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Research Article

Relations of Executive Function and Physical Performance in Middle Adulthood: A Prospective Investigation in African American and White Adults

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Abstract

Objectives: Previous studies in older adults found robust associations between executive functions (EF) and physical performance, as well as sociodemographic variation in physical performance decline. To examine these associations earlier in the adult lifespan, we investigated relations of EF, race, and sex with age-related physical performance decline during middle adulthood.

Method: Participants were 2,084 urban-dwelling adults (57.2% female; 57.8% African American; 37.3% living in poverty; mean baseline age = 48.1) from the Healthy Aging in Neighborhoods of Diversity across the Life Span study. Mixedeffects regression was used to examine interactive relations among EF, race, sex, and age (indexing time) with change in dominant and nondominant handgrip strength and lower extremity strength over approximately 5 years. All analyses adjusted for poverty status, and subsequently adjusted for education, body mass index, hypertension, and diabetes.

Results: There were no significant prospective associations between EF and decline in physical performance measures. Significant cross-sectional associations revealed that lower EF was associated with worse performance on all physical performance measures averaged across both time points (p < .05). A significant two-way interaction of Sex × Age (p = .019) revealed that men experienced greater age-related decline in lower extremity strength than women.

Discussion: Findings did not reveal prospective associations between EF and physical performance decline in middle adulthood. However, they identified robust cross-sectional associations between EF and physical performance, and unexpectedly greater decline in lower extremity strength in men than women. Ultimately, these findings may inform prevention and intervention strategies targeting groups at risk for poorer physical function status and decline.

Keywords: Grip strength, Health disparities, Lower extremity strength and endurance, Race, Sex

Assessment of physical functioning is critical in the evaluation of older adults in health settings (Guralnik et al., 1994). Poor performance in key domains of physical functioning is associated with increased risk for functional decline and age-related disability (Den Ouden, Schuurmans, Arts, & Van Der Schouw, 2011). Examples of such measures include the Short Physical Performance Battery (Guralnik et al., 1994) and the Hand Dynamometer Test (Bohannon, Peolsson, Massy-Westropp, Desrosiers, & Bear-Lehman, 2006), which measure lower extremity functioning and handgrip strength, respectively.

Executive functions (EF), which are top-down cognitive processes involved in the "orchestration of basic cognitive processes during goal-oriented problem-solving" (Roth, Isquith, & Gioia, 2013, p. 105), are involved in the planning and execution of movement (Mirabella, 2014) and are among the strongest cognitive correlates of functional status (Royall et al., 2007). In that regard, prospective and cross-sectional investigations have found robust associations between EF and select aspects of physical performance, such as gait speed and balance (Muir-Hunter et al., 2014; Watson et al., 2010). Associations between EF and other areas of physical performance, such as grip strength and lower extremity strength and endurance, have not been previously studied. Of note, associations between EF and physical functioning may, in part, reflect shared underlying neurobiological mechanisms; indeed, aspects of EF and physical performance are vulnerable to white matter disease affecting frontal systems (Parihar, Mahoney, & Verghese, 2013).

Previous studies have also reported variation in physical performance as a function of sociodemographic factors, namely sex and race. Generally, cross-sectional and longitudinal investigations have found that women and African Americans have greater vulnerability for poor physical performance and experience more rapid physical decline than men and Whites, respectively (Haas, Krueger, & Rohlfsen, 2012; Merrill, Seeman, Kasl, & Berkman, 1997; Seeman et al., 1994). There is a need to understand mechanisms underlying sex and racial disparities in physical function across the lifespan.

Sociodemographic disparities in EF trajectories may, in part, underlie racial and sex differences in age-related physical performance decline previously reported among older adults. However, despite substantial evidence of sex- and race-related disparities in age-related physical decline, the potential moderating role of sociodemographic factors in prospective associations of EF and physical performance has not been examined. Furthermore, it is plausible that the multitude of risk factors experienced by African Americans and women may increase their vulnerability to EF-related physical performance decline. For example, compared to Whites, African Americans are more likely to have lower socioeconomic position and be exposed to racial and other forms of discrimination, chronic disease, and environmental toxins, among several other risk factors (Glymour & Manly, 2008). Similarly, compared to men, women are more likely to experience gender discrimination (Pew Research Center, 2017), as well as higher rates of depression, anxiety disorders, and chronic stress (Eaton et al., 2007; Matud, 2004). Taken together, these vulnerability factors that can influence health and aging in their own right may also increase the vulnerability of these groups to EF-related physical performance decline, as well as declines in physical functioning overall.

In addition to focusing solely on gait speed and balance, to the best of our knowledge, previous prospective investigations of EF and physical function decline have utilized samples of older persons. Further, there have been few to no investigations of prospective sociodemographic trajectories in physical function during middle adulthood. The overwhelming focus on older adults, while relevant, has limited our understanding of these associations at earlier periods in the adult lifespan. Identification of potential cognitive and sociodemographic determinants of physical function decline during middle adulthood may assist in the prevention of age-related physical disability later in life.

