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Complex Walking Tasks and Risk for Cognitive Decline in High Functioning Older Adults

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Abstract

Background: Performance on complex walking tasks may provide a screen for future cognitive decline.

Objective: To identify walking tasks that are most strongly associated with subsequent cognitive decline.

Methods: Community-dwelling older adults with Modified Mini-Mental State (3MS) > 85 at baseline ($n = 223$; mean age = 78.7, 52.5% women, 25.6% black) completed usual-pace walking and three complex walking tasks (fast-pace, narrow-path, visuospatial dual-task). Slope of 3MS scores for up to 9 subsequent years (average = 5.2) were used to calculate a cognitive maintainer (slope θ) or decliner (slope <0) outcome variable. Logistic regression models assessed associations between gait speeds and being a cognitive decliner. A sensitivity analysis in a subsample of individuals ($n = 66$) confirmed results with adjudicated mild cognitive impairment (MCI) or dementia at 8–9 years post-walking assessment.

Results: Cognitive decliners were 52.5% of the sample and on average were slower for all walking tasks compared to maintainers. In models adjusted for demographic and health variables, faster fast-pace (OR = 0.87 per 0.1 m/s, 95% CI: 0.78, 0.97) and dual-task (OR = 0.84 per 0.1 m/s, 95% CI: 0.73, 0.96) gait speeds were associated with lower likelihood of being a cognitive

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decliner. Usual-pace gait speed was not associated (OR = 0.96 per 0.1 m/s, 95% CI: 0.85, 1.08). Results were nearly identical in analyses with adjudicated MCI or dementia as the outcome.

Conclusion: Fast-pace and dual-task walking may provide simple and effective tools for assessing risk for cognitive decline in older individuals with high cognitive function. Such screening tools are important for strategies to prevent or delay onset of clinically meaningful change.

Keywords

Cognitive disorders; Epidemiology; Geriatrics; walking speed

INTRODUCTION

Cognitive impairment and dementia increase with age and carry a heavy public health burden [1]. Early clinical indicators of risk for future cognitive impairment are needed in order to aid in prevention, planning, and treatment. Decline in gait speed over time has emerged as an early marker of risk for cognitive impairment [2] and age-related changes in gait may appear earlier than cognitive changes [3, 4]. Further, gait speed decline shares neural correlates with cognitive impairment, namely smaller hippocampal volume [2].

Several complex walking tasks have been utilized in older adults to challenge the overlearned motor task of walking in the environmentally-controlled settings of the clinic or laboratory [5]. These complex walking tasks tap into attentional networks [6] and thereby, provide a stress test of the central motor control system that may uncover deficits earlier than would be observed using usual gait speed. Therefore, complex walking tasks may have important clinical value in detecting early brain changes in those with high cognitive function, the group most likely to benefit from early detection. Complex walking tasks include cognitive dual-task, fast-pace, and narrow-path walking. Dual-task walking requires a person to walk while completing a concurrent, typically cognitively challenging, task. Greater gait slowing during cognitive dual-task walking is associated with conversion from either cognitively healthy status [7] or mild cognitive impairment (MCI) [8] to dementia. However, cognitive dual-task walking may be difficult to standardize clinically due to differences in types of secondary cognitive tasks [9] and difficulty in accounting for task prioritization [10]. Other complex walking tasks, such as fast-paced or narrow-path walking, may be just as effective at identifying individuals at risk for dementia [11, 12] but could be easier to implement in the clinic [5].

In a cohort of community-dwelling older adults without cognitive impairment, we compared associations of performance on several complex walking tasks with risk of cognitive decline for up to 9 years after walking assessment. We also assessed associations in a subsample who had adjudicated dementia status 8–9 years after the walking assessment.

