 69.9) triggered FAQ administration, and informants completed the FAQ for 2,705 (91.0%) participants. For the majority of participants, the FAQ was completed by a first degree relative (N = 1,110, 41.0%) or spouse/significant other (N = 1,066, 39.4%), followed by friend/acquaintance (N = 282, 10.4%), second or third degree relative (N = 134, 5.0%), family-in-law (N = 71, 2.6%), or other/unknown (N = 42, 1.6%). On average, participants that scored low enough on the MoCA to trigger FAQ administration were older (mean ± SD; 69.9 ± 9.9 years), more likely to be female, Black or Hispanic, and were less educated ($p < 0.001$). Participants whose FAQ was not obtained from an informant were more likely to be male and Black ($p < 0.01$; See Supplemental Table 1). In addition, Gait speed was collected from 974 adults ≥75 years.

Table 2 examines the univariate relationship between categories of FAQ severity and various subgroups. Overall, 61.4% (n = 1,661) of SPRINT participants who scored low enough on the MoCA to prompt FAQ administration had no functional

Table 1. Characteristics of SPRINT participants that did and did not prompt Functional Activities Questionnaire (FAQ) administration based on their Montreal Cognitive Assessment (MoCA) Score

	Triggered FAQ Administration N = 2,971	Did Not Trigger FAQ Administration N = 6,325	p-value
Age (years), mean (SD)	69.90 (9.94)	66.97 (9.03)	<0.001
Age < 75 years, No. (%)	1,108 (37.3)	1,504 (23.8)	<0.001
Female sex, No. (%)	1,120 (37.7)	2,181 (34.5)	0.003
Race/Ethnicity, No. (%)			<0.001
White	1,189 (40.0)	4,185 (66.2)	
Black	1,254 (42.2)	1,532 (24.2)	
Hispanic	459 (15.4)	505 (8.0)	
Other	69 (2.3)	103 (1.6)	
Education, No. (%)			<0.001
<12 years	599 (20.2)	267 (4.2)	
12 years	733 (24.7)	779 (12.3)	
>12 years	1,639 (55.2)	5,279 (83.5)	
Smoking status, No. (%)			<0.001
Never smoker	1,393 (46.9)	2,706 (42.8)	
Former smoker	1,163 (39.2)	2,791 (44.2)	
Current smoker	412 (13.9)	822 (13.0)	
Participation in vigorous activities, No. (%)			<0.001
Rarely or never	951 (32.1)	1,549 (24.6)	
1 to 3 times per month	460 (15.5)	1,047 (16.6)	
1 time per week	297 (10.0)	698 (11.1)	
2 to 4 times per week	844 (28.5)	2,172 (34.4)	
5 or more times per week	408 (13.8)	839 (13.3)	
Alcohol consumption, No. (%)			<0.001
Non-drinker	1,624 (54.7)	2,490 (39.4)	
Light Drinker	510 (17.2)	1,400 (22.1)	
Moderate Drinker	405 (13.6)	1,337 (21.1)	
Heavy Drinker	261 (8.8)	830 (13.1)	
Unknown	171 (5.8)	268 (4.2)	
Body Mass Index, No. (%)			0.007
Underweight (<18.5 kg/m^2)	14 (0.5)	33 (0.5)	
Normal weight (18.5 to <25 kg/m^2)	593 (20.0)	1,079 (17.2)	
Overweight (25 to <30 kg/m^2)	1,155 (39.0)	2,422 (38.6)	
Class I Obese (30 to <35 kg/m^2)	732 (24.7)	1,667 (26.6)	
Class II or III Obese (≥35 kg/m^2)	466 (15.7)	1,075 (17.1)	
History of CVD, No. (%)	691 (23.3)	1,169 (18.5)	<0.001
Gait Speed (m/s), mean (SD)[a]	0.85 (0.24)	0.95 (0.22)	<0.001
eGFR (ml/min/1.73 m^2), mean (SD)	70.63 (21.32)	73.23 (19.41)	<0.001
eGFR<60 ml/min/1.73 m^2, No. (%)	951 (32.2)	1,575 (25.0)	<0.001
Logical Memory (0–14), median [IQR]	6 [4, 8]	9 [7, 11]	<0.001
Digit Symbol (0–135), median [IQR]	42 [32, 51]	55 [46, 63]	<0.001