Given these gaps in the literature, the present study examined interactive relations of EF, race, and sex with age-related change in select aspects of physical performance over approximately 4–5 years within a sample of largely middle-aged (i.e., 30–64 years old at baseline), urban-dwelling African American and White adults. The dimensions of physical performance that were assessed included dominant and non-dominant grip strength and lower extremity strength and endurance. We hypothesized that age-related decline in physical function would be most pronounced among African American women with lower levels of EF.

Next, independent and interactive relations among EF, race, and sex with physical function trajectories may vary by age group within the broad period of middle adulthood. To examine this possibility, age-stratified analyses that were parallel to the analyses in the overall sample were run in younger to middle-aged participants (i.e., 30–49 years old at baseline) and middle-aged to older participants (i.e., 50–64 years old at baseline).

Finally, associations between EF and physical function trajectories may be explained, at least in part, by key biomedical variables. It is well-documented that cardiometabolic risk factors, such as obesity, diabetes, and hypertension, are associated with EF (Elias, Elias, Sullivan, Wolf, & D'Agostino, 2003; Nishtala et al., 2014) and aspects of physical performance (Mainous, Tanner, Anton, & Jo, 2015; Shen et al., 2015). Given these relations, it is plausible that cardiometabolic risk factors partially explain EF-physical performance associations. Likewise, educational attainment is among the strongest predictors of cognitive functioning, including EF (Strauss, Sherman, & Spreen, 2006) and has also been implicated in grip strength and lower extremity functioning (Hairi, Mackenbach, Andersen-Ranberg, & Avendano, 2010; Seeman et al., 1994). Therefore, the present study includes sensitivity analyses that examine whether significant effects of EF or its interaction with age, sex, and/or race in the overall sample were eliminated following adjustment for body mass index (BMI), diabetes, hypertension, and educational attainment. If effects became nonsignificant, the potential for mediation was considered. Changes in significant interactions among sex, race, and age following adjustment for these variables were also examined.

Method

Participants and Parent Study Procedures

Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) is an ongoing longitudinal investigation of age-related health disparities attributable to race and socioeconomic status (Evans et al., 2010). The HANDLS sample is a fixed cohort of urban-dwelling adults drawn from 13 neighborhoods (contiguous census tracts) in the city of Baltimore, Maryland. Neighborhoods were selected for their likelihood of yielding participants who were African American or White, men or women, and with adjusted annual household incomes above or below 125% of the 2004 federal poverty level. All HANDLS participants self-identified their race as African American or White and were between the ages of 30-64 years at baseline. The Institutional Review Board at the National Institute of Environmental Health Sciences approved the HANDLS protocol.

The first wave of HANDLS occurred between 2004 and 2009, and the next wave of complete data collection occurred between 2009 and 2013. Data were collected within participants' households and on medical research vehicles (MRV) located within participants' neighborhoods, where they completed a medical history and physical examination, physical performance battery, cognitive testing, and other assessments. After initial selection, participants were excluded from further participation in the larger HANDLS study if they were unable to provide informed consent; were pregnant; were within six months of active cancer treatment; self-reported a diagnosis of AIDS; were unable to provide valid government-issued identification; or did not have a verifiable address.

In total, 3,720 participants were enrolled in HANDLS, of whom 2,799 completed the baseline MRV visit and 2,468 completed the first examination follow-up visit. For the present study's data analyses, participants were excluded if they reported a history of dementia, stroke, transient ischemic attack, brain cancer, multiple sclerosis, Parkinson's disease, epilepsy, or HIV/AIDS. These criteria were chosen based on their likelihood of influencing EF and/or physical performance. To avoid biasing the dataset, if a participant met inclusion criteria at baseline but later developed one of these conditions prior to follow up, their baseline data were included in the study while their follow-up data were excluded. In the present study there were 2,084 participants (57.2% female; 57.8% African American; 40.0% living in poverty) with data for all predictors and at least one physical performance outcome at one or both time points. Of note, we did not exclude participants who had data at only one time point, as this is not necessary in linear mixedeffects regression (Gueorguieva & Krystal, 2004), and doing so would have risked biasing the sample. Therefore, the present study's sample comprised 1,556 participants with baseline data and 1,412 participants with follow-up data, of whom 884 participants with data at both waves.

Measures

Sociodemographic information

Participants reported their age, biological sex (0 = women, 1 = men), and self-identified race (0 = White, 1 = African American) at baseline. Annual household income at baseline (adjusted for household size) classified participants as living above (0) or below (1) 125% of the 2004 Health and Human Services poverty guidelines. Age, race, and sex were primary predictor variables and poverty status was an adjustment variable in all analyses.

EF composite measure

In order to assess a broad construct of EF, a composite score was computed from the summation of standardized scores (i.e., z-scores) from four neuropsychological tests of EF-related domains: (a) set-shifting, as measured by the Trail Making Test Part B; (b) auditory attention, as measured by Digit Span Forward; (c) working memory, as measured by Digit Span Backward; and (d) category verbal fluency, as measured by Animal Naming. All tests were administered on the MRV. The EF composite was an independent variable in all analyses. Composite variables of broad cognitive constructs, including EF, have been used extensively in the literature and are thought to be more reliable than individual cognitive tests (Bender, Austin, Grodstein, & Bynum, 2017; Tullberg et al., 2004). The tests that comprise the EF composite are described in the Supplementary Methods.

