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Metabolic Syndrome and Physical Performance: The Moderating Role of Cognition among Middle-to-Older-Aged Adults

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Abstract

Objective: Mobility limitation and cognitive decline are related. Metabolic syndrome (MetS), the clustering of three or more cardiovascular risk factors, is associated with decline in both mobility and cognition. However, the interrelationship among MetS, mobility, and cognition is unknown. This study investigated a proposed pathway where cognition moderates the relationship between MetS and Mobility. **Method:** Adults ages 45–90 years were recruited. MetS risk factors and mobility performance (Short Physical Performance Battery (SPPB) and gait speed) were evaluated. Cognition was assessed using a comprehensive neuropsychological battery. A factor analysis of neuropsychological test scores yielded three factors: executive function, explicit memory, and semantic/contextual memory. Multivariable linear regression models were used to examine the relationship among MetS, mobility, and cognition. **Results:** Of the 74 participants (average age 61 ± 9 years; 41% female; 69% White), 27 (36%) participants manifested MetS. Mean SPPB score was 10.9 ± 1.2 out of 12 and gait speed was 1.0 ± 0.2 m/s. There were no statistically significant differences in mobility by MetS status. However, increase in any one of the MetS risk factors was associated with decreased mobility performance after adjusting for age and gender (SPPB score: β (SE) -.17 (0.08), $p < .05$; gait speed: -.03 (.01), $p < .01$). Further adjusting for cognitive factors (SPPB score: explicit memory .31 (.14), $p = .03$; executive function 0.45 (0.13), $p < .01$; gait speed: explicit memory 0.04 (0.02), $p = .03$; executive function 0.06 (0.02), $p < .01$) moderated the relationships between number of metabolic risk factors and mobility. **Conclusion:** The relationship between metabolic risk factors and mobility may be moderated by cognitive performance, specifically through executive function and explicit memory.

Keywords: Gait speed, Cardiovascular diseases, Executive function, Aged, Neuropsychological tests

INTRODUCTION

Metabolic syndrome (MetS) is a collection of cardiovascular risk factors (abdominal obesity, hypertriglyceridemia, reduced levels of high-density lipoprotein–cholesterol (HDL-C), high blood pressure, and impaired glucose tolerance) and contributes to cardiovascular morbidity and mortality (Aguilar, Bhuket, Torres, Benny, & Wong, 2015; Alberti et al., 2009; Ford, Giles, & Dietz, 2002). In the United States, it is estimated that the prevalence of MetS is approximately 35% among adults and nearly half among older adults who are over 60 years of age (Aguilar et al., 2015). In addition to MetS being a risk factor for cardiometabolic and cerebrovascular diseases, accumulating evidence suggests the MetS is associated with a decline in mobility and cognitive performance.

Previous studies demonstrate that the manifestation of MetS is associated with self-reported mobility limitation and poorer physical performance (Beavers et al., 2013; Blazer, Hybels, & Fillenbaum, 2006; Everson-Rose et al., 2011; Penninx et al., 2009; Viscogliosi, Donfrancesco, Palmieri, & Giampaoli, 2017). In a cohort study of healthier older adults, researchers found that older adults with MetS had approximately 50% greater chance of developing mobility limitation over 4 years compared to older adults without MetS (Penninx et al., 2009). Interestingly, in addition to MetS status, researchers also observed significant associations between increase in any of the MetS risk factors with self-reported mobility limitation (Penninx et al., 2009),

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suggesting accumulation of any metabolic abnormality contributing to mobility limitation.

In addition, there is substantial evidence supporting the association between the presence of MetS and cognitive decline among older adults (Leritz, McGlinchey, Kellison, Rudolph, & Milberg, 2011). Specifically, MetS is associated with poorer performance on measures of attention (Wooten et al., 2019), executive function (Falkowski, Atchison, Debutte-Smith, Weiner, & O'Bryant, 2014; Rouch et al., 2014), memory (Rouch et al., 2014), and perceptual speed (Kazlauskaite et al., 2020). Several structural imaging studies reported associations between MetS and lesions in the white matter underlying frontal subcortical brain regions (Bokura, Yamaguchi, Iijima, Nagai, & Oguro, 2008; Portet et al., 2012; Tiehuis et al., 2014). Especially in the subcortical white matter, lesions are associated with decline in processing speed and executive function (Prins et al., 2005). Prior studies in our laboratory have observed relationships between MetS and reduced cortical thickness in frontal brain regions (Schwarz et al., 2018), supporting the idea that the multiple co-occurring risk factors of MetS seem to target frontal and prefrontal brain regions, including both the gray matter and the white matter underneath. Given what is known about the role of the frontal lobe and prefrontal cortex in multiple aspects of cognition, it logically follows that the neural impact of MetS may lead to declines in cognitive processes such as executive function and attention. More specifically, cognitive tasks that are more attentionally demanding and complex, such as those requiring selective attention, inhibition, and self-directed retrieval, are the most likely to be affected.