CVD denotes Cardiovascular Disease and eGFR estimated Glomerular Filtration Rate based on the CKD-EPI Study equation.
Values represent n (%)
[a]Only measured in participants 75 years or older.

difficulties in IADLs, 27.3% (n = 737) had mild functional difficulties, while 11.3% (n = 307) participants had moderate to severe functional difficulties. The prevalence of moderate to severe dysfunction was substantially higher for Hispanics compared to White participants (21.8% versus 8.4%), in participants with lower education (23.4% versus 7.2% in participants with <12 years and >12 years of education, respectively), and in participants with a slow walking speed (13.5% versus 6.2% in participants 75 years or older with a gait speed < 0.8 m/s versus a gait speed ≥ 0.8 m/s). When stratified by education and MoCA percentile groups (Table 2), poorer scores on the MoCA (relative to normative data) were generally associated with a higher prevalence of functional difficulties. For example, in participants with <12 years of education, 38.1% of participants scoring less than the normative fifth percentile were reported to have moderate to severe functional difficulties, compared to 14.7% in participants scoring at or above the 25th percentile.

Table 3 reports the adjusted association between MoCA score and FAQ Severity based on a multivariable partial proportional odds model. Compared with participants scoring at or above the 25th percentile on the MoCA, participants scoring

Table 2. Distribution of Functional Activities Questionnaire (FAQ) Severity categories in SPRINT participants by subgroups

	FAQ Severity			
	Moderate To Severe Dysfunction N = 307	Mild Dysfunction N = 737	No Dysfunction N = 1,661	p-value
Age				0.022
<75 years	188 (11.1)	435 (25.6)	1076 (63.3)	
75 years or older	119 (11.8)	302 (30)	585 (58.2)	
Sex				0.003
Male	162 (9.8)	449 (27.1)	1048 (63.2)	
Female	145 (13.9)	288 (27.5)	613 (58.6)	
Race/Ethnicity				<0.001
White	92 (8.4)	291 (26.7)	707 (64.9)	
Black	116 (10.3)	299 (26.6)	708 (63.0)	
Hispanic	94 (21.8)	129 (29.9)	209 (48.4)	
Other	5 (8.3)	18 (30)	37 (61.7)	
Education				<0.001
<12 years	129 (23.4)	158 (28.6)	265 (48)	
12 years	71 (10.6)	179 (26.7)	421 (62.7)	
>12 years	107 (7.2)	400 (27.0)	975 (65.8)	
Smoking status				0.003
Current smoker	50 (13.6)	91 (24.7)	227 (61.7)	
Former smoker	88 (8.4)	293 (27.8)	672 (63.8)	
Never smoker	169 (13.2)	353 (27.5)	760 (59.3)	
Missing	0 (0)	0 (0)	2 (100)	
Participation in vigorous activities				0.002
Rarely or never	124 (14.5)	237 (27.7)	496 (57.9)	
1 to 3 times per month	55 (13.2)	112 (26.9)	250 (60.0)	
1 time per week	24 (8.8)	81 (29.6)	169 (61.7)	
2 to 4 times per week	68 (8.7)	222 (28.5)	489 (62.8)	
5 or more times per week	34 (9.2)	83 (22.4)	253 (68.4)	
Missing	2 (25.0)	2 (25.0)	4 (50.0)	
Alcohol consumption				0.176
Non-drinker	188 (12.7)	402 (27.2)	886 (60)	
Light Drinker	37 (7.9)	131 (27.9)	301 (64.2)	
Moderate Drinker	38 (10.3)	106 (28.7)	225 (61)	
Heavy Drinker	25 (10.3)	64 (26.3)	154 (63.4)	
Unknown	19 (12.8)	34 (23)	95 (64.2)	
Body Mass Index				0.836
Underweight (<18.5 kg/m^2)	1 (7.7)	4 (30.8)	8 (61.5)	
Normal weight (18.5 to <25 kg/m^2)	59 (11.0)	147 (27.4)	330 (61.6)	
Overweight (25 to <30 kg/m^2)	115 (10.8)	281 (26.4)	670 (62.9)	
Class I Obese (30 to <35 kg/m^2)	75 (11.3)	183 (27.7)	403 (61.0)	
Class II or III Obese (≥35 kg/m^2)	55 (13.1)	118 (28.2)	246 (58.7)	
Missing	2 (20.0)	4 (40.0)	4 (40.0)	
History of CVD				0.058
No	222 (10.7)	559 (26.9)	1299 (62.5)	
Yes	85 (13.6)	178 (28.5)	362 (57.9)	
Gait Speed[a]				<0.001
≥0.8 m/s	16 (6.2)	58 (22.5)	184 (71.3)	
<0.8 m/s	97 (13.5)	238 (33.2)	381 (53.2)	
Missing	6 (18.8)	6 (18.8)	20 (62.5)	
eGFR				0.135
≥60 ml/min/1.73 m^2	205 (11.2)	476 (26)	1148 (62.8)	
<60 ml/min/1.73 m^2	101 (11.8)	258 (30)	500 (58.2)	
Missing	1 (5.9)	3 (17.6)	13 (76.5)	
MoCA Percentile Group[b]				
<12 years of education				<0.001
≥25th percentile	25 (14.7)	57 (33.5)	88 (51.8)	
10th to <25th percentile	40 (20.5)	50 (25.6)	105 (53.8)	
fifth to <10th percentile	27 (30.0)	24 (26.7)	39 (43.3)	
<fifth percentile	37 (38.1)	27 (27.8)	33 (34.0)	