Physical performance outcome measures

Three measures of physical performance were outcomes in the present study: (a) dominant handgrip strength, (b) nondominant handgrip strength, and (c) a chair stands task as a measure of lower extremity strength and endurance. These measures were chosen for their ability to provide gross estimates of upper and lower extremity functioning and the integrity of the skeletal muscle (Guralnik et al., 1994; Haas et al., 2012), as well as their feasibility of administration within the confines of the MRVs. Detailed descriptions of these measures are included in the Supplementary Methods.

Sensitivity Variables

BMI, diabetes, hypertension, and educational attainment were assessed as additional covariates in sensitivity analyses (see Supplementary Methods for detailed descriptions of these variables).

Statistical Analysis

Main analyses

Statistical analyses were conducted using the "lme4" package within R version 3.5.2 (Bates, Mächler, Bolker, & Walker, 2015; R Core Team, 2018). Linear mixed-effects regression models, with the intercept modeled as a random

effect, examined prospective interactive relations of EF, race, sex, and age (modeled to index time) with physical performance, adjusted for poverty status. We used a growth model formulation in which change in the cognitive measures were assessed by time, which is indexed by age in our analyses.1 Dominant and nondominant handgrip strength and the chair stands task were examined as outcomes in separate analyses. EF and the physical performance outcomes were modeled as time-varying, such that all available baseline and follow-up data were included in the analyses. Analyses began with all interactions (i.e., up to the fourway interaction of EF × Race × Sex × Age), and proceeded through backward elimination (Morrell, Pearson, & Brant, 1997). That is, nonsignificant higher-order interactions were removed from the analyses in a stepwise fashion until the highest-order significant interaction (i.e., p < .05) was identified. All significant interactions as well as lower-order interactions nested within them were then retained, while extraneous nonsignificant interactions were removed from analysis. Therefore, final models for each outcome contained the highest-level significant interaction(s), lowerlevel interactions nested within them, and all main effects and adjustment variables. Significant interactions were then plotted to assist with interpretation.

We opted to use linear-mixed effects regression analyses in this study for several reasons. Linear-mixed effects regression enabled us to include all available data in our analyses, even when some participants lacked complete repeated measures (Gueorguieva & Krystal, 2004). This is because in linear mixed-effects regression, all available data contribute to the overall means and standard errors, thus improving the precision of the results. In addition, selectively excluding participants who lack repeated measures (which is necessary in several other longitudinal analytic techniques, such as repeated-measures ANOVA) would risk biasing the dataset. Therefore, by including all available data, linear-mixed effects regression allowed us to avoid biasing our sample and findings.

Age was a modeled as a random effect to assess time in our repeated-measures analysis, such that within-person age differences represented the elapsed time between measurement waves. Age was also modeled as a fixed effect assessing individual differences associated with chronological age. Therefore, the regression coefficient for the age main effect in our analyses measures change in physical performance as a function of the slope of age change in the sample. The regression coefficients of any interactions with age (modeled as fixed effects) measure change in physical performance as a function of differences in the slopes of age change between levels of the moderating variables. For example, the interaction of Sex × Age with the chair stands task in the overall sample (see Results) indicates that men showed greater slowing in the chair stands task as a function of aging than women. All other variables were modeled as fixed effects, and interpretation of their regression coefficients is analogous to those in ordinary least squares regression; that is, they are interpreted as the mean change in the outcome per one-unit change in the predictor variable while holding other predictors in the model constant.

Age-stratified analyses

To examine differential rates of physical performance decline as a function of age, the main analyses were rerun after stratifying by baseline age. A cut-point of 50 years old was chosen given its widespread use in the literature and because it was reasonably near the median age for the HANDLS sample. The sample was split into two age groups: (a) younger to middle-aged participants aged 30–49 years old at baseline (n = 1,205), and (b) middle-aged to older participants aged 50–64 years old at baseline (n = 879). Like the main analyses, age-stratified analyses proceeded through backward elimination until final models were identified.

Sensitivity analyses

Two series of subsequent sensitivity analyses were conducted following the main analyses (see Supplementary Methods for detailed descriptions).

Results

Sample Characteristics

Table 1 contains sample characteristics. Histograms and Q-Q plots of all outcome variables indicated approximately normal distributions.²

Main Analyses

There were no significant interactions of EF with age, race, or sex for any of the physical performance outcomes (p > .05). However, there were significant main effects of EF with dominant handgrip strength, b = 0.40, $\beta = 0.10$, p < .001, nondominant handgrip strength, b = 0.39, $\beta = 0.09, p < .001$, and the chair stands task, b = -0.15, $\beta = -0.05$, p = .012 (Tables 2 and 3). Greater EF was associated with better performance on each of these tasks across baseline and follow-up (i.e., pooled overall effects; Figure 1). There was also a significant interaction of Sex × Age with the chair stands task (Table 3), b = 0.08, $\beta = 0.02$, p = .019, such that men experienced steeper decline in lower extremity strength and endurance than women (Figure 2). There were no further significant interactions among race, sex, or age with any of the physical performance outcomes.