METHODS

Sample

The Health Aging and Body Composition (Health ABC) study enrolled communitydwelling black and white adults at two sites in Pittsburgh and Memphis in 1997–1998. To be eligible, participants had to be 70–79 years old and be free of self-reported difficulties in performing activities of daily living, walking a quarter mile, or climbing 10 steps without resting. Men and black participants were oversampled. Participants at the Pittsburgh site were recruited to participate in a dual-task substudy during the 2002–2003 study visit ($n =$ 377) if they agreed to participate and were able to complete the tasks [13]. Cognitive data was obtained through 2012.

The primary analytic sample included participants who completed a cognitive dual-task, fast-paced, and narrow-path walking in 2002–2003, had a Modified Mini-Mental State (3MS) [14] score 85 at the 2001–2002 visit, and had at least one additional 3MS through the end of follow-up in 2012 ($n = 223$). Surviving participants were invited for an in-depth neurocognitive study from 2006–2012; a subset comprised the secondary analytic sample and included those with complete dual-task data, a 3MS score 85 at the 2001–2002 visit, and cognitive adjudication in 2010–2012 ($n = 66$).

Compared to participants who attended the 2002–2003 visit at the Pittsburgh site but were not included in our sample, participants in our primary analytic sample were less likely to be black (25.6% versus 42.9%, $p < 0.001$), to have high school or less education (47.7% versus 58.8%, $p = 0.001$), and to have diabetes (20.6% versus 27.2%, $p = 0.03$). Compared to those excluded, participants in our primary analytic sample also had a higher body mass index (BMI; 28.3 \pm 4.6 versus 27.2 \pm 5.0, $p = 0.001$), fewer depressive symptoms (6.2 \pm 6.4 versus 7.8 \pm 7.1, $p = 0.002$), higher 3MS scores (by definition of our analytic sample: 95.0 ± 3.8 versus 89.6 \pm 9.4, p < 0.0001), and faster usual walk pace (1.16 \pm 0.24 m/s versus 1.05 \pm 0.30 m/s, p < 0.0001). No other demographic or health differences were observed.

Walking tasks

Usual pace, fast-paced, and narrow-path gait were collected as part of the clinical visit in 2002–2003. For all tasks, participants began walking before the start line and time was measured from the first footfall over the start line until the first footfall after the finish line. Walk times were converted to m/s. Participants were first asked to walk at their usual pace along a 20-m corridor. They were then asked to "walk as fast as you can" along the same 20 m corridor. During narrow-path walking, participants were asked to walk a 6-m long path marked with tape on the floor. The path was 20 cm wide and participants were instructed to walk at a comfortable pace and keep their feet within the lines [15]. Up to three attempts were made and only walk times where participants did not step outside of the lines were used.

The cognitive dual-task walking paradigm using a visuospatial cognitive task was previously described [16]. Briefly, participants were given a time of day prompt and were asked to visualize the time of day as displayed on an analog clock. Participants then responded 'same' or 'different' based on whether the hands of the clock were on the same side of a line

passing through the 12 and 6 on the clock face or on different sides. The visuospatial task was completed both while seated and while walking along a 20-m corridor to allow for assessment of cognitive performance during both single- and dual-task. Response accuracy and reaction time were recorded, but largely did not differ between seated and walking conditions and were not assessed further. Single-task, usual pace walking was also completed during the same visit along the same corridor. Walk times were recorded from the time that the first toe crossed the start and finish lines marked by tape on the floor and were converted to m/s.

Percent change in gait speed from usual to complex conditions were calculated as secondary outcomes for each walking task. For narrow-path and dual-task conditions, this represents the cost in gait speed from adding the secondary task (staying within the narrow-path or cognitive challenge). Narrow-path percent change in gait speed was calculated as: ((narrowpath speed – usual pace speed)/usual pace speed) *100. Dual-task percent change in gait speed was calculated as: ((Dual-task gait speed – single-task gait speed)/single-task gait speed)*100. For fast-pace, the percent change in gait speed indicates the participant's ability to increase their speed on command. Fast-paced percent change in gait speed was calculated as: ((fast-paced gait speed – usual pace speed)/usual pace speed)*100). For all of our percent change in gait speed variables, negative values indicate the participant slowed down from usual-pace to complex walking whereas positive values indicate they sped up.