A good deal of research demonstrates a close association between cognitive decline and mobility limitation (Ambrose et al., 2010; Mielke et al., 2013; Pedersen et al., 2014; Rodriguez-Molinero et al., 2019). For example, walking may seem like a simple task but it is quite complex. Beyond the physical capabilities, walking requires the ability to navigate and pay attention to various environmental and postural conditions (Mirelman, Shema, Maidan, & Hausdorff, 2018; Montero-Odasso, Verghese, Beauchet, & Hausdorff, 2012). Thus, successful walking draws upon cognitive functions such as executive function and attention (Mirelman et al., 2018; Montero-Odasso et al., 2012). Evidence suggests that gait instability and slow gait speed are associated with decline in attention, executive function, and working memory (Montero-Odasso et al., 2012). In fact, brain regions linked to executive function and attention (prefrontal cortex and frontal lobes) are activated during walking-while-talking conditions, during which participants are typically asked to perform a moderately complex mental task while talking (Doi et al., 2013; Holtzer et al., 2011; Poole et al., 2018). The fact that this multitasking recruits these regions provided additional support for the connection between cognition and walking. Furthermore, decline in executive function and attention is associated with mobility limitation and progression to dementia (Montero-Odasso et al., 2012).

Despite the general consensus of the impact of MetS on mobility and cognition, little is known about the interrelationship among MetS, mobility, and cognition. Among the studies that examined the relationship between MetS and mobility and accounted for cognitive function, cognitive function did not statistically influence the relationship between MetS and mobility limitation, leading to the conclusion that the relationship between MetS and mobility limitation was independent of cognitive status (Blazer et al., 2006; Viscogliosi et al., 2017). However, these studies implemented general measures of global cognition using Mini-Mental State Examination (MMSE) (Viscogliosi et al., 2017) or 10-item short Portable Mental Status Questionnaire (PMSQ) (Blazer et al., 2006) rather than more broadly examining cognitive domains that may impact MetS and mobility such as attention, executive function, and memory; thus, they may have used measures insensitive to detect the association. Therefore, the purposes of this study were (1) to investigate the relationship between MetS and mobility limitation and (2) to examine the impact of broad cognitive domains including attention, memory, executive function, and language in the relationship between MetS and mobility. We hypothesized that MetS is associated with mobility limitation and this relationship would be moderated specifically by executive function.

METHODS

This study was an ancillary study conducted from the Cerebrovascular Integrity and Risk for Cognitive decline in Aging (CIRCA) (Wooten et al., 2019). CIRCA was a cross-sectional study of middle-to-older-aged adults designed to investigate the effects of vascular risk factors on cognition (Wooten et al., 2019). A total of 150 participants were enrolled in the CIRCA study and 81 participants completed physical performance testing. Physical performance was introduced after enrollment of the CIRCA study was initiated; hence, the first 70 participants completed their assessment without undergoing the physical performance measures. Of the 81 participants, five participants missed several medical examination values; thus, 76 participants' physical performance measures were evaluated in the present study. All study protocol and consent procedures were approved by the Institutional Review Board of the Department of Veterans Affairs Boston Healthcare System.

Recruitment/Eligibility

Targeted recruitment was used to enroll middle-to-older-aged adults at a high risk for MetS through direct clinic recruitment in the Department of Veterans Affairs Boston Healthcare System. Additional recruitments were conducted throughout the greater Boston, MA, area via postings on the Massachusetts Bay Transit Authority (MBTA) subway system. The inclusion criteria for CIRCA were participants had to be between 45 and 90 years of age and ability to communicate in English. Exclusion criteria for the study included significant medical disease (e.g., overt cardiovascular,

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hepatic, or renal disease), prior major surgery (e.g., brain or cardiac surgery), head trauma (e.g., loss of consciousness for more than 30 min), neurological disorders (e.g., Parkinson's disease or dementia), history of severe or current psychiatric disorders (e.g., schizophrenia or major depressive disorder), history or current diagnosis of drug abuse or dependency, or any contraindication to magnetic resonance imaging (MRI). Participants were not excluded based on their self-reported diabetes status.