² Examination of histograms and Q-Q plots revealed some extreme values for dominant handgrip strength (n = 1), nondominant handgrip strength (n = 1), and the chair stands task (n = 2). When these values were excluded, they did not substantially change results of the main analyses or sensitivity analyses. One difference was observed in the age-stratified analyses, such that a significant interaction of Sex × Age with dominant handgrip strength attenuated to nonsignificance after removal of an extreme value, as is described in the Results. Nonetheless, given the overwhelming consistency across the models, these extreme values were retained in the study.

		(a) Baseline	Ischine				
Variable	AA $(n = 851)$	White $(n = 705)$	sig.	Women $(n = 879)$	Men ($n = 677$)	sig.	All $(N = 1,556)$
African American, n (%)		I		475 (54.0%)	376 (55.5%)		851 (54.7%)
Women, n (%)	475 (55.8%)	404 (57.3%)		I	I		879 (56.5%)
Below poverty, $n (\%)$	349(41.0%)	203 (28.8%)	* *	319 (36.3%)	233 (34.4%)		552 (35.5%)
Age, M (SD)	48.0 (9.3)	48.2 (9.4)		48.3 (9.4)	47.8 (9.3)		48.1 (9.3)
Education, $M(SD)$	12.2 (2.2)	12.4 (2.9)		12.3 (2.5)	12.2 (2.6)		12.3 (2.5)
Body mass index, M (SD)	29.9 (7.7)	30.1 (7.6)		31.4(8.3)	28.3 (6.3)	* * *	30.0 (7.6)
Hypertension, $n (\%)$	390 (45.8%)	263 (37.3%)	* * *	382 (43.5%)	271 (40.0%)		653 (41.9%)
Diabetes, $n % = \frac{1}{2} \sum_{i=1}^{n} \frac{1}{2} $	141 (16.6%)	105(14.9%)		145(16.5%)	101 (14.9%)		246 (15.8%)
Executive functions composite, M (SD)	-0.7 (2.6)	1.0(2.8)	* * *	0.1(2.9)	0.1(3.0)	*	0.1(2.8)
Dominant handgrip strength, kg, M (SD)	35.7(11.3)	33.9 (10.8)		28.3(6.9)	43.4 (9.6)	* * *	34.9(11.1)
Nondominant handgrip strength, kg, M (SD)	35.7(11.9)	33.8 (11.4)	* * *	27.8 (7.0)	44.1 (10.1)	* * *	34.9 (11.7)
Chair stands task, seconds, M (SD)	33.8 (8.4)	33.5 (8.1)		34.2 (8.0)	33.1(8.5)		33.7 (8.2)
		(b) Fol	(b) Follow-up				
Variable	AA $(n = 852)$	White $(n = 560)$	sig.	Women $(n = 826)$	Men $(n = 586)$	sig.	All $(N = 1, 412)$
African American, n (%)		1		498 (60.3%)	354 (60.4%)		852 (60.3%)
Women, n (%)	498 (58.5%)	232 (58.6%)					826 (58.5%)
Below poverty, n (%)	355 (41.7%)	163 (29.1%)	* * *	326 (39.5%)	225 (32.8%)	*	518 (36.7%)
Age, M (SD)	51.9(9.0)	52.7 (9.1)		52.3 (9.4)	52.1 (8.8)		52.2 (9.1)
Education, M (SD)	12.3 (2.3)	12.8 (2.9)		12.0(2.6)	12.6 (2.7)		12.5 (2.6)
Body mass index, M (SD)	30.7 (7.9)	30.7 (7.6)		32.0 (8.4)	28.9 (6.4)	* * *	30.7 (7.8)
Hypertension, $n (\%)$	501 (59.1%)	264(47.1%)	* *	471 (57.0%)	294 (50.2%)	* *	765 (54.2%)
Diabetes, $n \%$	171 (20.3%)	89(15.9%)	*	162 (19.6%)	98 (16.7%)		260~(18.4%)
Executive functions composite, M (SD)	-0.2 (2.5)	1.88(2.8)	* *	0.2 (2.7)	0.5 (2.9)	*	0.3 (2.8)
Dominant handgrip strength, kg, M (SD)	36.8 (12.4)	35.2(10.8)	*	28.9 (7.6)	46.4(10.5)	* * *	36.2 (12.4)
Nondominant handgrip strength, kg, M (SD)	36.2 (12.6)	35.1(11.4)	* *	28.3 (7.5)	46.3 (11.0)	* *	35.8 (12.7)
Chair stands task, seconds, M (SD)	33.4 (7.4)	33.6(8.1)		34.2 (7.4)	32.5 (7.2)	* * *	33.5 (7.4)

Table 1. Participant Characteristics Stratified by Self-identified Race and Sex and in the Overall Sample at Baseline and Follow-up

Note: AA = African American. Independent samples t tests and chi-square tests of independence were used to assess differences between race and sex groups, * b < .05, ** b < .01, *** b < .001.