Cognitive decline

Participants were classified as cognitive maintainers or decliners based on repeated 3MS assessments for up to 9 years after the walking assessment, consistent with previous studies [17, 18]. Briefly, changes in 3MS scores over time were defined using a linear mixed model with random intercepts and slopes, adjusted for age, sex, race, education, and time between first and last 3MS assessment. The 3MS was measured in the full sample during clinic visits at years 2001–2002, 2006–2007, and 2007–2008. In addition, a subset of participants completed the 3MS in years 2003–2004 and 2005–2006 and in 2009–2010 and 2011–2012. Mixed models utilized 3MS scores from all available time points for all participants. Participants with predicted slopes of 0 or greater, indicating no change or improvement in 3MS over time, were classified in maintainers. Participants with predicted slopes of less than 0 were classified as decliners.

Dementia adjudication

Cognitive status was clinically adjudicated among participants at the Pittsburgh site during the 2010–2012 site visit from data collected at that and prior visits, as described elsewhere [19]. Participants were characterized as having normal cognition, MCI, or dementia. Due to the small sample sizes, outcomes were analyzed as cognitively normal or cognitively impaired (MCI or dementia).

Covariates

At baseline, demographic data including age, race, sex, and education were self-reported. Depressive symptoms were assessed by the Center for Epidemiologic Studies Depression Scale (CES-D) short form [20]. Digit Symbol Substitution Test (DSST) scores were

collected at baseline as a measure of processing speed. Prevalent and incident diabetes mellitus, coronary heart disease (CHD), and hypertension were based on both self-report and physician diagnoses, recorded medications and laboratory data throughout the study. Height and weight were recorded and BMI was calculated using standard methods [21]. Apolipoprotein E (APOE) genotype was quantified by standard single nucleotide polymorphism genotyping and was coded as being an APOE ε4 allele carrier versus no allele. Participants self-reported number of falls in the previous 12 months; recurrent fallers were those reporting 2 or more falls.

Statistical analyses

Demographic characteristics, medical comorbidities, cognition, and gait speed measures were compared by cognitive maintainer status. Chi-square tests or *t*-tests were used, as appropriate, to determine if there were significant differences across these characteristics by cognitive maintainer status.

Unadjusted logistic regression models investigated the associations of gait speed (m/s) and percent change predictors with cognitive maintainer outcome status. For all gait speed models, odds ratios were calculated for 0.1 m/s differences in gait speed for more meaningful interpretation. Models were then adjusted for race, CHD, and DSST scores, as these variables significantly differed by cognitive maintainer status in bivariate analyses. Baseline 3MS score also differed by cognitive maintainer status, but was not used as a covariate as it was used to define the cognitive maintainer variable.

Sensitivity analyses in a sub-sample of 66 participants tested the association between the gait speed and percent change measures with adjudicated cognitive status (cognitively normal versus cognitively impaired (MCI or dementia)). Logistic regression models were run both unadjusted and adjusted for race, CHD and DSST scores.

RESULTS

The primary analytic sample had an average baseline age of 78.7 ($SD = 3.0$) years, 52.5% were female, and 25.6% were black. The average slope of 3MS over follow-up was –0.38 points per year (SD = 0.88). There were 106 (47.5%) cognitive maintainers and 117 (52.5%) cognitive decliners over an average of 5.2 years of follow-up (Table 1). Compared to maintainers, cognitive decliners were more likely to be black (30.8% versus 19.8%, $p =$ 0.06), were less likely to have CHD (16.2% versus 30.2%, $p = 0.01$), and had lower baseline DSST (39.50 versus 44.08, $p = 0.001$) and 3MS scores (94.06 versus 95.98, $p = 0.0001$; Table 1).