Metabolic Syndrome Risk Factors

All participants were evaluated for the MetS risk factors and stratified to either the MetS or non-MetS group. MetS classification was based on the National Cholesterol Education Program Adult Treatment Program (NCEP ATP-III) guidelines (Alberti et al., 2009). Participants were categorized to MetS if they met three or more MetS risk factors and participants were categorized to non-MetS if they had less than three of the following MetS risk factors: (1) abdominal obesity (waist circumference ≥ 102 (men)/88 (women) cm); (2) hypertriglyceridemia (triglycerides ≥ 150 mg/dL or medication for elevated triglycerides); (3) reduced levels of HDL–C (HDL-C < 40 (men)/50(women) mg/dL or medication for treating low HDL-C); (4) high blood pressure (systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg or medication for hypertension); and (5) impaired glucose tolerance (fasting plasma glucose ≥ 100 mg/dL or medication for elevated glucose) (Alberti et al., 2009). Blood pressure was taken while seated, and an average of two measurements was used to determine the final BP value. Primary focus of the study was the comparison between MetS and non-MetS. In addition to the MetS status, the number of positive MetS risk factors was used as a continuous independent variable for the present study.

Neuropsychological Assessment

Participants underwent a comprehensive neuropsychological battery, assessing broad domains of cognition: attention, memory, executive function, and language. Neuropsychological tests including the Digit Span from the Wechsler Adult Intelligence Scale (WAIS; (Lezak, Howieson, Loring, Hannay, & Fischer, 2004)), the Boston Naming Test (BNT; (Kaplan, Goodglass, & Weintraub, 1983)), the California Verbal Learning Test (CVLT; (Delis, Kramer, Kaplan, & Ober, 1987)), Brief Visuospatial Memory Test (BVMT; (Benedict, Schretlen, Groniner, Dobraski, & Shpritz, 1996)), Delis-Kaplan Executive Function System (D-KEFS; (Delis, Kaplan, & Kramer, 2001)), and Wechsler Memory Scale (WMS; (Wechsler, 1945)) were assessed. Specifically, total raw scores were used for Digit Span (forward, backward, sequencing) and BNT and total and delayed recalls were used for BVMT. Total score (trial 1–5) and long delay free recall were used for CVLT. Immediate and delayed logical story memory scores were used from the WMS. Subsets of D-KEFS including color-word interference (inhibition total time), verbal fluency (letter fluency score/category fluency score), number/letter switching trails (total time), which assess a variety of verbal and nonverbal executive functions, were used. Participants with inadequate task efforts during neuropsychological tests were excluded. Suboptimal effort was defined using the forced choice recognition trial of CVLT (total score < 16; (Schwartz et al., 2016)) and the Reliable Digit Span ((total RDS < 8) (Schroeder, Twumasi-Ankrah, Baade, & Marshall, 2012)).

Physical Performance

Physical performance was assessed using the Short Physical Performance Battery (SPPB). The SPPB is a composite measure assessing three functional tasks: balance, walking, and chair stand (Guralnik et al., 1994). The balance score is based on participants' ability to stand for 10 s with feet in different standing positions (side by side, semitandem, and tandem). The walking score is based on participants' walking time over a 4 meter walking course. Lastly, chair stand score is based on participants' time to complete five chair stands, as quickly as possible. Each domain is scored between 0 and 4 with a maximum score of 12 (higher score—better performance). Small and large clinically meaningful changes in SPPB are 0.5 point and 1.0 point, respectively (Pahor et al., 2006; Perera, Mody, Woodman, & Studenski, 2006). For the present study, total SPPB score and gait speed, which was calculated by dividing the distance (4-meter) by walking time, were used as mobility outcomes. Small and large clinically meaningful changes in gait speed are characterized as 0.05 m/s and 0.10 m/s, respectively (Pahor et al., 2006; Perera et al., 2006).

Other Measures

Sociodemographic and health information including age, gender, race, educational attainment, and self-reported general health was recorded. Height and weight were measured using standard methods and body mass index (BMI) was calculated.