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Table 2. Mixed-Effects Regression Models for Dominant and Nondom	inant Handgrip Strength
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(a) Dominant handgrip strength $(n = 2,056)^{a}$						
	Model 1	Model 2	Model 3	Model 4		
Poverty status	-0.98**	-0.98***	-0.98***	-0.98**		
Age	-0.20***	-0.20***	-0.19***	-0.16***		
Executive functions	0.41**	0.41***	0.37**	0.40***		
Race	2.32***	2.33***	2.35***	2.60***		
Sex	15.65***	15.66***	15.57***	15.93***		
Executive Functions × Age	0.00	0.00	0.00			
Executive Functions × Race	-0.17	-0.17	-0.10			
Executive Functions × Sex	0.10	0.10	0.18			
Age × Race	0.07	0.07	0.07			
Age × Sex	-0.01	-0.01	-0.01			
Race × Sex	0.67	0.65	0.68			
Executive Functions × Age × Race	-0.01	-0.01				
Executive Functions × Age × Sex	-0.00	0.00				
Executive Functions × Race × Sex	0.14	0.14				
Age × Race × Sex	0.00	0.00				
Executive Functions × Age × Race × Sex	0.01					

(b) Nondominant handgrip strength $(n = 2,049)^{b}$						
	Model 1	Model 2	Model 3	Model 4		
Poverty status	-1.21**	-1.22**	-1.21**	-1.23**		
Age	-0.20***	-0.20***	-0.20***	-0.18***		
Executive functions	0.44**	0.44***	0.40***	0.39***		
Race	2.26***	2.24***	2.30***	2.29***		
Sex	16.95***	16.94***	16.78***	16.80***		
Executive Functions × Age	0.00	0.00	0.01			
Executive Functions × Race	-0.18	-0.18	-0.10			
Executive Functions × Sex	0.05	0.05	0.11			
Age × Race	0.06	0.06	0.06			
Age × Sex	-0.05	-0.04	-0.03			
Race × Sex	0.00	0.04	0.04			
Executive Functions × Age × Race	-0.00	-0.01				
Executive Functions × Age × Sex	0.03	0.02				
Executive Functions × Race × Sex	0.14	0.15				
Age × Race × Sex	0.01	0.01				
Executive Functions × Age × Race × Sex	-0.01					

Note: Unstandardized regression coefficients (*b*) across four model iterations for dominant and nondominant handgrip strength. Model 4 (shown in bold above) was retained as the final linear mixed-effects regression model for both outcomes.

 $^{a}N = 2,056$ participants with data for dominant handgrip strength (n = 1,514 with data at baseline and n = 1,389 with data at follow-up, of whom n = 839 had data at both waves).

 $^{b}N = 2,049$ participants with data for nondominant handgrip strength (n = 1,509 with data at baseline and n = 1,376 with data at follow-up, of whom n = 836 had data at both waves).

p < .01, p < .001.

Age-Stratified and Sensitivity Analyses

Detailed descriptions of the age-stratified and sensitivity analyses are included in the Supplementary Results. Briefly, findings were largely consistent with results of the main analyses, with the exception of an additional interaction of Sex × Age with dominant handgrip strength among younger to middle-aged participants in the age-stratified analyses, such that women showed greater decline in dominant handgrip strength than men, b = 0.14, $\beta = 0.03$, p = .044. However, these differences were minimal upon visual inspection when plotted (see Supplementary Figure 4). Further, this interaction attenuated to nonsignificance with the removal of an extreme value for dominant hand-grip strength (p = .051). Of note, the Sex × Age interaction with the chair stands task was significant in the middle-aged to older participants (consistent with the overall

sample; p = .014), but nonsignificant in the younger to middle-aged participants (inconsistent with the overall sample; p = .204). Conversely, the EF main effect with the chair stand task was significant in the younger to middle-aged participants (consistent with the overall sample; p = .008), but nonsignificant in the middle-aged to older participants (inconsistent with the overall sample; p = .224).

Discussion

To the best of our knowledge, this was the first study to examine interactive relations among EF, race, and sex with age-related change in key domains of physical performance. Our hypothesis that age-related decline in physical function would be most pronounced among African American women with lower levels of EF was not supported by our findings. Indeed, contrary to our expectations, we did not

Table 3	Mixed-Effects	Regression	Models for	r the Chair	Stands Task	(<i>n</i> = 1,880)
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	Model 1	Model 2	Model 3	Model 4
Poverty status	1.69***	1.69***	1.69***	1.68***
Age	0.21***	0.22***	0.19***	0.16***
Executive functions	-0.18	-0.18	-0.09	-0.15*
Race	-0.26	-0.24	-0.19	-0.43
Sex	-1.25*	-1.24*	-0.97	-1.29***
Age × Sex	0.04	0.02	0.08*	0.08*
Executive Functions × Age	0.00	-0.00	0.00	
Executive Functions × Race	0.02	0.03	-0.15	
Executive Functions × Sex	0.19	0.20	0.03	
Age × Race	-0.09	-0.10*	-0.05	
Race × Sex	-0.33	-0.38	-0.55	
Executive Functions × Age × Race	-0.01	0.01		
Executive Functions × Age × Sex	-0.00	-0.01		
Executive Functions × Race × Sex	-0.31	0.01		
Age × Race × Sex	0.09	0.10		
Executive Functions \times Age \times Race \times Sex	0.01			

Note: Unstandardized regression coefficients (*b*) across four model iterations for the chair stands task. Model 4 (shown in bold above) was retained as the final regression model. N = 1,880 participants had data for dominant handgrip strength (n = 1,389 with data at baseline and n = 1,227 with data at follow-up, of whom n = 736 had data at both waves).

p < .05, p < .001.