(*continued on next page*)

Table 2. (*continued*)

	FAQ Severity			
	Moderate To Severe Dysfunction N = 307	Mild Dysfunction N = 737	No Dysfunction N = 1,661	p-value
12 years of education				0.014
≥25th percentile	10 (8.8)	25 (22.1)	78 (69.0)	
10th to <25th percentile	19 (7.3)	63 (24.0)	180 (68.7)	
fifth to <10th percentile	18 (12.5)	44 (30.6)	82 (56.9)	
<fifth percentile	24 (15.8)	47 (30.9)	81 (53.3)	
>12 years of education				0.980
≥25th percentile	1 (4.5)	5 (22.7)	16 (72.7)	
10th to <25th percentile	27 (6.5)	117 (28.1)	273 (65.5)	
fifth to <10th percentile	21 (7.0)	81 (27.2)	196 (65.8)	
<fifth percentile	58 (7.8)	197 (26.4)	490 (65.8)	

CVD denotes Cardiovascular Disease and eGFR estimated Glomerular Filtration Rate based on the CKD-EPI Study equation.
Values represent mean ± standard deviation
[a]Only measured in participants 75 years or older.
[b]Percentile ranks relative to normative data from the Irish Longitudinal Study of Ageing, see methods.

Table 3. Association of performance on the Montreal Cognitive Assessment (MoCA) and Gait Speed (participants 75 years or older) with the Functional Activities Questionnaire (FAQ) Severity Score based on multivariable partial proportional odds model

	Adjusted Odds Ratio (95% CI)	p-value
All participants		
MoCA Percentile Group		
≥25th percentile	Referent	-
10th but <25th percentile	1.71 (1.26, 2.31)	<0.001
fifth to <10th percentile	2.38 (1.70, 3.33)	<0.001
<fifth percentile	3.21 (2.29, 4.49)	<0.001
Participants 75 years or older		
MoCA Percentile Group		
≥25th percentile	Referant	
10th but <25th percentile	1.68 (1.10, 2.58)	0.016
fifth to <10th percentile	1.88 (1.14, 3.09)	0.013
<fifth percentile	2.78 (1.67, 4.63)	<0.001
Gait Speed		
≥1.0 m/s	Referant	-
<1.0 m/s but ≥0.8 m/s	1.36 (0.93, 1.98)	0.109
<0.8 m/s	2.54 (1.74, 3.69)	<0.001

Odds ratios represent odds of reporting higher FAQ severity, i.e. more dysfunction. Odds ratios are adjusted for age, sex, race/ethnicity, education, body mass index, smoking status, alcohol consumption, participation in vigorous physical activity, eGFR<60 ml/min/1.73 m^2, history of cardiovascular disease, and self-reported history of stroke. MoCA percentile ranks relative to normative data from The Irish Longitudinal Study of Ageing, see methods.