Statistical Analysis

The dependent variable for the study was mobility (SPPB score and gait speed). To investigate the relationship between MetS and mobility, we first compared mobility performance by MetS status. Secondly, we examined the association between mobility performance and the number of positive MetS risk factors as continuous variables. To examine the impact of cognition on the relationship between MetS and mobility, we investigated the moderating effect of cognition in the relationship between mobility and number of positive MetS risk factors. Statistical analyses were performed using SPSS software (Version 26, Armonk, NY: IBM Corp.). Statistical significance was determined with a two-tailed test at p value of less than 0.05. Findings were also interpreted in terms of effect sizes and clinically meaningful differences. Effect sizes (cohen's d) were calculated by taking the mean difference between MetS and non-MetS and dividing by the pooled standard deviation (Cohen, 1989). Effect sizes of .20,

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Table 1. Participant characteristics according to metabolic syndrome ($N = 74$)

	All ($N = 74$)	MetS − ($n = 47$)	MetS + ($n = 27$)	p value*
		Mean ± SD		
Age (years)	61.86 ± 9.29	59.47 ± 8.99	66.04 ± 8.42	<.01
BMI (kg/m^2)	28.14 ± 6.07	26.89 ± 6.38	30.33 ± 4.86	.02
SPPB Score	10.91 ± 1.16	11.09 ± 1.14	10.59 ± 1.15	.08
Gait Speed (m/s)	0.99 ± 0.16	1.01 ± 0.17	0.94 ± 0.14	.06
Chair Stands (s)	11.75 ± 3.98	11.42 ± 4.29	12.33 ± 3.36	.35
Balance Score	3.88 ± 0.40	3.94 ± 0.32	3.78 ± 0.51	.11
		n (%)		
Race: White	50 (69.4)	30 (66.7)	20 (74.1)	.60
Sex: Female	30 (40.5)	21 (44.7)	9 (33.3)	.46
Education:				
Some HS or HS grad	8 (10.8)	5 (10.6)	3 (11.1)	.99
Some college	17 (23.0)	10 (21.3)	7 (25.9)	
College graduate	18 (24.3)	12 (25.5)	6 (22.2)	
Postgraduate education	31 (41.9)	20 (42.6)	11 (40.7)	
General Health:				
Excellent	22 (29.7)	19 (40.4)	3 (11.1)	.01
Good	45 (60.8)	26 (55.3)	19 (70.4)	
Fair	7 (6.5)	2 (4.3)	5 (18.5)	

*Independent t test or chi-square.

.50, and .80 have been used to represent small, moderate, and large effect sizes, respectively (Cohen, 1989).

A factor analysis was used to reduce the neuropsychological data to empirically derived neuropsychological factors (DeCoster, 1998). A total of 12 raw neuropsychological test scores was included in the principal component analysis. A minimum eigenvalue for extraction was set to one and varimax rotation was used to derive orthogonal factor scores. Items with a minimum factor loading of |0.40| were considered relevant.

The distribution of all variables was inspected using descriptive statistics. Demographic, health characteristics, and mobility performance were examined according to MetS status using independent t tests for continuous measures or chi-square tests for categorical measures. Multivariable linear regression models adjusting for potential confounders including age and gender (model 1) and cognitive domain factors uncovered from the factor analysis (model 2) were used to examine the relationships between the number of MetS risk factors, mobility performance, and cognition.

The influence of outliers on all resulting models was tested by calculating Cook's distance and leverages. We used the thresholds of $4/(n\text{-}k\text{-}1)$ for Cook's distance (Hair, Anderson, Tatham, & Black, 1998) and $2\,p/n$ for leverage (Hoaglin & Welsch, 1978), where n is the number of observations and k/p is the number of predictors to identify overly influential values, which were deemed as outliers and removed from the final analyses.

RESULTS

Of the 76 participants, two statistically influential outliers for mobility performance were identified and removed from the analyses as described in the methods. There was no difference in participant characteristics, mobility performance, and number of MetS risk factors between participants who were included in the data and participants who had missing or influential outliers.