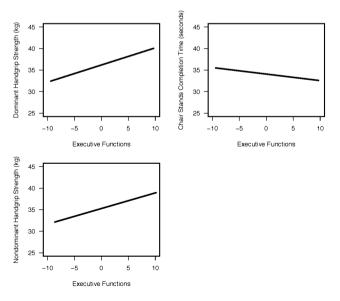


Figure 1. Significant associations of executive functions with dominant handgrip strength (top left panel), nondominant handgrip strength (bottom left panel), and lower extremity strength and endurance (top right panel) averaged across baseline and follow-up.

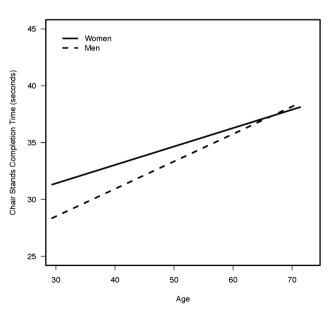


Figure 2. Significant interaction of Sex \times Age with lower extremity strength and endurance.

find prospective relations of EF with age-related physical performance decline over time in race or sex subgroups, or within the sample as a whole. These findings are inconsistent with prior longitudinal studies demonstrating that EF is associated with declines in physical performance; no prior literature has integrated potential moderating roles of race and sex. However, to the best of our knowledge, previous studies that demonstrated prospective associations between EF and physical performance decline primarily used gait speed to measure of physical functioning (Atkinson et al., 2007; Watson et al., 2010), and none measured the dimensions of physical function assessed in this study. It is plausible that gait speed tasks place greater demands on EF due to their complex nature. Furthermore, such studies have utilized samples of older adults; in contrast, our study focused on decline over an approximately five-year period in a sample of largely middle-aged adults (aged 30-64 years at baseline). Thus, it is possible that different levels of EF are not associated with decline trajectories until older ages. Future research should examine prospective trends in EF-physical performance associations over longer periods and further into older adulthood. Finally, the present study examined whether different levels of EF predicted differential decline in physical performance outcomes, whereas change in EF was not examined. It is plausible that differences in rates of change in EF influence rates of physical performance decline more strongly than differences in levels of EF.

Our study revealed robust cross-sectional relations between EF and physical function across baseline and follow-up. Specifically, we found significant main effects of EF with dominant and nondominant handgrip strength and lower extremity strength and endurance, such that greater EF (across baseline and follow-up) was associated with better performance on those tasks (also across baseline and follow-up). These findings are consistent with prior literature indicating that EF is closely related to planning and executing movement (Mirabella, 2014) and directly associated with aspects of physical functioning such as gait speed (Parihar et al., 2013; Yogev-Seligmann, Hausdorff, & Giladi, 2008) and balance (Muir-Hunter et al., 2014). Results are also generally supported by prior longitudinal and cross-sectional investigations demonstrating that greater decline and poorer performance in EF is associated with decline in overall functional status (Royall et al., 2007). These findings extend previous literature by demonstrating associations between EF with handgrip strength and lower extremity and endurance during middle adulthood.

It is possible that EF more strongly predicts decline in key aspects of physical functioning at older developmental periods than those measured in the present study. Our study focused on decline over an approximately five-year period during middle adulthood, prior to the onset of agerelated physical disability found more commonly in older adults. Cross-sectional associations observed between EF and handgrip and lower extremity strength in the present study may portend prospective change over longer periods of follow-up and with an aging sample. Future researchers should examine prospective trends in EF-physical performance associations over longer periods.

Importantly, associations between EF and physical performance were observed in both the main and agestratified analyses. This suggests that EF may be implicated in physical functioning for several decades prior to older adulthood, the developmental period that has been the predominant focus of previous research. The only discrepancy in EF-physical performance associations between our main and age-stratified analyses was the null association between EF and performance on the chair stands task among the middle-aged to older participants. This is largely inconsistent with previous research suggesting links between EF and select aspects of physical functioning (e.g., gait speed and balance; Muir-Hunter et al., 2014; Watson et al., 2010). Given that associations between EF and chair stands tasks have not been previously examined, it is possible that associations between EF and lower extremity strength and endurance become nonsignificant at older ages, perhaps reflecting differential effects between those who live to older age and those who do not. However, it is likely that this null finding was influenced, at least in part, by reduced statistical power resulting from the smaller sample. Therefore, findings should be replicated in larger samples of middle-aged to older adults before concluding that associations between EF and lower extremity functioning are stronger earlier in middle adulthood.