lower on the MoCA had higher adjusted odds of their informant indicating dysfunction on the FAQ, with odds ratios of 1.71 (95% confidence interval [CI], 1.26 to 2.31) in the 10th to <25th, 2.38 (95% CI, 1.70 to 3.33) in the fifth to <10th, and 3.21 (95% CI, 2.29 to 4.49) for participants scoring <fifth percentiles, respectively. A similar pattern of results was observed in the subgroup of participants 75 years or older (mean age 79.9) at baseline. In addition, within that subgroup of participants, slower gait speed was also associated with more functional difficulties on the FAQ. Specifically, participants with a gait speed <0.8 m/s (slow walkers) had adjusted odds of 2.54 (95% CI, 1.74 to 3.69) of their informant reporting more dysfunction compared to participants with a gait speed ≥1.0 m/s.

Supplementary Table 2 displays the association between the individual items on the FAQ (normal versus any difficulty) and scores on neuropsychological tests (MoCA, Logical Memory I, and Digit Symbol Coding test) modeled using quantile regression, adjusting for age, sex, race/ethnicity, and education. In general, the effects of functional limitations (all FAQ items) changed across the distribution of neuropsychological tests, meaning for every unit of change on FAQ corresponded with lower cognitive performance. For example, the FAQ item difficulty writing checks, paying bills, or balancing their checkbook was associated with a decrease of 1.29 points on the median MoCA score (95% CI, -1.91 to -0.68; $p < 0.001$). Similarly, difficulty with individual FAQ items was associated with lower scores on the Logical Memory I test, with the

strongest associations being a median decrease of 1.17 points (95% CI, -1.63 to -0.72; $p < 0.001$) for writing checks, paying bills, or balancing checkbook and a 1.0 median decrease (95% CI, -1.55 to -0.45; $p = <0.001$) for "difficulty paying attention to and understanding a TV program, book, or magazine". Furthermore, results for all informant reported FAQ items, was significantly associated with lower scores on the MoCA, Logical Memory, and Digit Symbol ($p < 0.05$) indicating those with lower cognitive performance have reduced functional abilities proportionate to their cognitive performance.

DISCUSSION

Our results show that global cognitive function was associated with functional impairment in a graded manner in a large, diverse sample of hypertensive, older adults. More than one-third of SPRINT participants (37%) who had FAQs obtained exhibited very low MoCA scores (<fifth percentile compared to normative data from TILDA) (Borland et al., 2017; Czaja et al., 2017; Kenny et al., 2013). However, 61.4% of the informants did not report functional deficits; this is inconsistent with previous work (Brown et al., 2011; Teng et al., 2010). MoCA scores were significantly associated with all FAQ items, as expected, supporting previous empirical data of the relationship between cognitive and functional status (Blazer, Yaffe, Liverman, 2015; CDC, 2013; Farias et al., 2017; Giovannetti et al., 2007). We also found that FAQ deficits were more likely in individuals with lower MoCA scores in terms of selected cognitive domains on the MOCA for IADLs such as keeping track of current events and writing checks.

The relative contribution of physical and cognitive problems to functional limitations in hypertensive older adults is currently poorly understood, partly due to heterogeneous assessment strategies. A few studies have focused on the functional impact of cognitive impairment (Rozzini et al., 2007; Teng et al., 2010). In SPRINT participants 75 years or older, there was an association between gait speed and greater functional difficulties based on the FAQ. Such findings are not unexpected (Farias et al., 2017). Our results suggest that there is an elastic relationship between cognitive performance and FAQ rated functional limitations; those with lower cognitive performance have reduced functional abilities that commensurate to their cognitive performance, as observed in previous research (Teng et al., 2010). Assessing the contribution of concomitant physical limitations to overall FAQ score is complex especially as physical abilities such as gait speed scale with cognitive performance as well as age and physical limitations such as advanced osteoarthritis. Overall, this study of a large cohort provides support to a limited body of literature that subtle cognitive impairments affect functional capacity in non-diabetic hypertensive patients.