The average age for the remaining 74 participants was 62 ± 9 years. Totally, 41% were female, more than half (66%) had a college degree, 69% were of white race, and 11% self-reported diabetes. A total of 36% of the participants had MetS and had an average SPPB score of 10.9 ± 1.2 points and gait speed of 0.99 ± 0.16 m/s. Table 1 provides a description of participants' characteristics and mobility outcomes according to MetS status. Compared to participants who did not have MetS, participants with MetS were older (7 ± 2 years), had higher BMI (3.4 ± 1.4 m/kg^2), and reported fair health (all $p < .05$). We observed effect sizes nearing moderate effect and clinically meaningful but not statistically significant differences as a function of MetS status in mobility performance (SPPB score: 0.05 ± 0.3 points, $p = .08$, $d = .44$; gait speed: 0.07 ± 0.04 m/s, $p = .06$, $d = .45$). Figure 1 displays the description of mobility performance based on the number of MetS risk factors. We did not observe statistically significant differences in either the SPPB score ($p = .24$) or gait speed ($p = .08$) based on the number of MetS risk factors.

Factor analysis yielded three factors (Table 2). The three factors explained a total of 73.4% of the variance for the entire set of variables. The first factor extracted was "explicit memory" and accounted for 51.7% of the variance, with high loading from CVLT and BVMT items. The second factor was "executive function" and accounted for 12.9% of the variance with high loading from D-KEFS and Digit Span. The third factor was "semantic/contextual memory" and accounted for 8.8% of variance, with loading from WMS and BNT.

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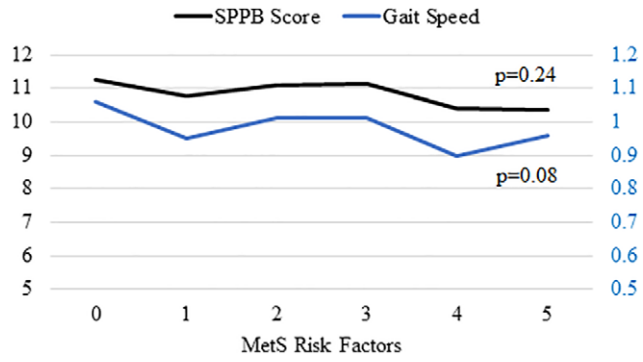

Fig. 1. Mobility Performance based on the number of MetS risk factors.

Table 3 displays the coefficients describing the relationship between the number of MetS risk factors and SPPB score. On average, an increase in one MetS risk factor was associated with 0.17 (SE: .08, $p = .04$) point decrease in total SPPB score after adjusting for age and gender. Further adjustments for cognitive domain factors attenuated the relationship between the number of MetS risk factors and SPPB score. Greater explicit memory and executive function scores were associated with higher SPPB scores (explicit memory: $\beta = .31$ (SE: .14), $p = .03$; executive function: $\beta = .45$ (SE: .13), $p < .01$).

Table 4 displays the coefficients describing the relationship between the number of MetS risk factors and gait speed. On average, an increase in any one of MetS risk factors was associated with .03 m/s (SE: .01, $p < .01$) reduction (worse) in gait speed after adjusting for age and gender. Further adjustments for cognitive domain factors attenuated the relationship between number of MetS risk factors and gait speed ($p > .05$). Increase in explicit memory and executive function scores were associated with faster gait speed (explicit memory: $\beta = .04$ (SE: .02), $p = .03$; executive function: $\beta = .06$ (SE: .02), $p < .01$).

DISCUSSION

The major findings of this study demonstrate that the manifestation of MetS has a negative impact on mobility among middle-to-older-aged adults and increase in any of the MetS risk factors is associated with poorer mobility performance. The findings also support the overarching hypothesis that the relationship between MetS and mobility is moderated by cognitive performance, specifically through executive function and explicit memory. We observed a clinically meaningful and close-to-moderate effect sizes but not statistically significant difference in mobility performance based on MetS status. Specifically, the differences observed in both SPPB and gait speed as a function of MetS status exceeded the clinically meaningful differences for both parameters and approached statistical significance. Furthermore, an increase in any one of the MetS risk factors (abdominal obesity, hypertriglyceridemia, reduced levels of HDL-C, high blood pressure, impaired glucose tolerance) was associated with lower total physical performance score and slower gait speed. As hypothesized, cognitive domains, specifically executive function and explicit memory, moderated the relationship between MetS and mobility.

Our results are consistent with other studies that examined the relationship between MetS and mobility, which found that MetS was associated with poorer mobility (Beavers et al., 2013; Blazer et al., 2006; Everson-Rose et al., 2011; Okoro et al., 2006; Penninx et al., 2009; Viscogliosi et al., 2017). In addition, similar to previous studies that examined the relationship between the number of MetS risk factors and mobility (Okoro et al., 2006; Penninx et al., 2009), we also observed a strong linear relationship between the number of MetS risk factors and mobility performance, implying that an increase in any metabolic risk factors is associated with poorer mobility performance.