Findings from neuroimaging research suggest that underlying white matter pathology is related to both EF (Gunning-Dixon & Raz, 2000) and aspects of physical performance, including handgrip strength (Sachdev, Wen, Christensen, & Jorm, 2005) and lower extremity strength and endurance (as measured by chair stands task; Su et al., 2017; Viana-Baptista et al., 2011). In addition, several cortical and subcortical gray matter regions may be implicated in the EF-physical performance associations observed in this study. For example, the supplementary motor cortex, prefrontal cortex, and basal ganglia are brain regions involved in various aspects of EF (Elliott, 2003; Graybiel, 2000; Miller & Cohen, 2001), as well motor planning and control (Monchi, Petrides, Strafella, Worsley, & Doyon, 2006; Nachev, Kennard, & Husain, 2008). Therefore, it is possible that EF partially mediates significant associations between the status of key neuroanatomical regions and physical functioning. However, most previous research linking these regions to physical functioning has focused on gait speed, balance, and postural control, which were not measured in this study. Therefore, future research is needed to determine whether the structure or functioning of these anatomical regions is specifically linked to handgrip and lower extremity strength, as well as the potential mediating role of EF in any associations observed. Alternatively, neurobiological differences may explain both lower EF and physical functioning.

It is further plausible that cardiovascular risk factors that contribute to cerebrovascular disease (Howard et al., 1998; Shimada, Kawamoto, Matsubayashi, & Ozawa, 1990) might damage these neighboring regions (via white matter disease), thus promoting simultaneous declines in EF and physical function. Of note, adjustment for biomedical risk factors (i.e., BMI, hypertension, and diabetes), as well as educational attainment, did not significantly alter main effects of EF. Therefore, these variables were not considered to be likely mediators of EF-physical performance associations in the present study. Nonetheless, future studies should use more comprehensive assessment of cardiovascular disease risk factors to better assess their contributions to EF-related physical performance differences. Likewise, future studies should utilize formal mediation analyses, such as through structural equation modeling, to examine the role of biopsychosocial risk factors in EF-related differences and trajectories in physical performance outcomes.

With regard to sociodemographic differences in physical performance decline-irrespective of EF-we found that men demonstrated greater age-related decline in lower extremity strength and endurance than women. This is inconsistent with most prior studies that have shown that women perform more poorly on measures of physical function, experience greater decline in physical functioning, and have higher rates of self-reported disability than men (Kennedy, Stratford, Pagura, Walsh, & Woodhouse, 2002; Merrill et al., 1997). However, a study by Botoseneanu and colleagues (Botoseneanu, Allore, Gahbauer, & Gill, 2013), which examined sex-related trajectories in physical performance decline after statistically adjusting for mortality bias, found that older men (versus older women) demonstrated greater age-related decline in lower extremity function over time. Furthermore, another study by the same research group demonstrated that despite having faster accumulation of self-reported disability, older women experienced slower decline in physical performance than men over 13.5 years after adjustment for length-of-survival and other sociodemographic and health factors (Botoseneanu, Allore, Mendes de Leon, Gahbauer, & Gill, 2016). Although our study did not address mortality effects, the use of a relatively younger sample (i.e., primarily middle-aged adults between 30 and 64 years old at baseline) with lower agerelated mortality risk than older samples used in prior studies may have unintentionally accomplished this. This finding emphasizes the importance of considering mortality effects in prospective studies of physical functioning and why it is crucial to assess decline in functional abilities prior to older adulthood.

A range of biopsychosocial risk factors may have contributed to our finding of sex-related disparities in lower extremity decline. As with the EF-related findings, adjustment for biomedical risk factors, namely BMI, hypertension, and diabetes, as well as educational attainment did not significantly alter the two-way interaction of Sex × Age with decline trajectories in lower extremity function. As described above, a more comprehensive assessment of cardiovascular disease risk factors, as well as formal mediation analyses, could allow for more sensitive examination of their potentially cumulative impact on sex-related physical performance trajectories.

In addition, sex-related behavioral and occupational factors may have contributed to our finding of sex-related disparities in lower extremity function decline. For example, cigarette smoking is more prevalent among men than women (Centers for Disease Control and Prevention, 2018) and may be associated with worse lower extremity functioning (Strand, Mishra, Kuh, Guralnik, & Patel, 2011). Men also have higher rates of use of most illicit substances than women (Cotto et al., 2010). In addition, sex-related occupational factors may have contributed to our findings. Men are far more likely to work in some manual occupations than women (e.g., representation in natural resources, construction, and maintenance occupations is 94.6% male; Bureau of Labor Statistics, 2019). As has been suggested previously (Haas et al., 2012; Krueger & Burgard, 2011; Toivanen et al., 2010), participation in such physically demanding jobs may initially confer musculoskeletal benefits, but with greater risk for decline over the long-term due to work-related toxic exposures, diseases, injuries, and pain. This could partly explain why men had better lower extremity functioning at younger ages, but greater decline at older ages, than women in our study (Figure 2). This interpretation is also supported by the age-stratified analyses, which found sex-related differences in lower extremity strength trajectories among the middle-aged to older participants, but not the younger to middle-aged participants. Musculoskeletal benefits associated with social and occupational factors among men may serve as protective factor through younger adulthood but give way to risk factors at older ages.