A strength of our study is that it is the first to examine the relationship between scores on the MoCA and functional deficits drawn from a large population of non-demented, hypertensive older adults. It is also important to point out that SPRINT participants were not adjudicated for cognitive impairment at baseline, and we inferred suspected cognitive impairment using age and education specific normative data, unlike previous work (Smith et al., 2017); thus, these analyzes should be interpreted cautiously. Our study was not focused primarily on cognitive performance and classification, but the results suggest that it is not uncommon in a diverse population of older hypertensive adults. A limitation of the FAQ is that it is based on informant report. Informants may not be able to provide responses on certain items, either because the subject never performed the task regardless of their cognitive status or because the informant had insufficient information and/or speculated on subject's potential to rate an individual's current performance. Therefore, relying on collateral sources of information may underestimate an individual's functional ability.

Conclusion

The MoCA was developed initially to provide a quick, easily administered omnibus cognitive test to distinguish MCI and Alzheimer's Disease (AD) from normal individuals (Nasreddine et al., 2005). SPRINT provided assessment of cognitive function via the MoCA in a racially and ethnically diverse population, coupled with other tests assessing domains not covered in MoCA, such as functional ability. Previous studies of the FAQ have looked at its performance with cognitive exams such as the MMSE or the Alzheimer's Disease Neuroimaging Initiative (ADNI) battery (Liu-Seifert et al., 2015; Tekin, Fairbanks, O'Connor, Rosenberg & Cummings, 2001); but our study is the first to report this relationship of the FAQ and MoCA in a large cohort. Trzepacz et al. (2015) also found that large variability and overlap between normal, MCI, and AD subjects in FAQ scores though they did not report on the proportions of subjects scoring completely normally on the FAQ. Our major finding was that the MoCA global cognitive function was strongly associated with IADL deficits assessed via the FAQ. A substantial proportion of informants indicated no functional difficulties in SPRINT participants despite relatively low MoCA scores. Understanding the causes of this apparent variability is important as it may stem from 1) variability in test administration methods, 2) variability in the relationship between subject and informant, such as amount of daily contact, and 3) overall

perception of the subject by the informant. In a diverse cohort such as SPRINT, living circumstances (rural versus urban), demographics (married versus living alone), and medical factors such as depression, or medical conditions including cardiovascular disease may also alter a subject's functional abilities. The contribution of ethnic and racial differences to expectations and perceptions of "normal" function is important but beyond the scope of this current study. Overall, our findings and limitations can help with designing future studies that aim to detect mild cognitive impairment and/or dementia in large, community-dwelling populations.

Supplementary Material

Supplementary material is available at *Archives of Clinical Neuropsychology* online.

Funding

The Systolic Blood Pressure Intervention Trial (SPRIN) is funded with Federal funds from the National Institutes of Health (NIH), including the National Heart, Lung, and Blood Institute (NHLBI), the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the National Institute on Aging (NIA), and the National Institute of Neurological Disorders and Stroke (NINDS), under Contract Numbers HHSN268200900040C, HHSN268200900046C, HHSN268200900047C, HHSN268200900048C, HHSN268200900049C, and Inter-Agency Agreement Number A-HL-13-002-001. It was also supported in part with resources and use of facilities through the Department of Veterans Affairs.

Conflict of interest

None Declared

Acknowledgements

The SPRINT investigators acknowledge the contribution of study medications (azilsartan and azilsartan combined with chlorthalidone) from Takeda Pharmaceuticals International, Inc. All components of the SPRINT study protocol were designed and implemented by the investigators. The investigative team collected, analyzed, and interpreted the data. All aspects of manuscript writing and revision were carried out by the coauthors. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH, the U.S. Department of Veterans Affairs, or the United States Government.

We also acknowledge the support from the following CTSAs funded by NCATS: CWRU: UL1TR000439, OSU: UL1RR025755, U Penn: UL1RR024134& UL1TR000003, Boston: UL1RR025771, Stanford: UL1TR000093, Tufts: UL1RR025752, UL1TR000073 & UL1TR001064, University of Illinois: UL1TR000050, University of Pittsburgh: UL1TR000005, UT Southwestern: 9U54TR000017-06, University of Utah: UL1TR000105- 05, Vanderbilt University: UL1 TR000445, George Washington University: UL1TR000075, University of CA, Davis: UL1 TR000002, University of Florida: UL1 TR000064, University of Michigan: UL1TR000433, Tulane University: P30GM103337 COBRE Award NIGMS.

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