Nevertheless, our study is the first to identify cognitive domains such as executive function and explicit memory that potentially moderate the association between MetS and mobility. While prior studies desired to test these relationships, they used general measures of basic cognitive functioning (MMSE (Viscogliosi et al., 2017), PMSQ (Blazer et al., 2006)), as opposed to a more comprehensive assessment. In our sample, when we included the three cognitive factors (explicit memory, executive function, and semantic/contextual memory) in the models that evaluated the relationship between the number of MetS risk factors and mobility, the previous associations attenuated. These findings suggest that cognitive domains specifically executive function and explicit memory explained a portion of the association between the number of MetS risk factors and mobility.

We found that the executive function factor score was a significant moderator in the relationship between greater vascular risk and lower SPPB score and slower gait speed. This is consistent with prior findings of higher levels of cardiovascular risks and poorer performance on tasks purported to assess executive function (Alcorn et al., 2019; Rouch et al., 2014). Furthermore, there is substantial evidence supporting the important role executive function plays in controlling gait (Parihar, Mahoney, & Verghese, 2013), where decline in executive function is associated with gait dysfunction and slowing of gait (Mirelman et al., 2018; Montero-Odasso et al., 2012; Poole et al., 2018). Given that brain regions linked to executive function and attention (prefrontal cortex and frontal lobes) are activated during walking (Doi et al., 2013; Holtzer et al., 2011; Poole et al., 2018), problems in gait and cognition may share common underlying neural substrates. Therefore, it is possible that the metabolic risk factors, also shown to affect brain regions that support executive function, may lead to executive dysfunction, thus leads to poorer physical performance and slowing of the gait.

Furthermore, although there is a general consensus that executive function has the strongest association with gait speed among the cognitive domains (Doi et al., 2014; Toots, Taylor, Lord, & Close, 2019), previous studies also observed the association between gait speed and verbal, visual, and episodic memory (explicit memory) (Doi et al., 2014;

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Table 2. Item loadings from factor analysis of neuropsychological variables using Varimax rotation

	Factors		
	Explicit memory	Executive function	Semantic/contextual memory
CVLT, Total Trial 1–5	**.845**	.294	.215
CVLT, Long Delay Free Recall	**.826**	.316	.073
BVMT, Total Recall	**.780**	.117	**.440**
BVMT, Delayed Recall	**.767**	–.004	**.440**
D-KEFS, Letter Fluency	.248	**.797**	.168
D-KEFS, Category Fluency	.394	**.727**	.033
D-KEFS, Inhibition	.018	**–.655**	–.091
DS, Total	.168	**.624**	**.509**
D-KEFS, Trails	–.342	**–.540**	**–.434**
WMS, Imeediate Memory	.388	.030	**.853**
WMS, Delayed Memory	**.400**	.256	**.767**
BNT, Total	.047	**.530**	**.690**

Note. CVLT = California Verbal Learning Test; BVMT = Brief Visuospatial Memory Test; D-KEFS = Delis–Kaplan Executive Function System; DS = Digit Span; WMS = Wechsler Memory Scale; BNT = Boston Naming Test.
The bold values are the factor loading >|.40| were considered relevant items of the factor.

Table 3. Association between total SPPB score with number of MetS risk factors: adjusted for age, gender, and cognitive domains ($n = 74$)

	Model 1 ($n = 74$)			Model 2 ($n = 72$)		
Variable	β (SE)	p-value	R^2	β (SE)	p-value	R^2
# MetS Risk Factors	–.17 (.08)	.04	.07	–.08 (.08)	.33	.26
Age	.01 (.02)	.59		–.002 (.02)	.90	
Gender	.07 (.28)	.80		–.11 (.27)	.70	
Factor 1 (Explicit Memory)				.31 (.14)	.03	
Factor 2 (Executive Function)				.45 (.13)	<.01	
Factor 3 (Semantic/Contextual Memory)				–.20 (.13)	.89	

Multivariable linear regression models with total SPPB score as dependent variables.