Importantly, age-stratified analyses revealed a significant interaction of Sex × Age with dominant handgrip strength among younger to middle-aged adults, but not middle-aged to older adults. This finding suggested that women (versus men) experienced greater dominant handgrip strength decline than men. This finding is consistent with the much of the physical performance literature that has shown women to be at greater risk for physical performance decline and age-related disability than men (Kennedy, Stratford, Pagura, Walsh, & Woodhouse, 2002; Merrill et al., 1997). However, this finding is inconsistent with sex-related patterns observed with the chair stands task in the overall sample and the older age group, which showed men experiencing greater lower extremity function decline than women. Additionally, there were no significant sex-related differences in grip strength trajectories among the older sample. As described above, men may experience musculoskeletal benefits related to social and occupational factors at younger ages, which could partially contribute to their slower rate of decline in dominant handgrip strength than men during younger to middle

adulthood. However, this finding must be interpreted with caution for several reasons. First, visual analysis of the plot (see Supplemental Figure 4) appeared to show minimal differences in dominant handgrip strength trajectories between women and men. Second, the interaction effect attenuated to nonsignificance following removal of a single extreme value, suggesting that the finding may have been spurious. Finally, the analysis may have been capitalizing on chance given that the lower sample size reduced the degrees of freedom of the age-stratified analyses. Replication in a unique sample is necessary to support or refute the reliability of this finding among younger to middle-aged adults.

Study Strengths and Limitations

This study contributed uniquely to the literature in several ways. To our knowledge, this was the first study to examine interactive relations among EF, race, and sex with age-related physical performance decline. This was also the first study to examine associations between EF and physical performance trajectories during middle adulthood. Further, the diverse HANDLS sample expanded on previous studies in this research area by including men and women who were African American and White with household incomes above and below the poverty level. Our findings suggest that a lifespan perspective that considers individual differences in EF is crucial when studying age-related decline in physical functioning.

The current study also has limitations. We only examined two time points approximately five years apart, which likely made detecting prospective effects challenging. It is possible that the absence of prospective relations of EF with age-related physical performance decline is due to the relatively short time span between measurement waves. Increasing the number of measurement time points over longer periods may elucidate long-term and nonlinear trends in physical performance outcomes. Relatedly, the potential for ceiling effects in physical performance tasks, particularly among the younger participants, may have made change difficult to detect. Future studies should examine prospective associations between EF and physical performance decline over multiple time points and longer periods. Our use of an EF composite did not allow for specific examination of different EF subdomains. Although composite variables of cognitive domains, including EF, have been used previously in the literature (Bender et al., 2017; Tullberg et al., 2004), individual tests of different executive subdomains may also be useful to parse aspects of EF that are implicated in physical performance changes over time. In addition, the present study limited its examination of cognitive domains to those under the EF umbrella. Changes in other cognitive domains, such as memory and psychomotor speed, might also be important to consider in relation to age-related physical performance decline. Future research should consider measuring

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key subdomains of EF, as well as other cognitive domains, in relation to physical performance decline. Similarly, our study only included measures of grip strength and lower extremity strength and endurance. Other dimensions of physical performance, such as gait speed, should be investigated in future studies. Next, our analyses did not adjust or exclude for other potentially impactful biomedical variables, such as use of select medications or functional comorbidities, which may have impacted the findings. Although this study adjusted for poverty status, we did not examine how poverty and other indicators of socioeconomic status (e.g., education, occupational status) interact with EF, race, or sex to predict age-related physical function decline. Future studies seeking to examine within-group heterogeneity should probe the role of socioeconomic status in these associations. Finally, our results should be interpreted cautiously given their exploratory nature and that we did not apply *p*-value adjustments for multiple-comparisons. Overall, the findings should be viewed as preliminary pending replication in a unique sample.

Summary and Conclusions

This was the first study to examine interactive relations among EF, race, and sex with age-related physical performance decline in a sample of primarily middle-aged adults. Contrary to our expectations, we did not find prospective associations of EF with age-related decline in physical functioning in the overall sample or in any race/sex subgroups. However, our findings revealed robust cross-sectional relations between EF and physical performance averaged across baseline and follow-up. This finding is consistent with previous research indicating that EF is involved in planning and execution of movement, as well functional and disability status in older adults. Future studies should expand on this work by examining how rates of change in EF, in addition to levels of EF, influence rates of physical performance decline in diverse populations. We also found that sex-related variation in lower extremity strength and endurance over time that challenges the consensus that women are at greater risk for age-related physical disability than men. Rather, during middle age, our findings suggest that men may be more vulnerable to decline in lower extremity strength and endurance. Finally, these effects persisted following adjustment for potential mediating variables, namely BMI, hypertension, diabetes, and educational attainment.

Our study may provide useful information for screening of individuals at risk for age-related physical function decline or disability. Because the present study's sample was younger than those used in most prior studies, these results may indicate early signs of emerging physical disability. Future research should focus on elucidating biopsychosocial mediators of the associations observed in this study, as well as examining withingroup heterogeneity in physical function trajectories. In particular, our study offers justification for prospective neuroimaging

Supplementary Material

Supplementary data is available at *The Journals of Gerontology, Series B: Psychological Sciences and Social Sciences* online.

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Data Availability: Data and analytic methods are available upon request to researchers with valid proposals who agree to the confidentiality agreement required by our Institutional Review Boards. We publicize our policies on our website (https://handls.nih.gov/). Requests for data access may be sent to A. B. Zonderman (coauthor) or the study manager, Jennifer Norbeck, at norbeckje@mail.nih. gov. This study was not preregistered.

Conflict of Interest

None reported.

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