Table 4. Association between gait speed with number of MetS risk factors: adjusted for age, gender, and cognitive domains ($n = 74$)

	Model 1 ($n = 74$)			Model 2 ($n = 72$)		
Variable	β (SE)	p-value	R^2	β (SE)	p-value	R^2
# MetS Risk Factors	–.03 (.01)	<.01	.11	–.02 (.01)	.18	.27
Age	.003 (.002)	.15		.001 (.002)	.75	
Gender	–.04 (.04)	.26		–.05 (.04)	.18	
Factor 1 (Explicit Memory)				.04 (.02)	.03	
Factor 2 (Executive Function)				.06 (.02)	<.01	
Factor 3 (Semantic/Contextual Memory)				.02 (.02)	.264	

Multivariable linear regression models with gait speed as dependent variables.

Holtzer, Wang, & Verghese, 2012; Watson et al., 2010). In our study, we observed the strongest moderating effect from the executive function factor but also observed significant moderating effects from explicit memory factor.

Furthermore, it is also possible that the two cognitive domains identified in the present study, executive function and explicit memory, are reflective of two pathways in which metabolic risk factors may affect mobility. Dementia is a disease that affects memory, language, planning, and problem-solving, and most prevalent subtypes of dementia are Alzheimer's disease and vascular dementia (Javanshiri et al., 2018). While Alzheimer's disease is neuropathologically defined as the presence of amyloid plaques and accumulation of neurofibrillary tangles composed of filamentous tau

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protein (Perl, 2010), vascular dementia is a cognitive disorder that is derived from cerebrovascular cases (Iadecola, 2013). Previously, cardiovascular disease, cerebrovascular disease, atherosclerosis, hypertension, diabetes mellitus, and stroke were considered risk factors for developing vascular dementia (Song, Lee, Park, & Lee, 2014). However, recent evidence suggests that these risk factors are also common in Alzheimer's disease (Javanshiri et al., 2018); thus, cardiometabolic abnormalities may impact both dementia subtypes. While Alzheimer's disease is commonly associated with impaired explicit memory (Bondi & Kaszniak, 1991), executive dysfunction is associated with both Alzheimer's disease and vascular dementia (McGuinness, Barrett, Craig, Lawson, & Passmore, 2010). Hence, the results from our moderation analyses may be reflective of the two pathways derived from the dementia subtypes where executive function and explicit memory moderate the relationship between cardiometabolic risk factors and mobility performance.

Alternatively, the memory measures that comprised the explicit memory factor were those that are thought to rely more on executive function abilities than those that loaded onto other factors (Logical Memory) (Brooks, Weaver, & Scialfa, 2006; Delis et al., 1987; Stuss & Levine, 2002). Successful performance on the CVLT, a word-list learning task, relies on an individual's ability to successfully organize, encode, and retrieval of item-specific information (Vanderploeg, Schinka, & Retzlaff, 1994). To add, BVMT is nonverbal memory task that, by nature, is more novel and thus more reliant on executive abilities. While these abilities primarily reflect explicit memory, there are considerable aspects to this that rely on executive function. Thus, the relationship between MetS and mobility may be primarily influenced by aspects of executive function.

There are limitations to our study that have to be addressed. The sample size of the present study was relatively small; thus, our nonstatistical significant findings that exceeded clinically meaningful thresholds with medium effect sizes could be due to a lack of statistical power. Our study was a cross-sectional study and causality cannot be ascertained. Thus, we have not established a temporal relation between change in MetS status, mobility performance, and cognitive function. Longitudinal studies are necessary to examine the causal relationship between MetS, cognition, and mobility. In addition, our sample population is relatively well educated and since education impacts cognitive performance (Guerra-Carrillo, Katovich, & Bunge, 2017), our results may not generalize the larger population at hand.

Despite these limitations, several strengths of this study are noteworthy. We used well-studied, validated tests to assess for both mobility and neuropsychological measurements. This study is the first to examine the relationship between MetS and mobility and how cognition may influence this relationship using standardized neuropsychological measurements. Our study is an important step in developing scientific understanding of the relationship between MetS, mobility, and cognition, which will help assist in the development of new strategies and treatments to improve cognition and mobility in older adults with MetS.

CONCLUSION

In conclusion, MetS is associated with mobility limitation and an increase in any one of MetS risk factors was associated with poorer mobility performance. Our findings suggest that lower mobility performance may be explained by performance on measures of executive function and explicit memory. Longitudinal research is needed to establish the causal pathways among MetS, mobility, and cognition.

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CONFLICT OF INTEREST

The authors have nothing to disclose.

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