In bivariate analyses, cognitive decliners were slower in all gait conditions and had higher percent change in gait speed under fast-pace and dual-task conditions $(p < 0.05)$ (Table 1). Faster usual pace gait speed was associated with decreased odds of being a cognitive decliner, as opposed to a maintainer (OR = 0.89 per 0.1 m/s, 95% CI: 0.80 , 0.99); this association was attenuated after adjustment for race, CHD, and baseline DSST scores (Table 2). Similarly, faster fast-paced gait speed was associated with decreased odds of being a cognitive decliner, as opposed to a maintainer ($OR = 0.83$ per 0.1 m/s, 95% CI: 0.75, 0.91);

this association was robust to adjustment by race, CHD, and baseline DSST scores (OR $=$ 0.87 per 0.1 m/s, 95% CI: 0.78, 0.97; Table 2). Dual-task gait speed was also associated with being a cognitive decliner versus maintainer ($OR = 0.79$ per 0.1 m/s, 95% CI: 0.69, 0.90) and the relation was unchanged after adjustment for covariates (Table 2). The percent change variables for fast-pace and narrow walk were not significantly associated with being a cognitive decliner. Dual-task percent change in gait speed was associated, but only weakly (Table 2). Dual-task performance and percent change on the visuospatial cognitive task were not related to being a cognitive decliner (data not shown).

The subset of 66 participants with cognitive status adjudication had an average baseline age of 78.2 (SD = 2.7) years, 51.5% were female, and 28.8% were black. Compared to the primary analytic sample, participants in the subset with adjudicated cognitive status had faster dual-task gait speed (1.27 versus 1.18, $p = 0.006$) and lower dual-task percent change in gait speed (1.33 versus -1.27 , $p = 0.03$), but did not significantly differ by any other demographic, health, or gait speed characteristics. Average follow-up from gait assessment to cognitive adjudication was 8 years. Of the participants with adjudicated cognitive status, 32 were cognitively normal, 19 had MCI and 15 had dementia. Results for associations of gait characteristics with adjudicated cognitive outcomes were similar to those for cognitive decliner/maintainer status (Table 3). Faster fast-paced gait speed (OR = 0.83 per 0.1 m/s, 95% CI: 0.70, 0.98) and dual-task gait speed (OR = 0.72 per 0.1 m/s, 95% CI: 0.56, 0.93) were the strongest predictors of remaining cognitively normal, as opposed to developing MCI or dementia (Table 3). These results remained statistically significant after adjustment for race, CHD, and baseline DSST scores.

DISCUSSION

In a sample of community-dwelling older adults with initially high cognitive function, we found that gait speed under fast-pace and cognitive dual-task conditions was predictive of declining cognition in the years after gait assessment. These results were robust to covariate adjustment and were repeated in the sub-sample with clinically adjudicated dementia outcomes at the end of the study. In contrast, gait speed during usual pace and narrow walk conditions was not associated with cognitive outcomes after adjustment. Further, a calculation of percent change (i.e., cost) in gait speed from usual pace to complex walking was only weakly associated with cognitive outcomes for the dual-task condition, and percent change in gait speed from other conditions was not associated.

Gait speed is emerging as an important early indicator of risk for cognitive decline and cognitive impairment [22]. However, usual pace gait speed measured at a single time point in higher functioning older adults may not predict cognitive decline [2], thereby limiting its clinical utility. Complex walking tests challenge the overlearned task of walking and could serve as stress tests of central motor control. Prior studies have indicated that there is overlap in the brain regions responsible for central motor control and those involved in cognitive decline [2, 23, 24]. Therefore, these complex walking tests may uncover latent pathology that puts individuals at increased risk for cognitive decline and dementia.

Prior studies have found evidence that fast-pace and cognitive dual-task walking tasks can predict changes in cognitive function. A study of non-demented individuals compared multiple metrics obtained while dual-tasking and found that variability but not speed was associated with higher probability of converting to dementia over 2 years [7]. In a separate cohort, slower fast-pace gait speed was associated with increased risk of Alzheimer's disease over 11 years of follow-up among initially cognitively normal older adults [25]. In another study, inability to speed up by >0.1 m/s during fast-pace walking and inability to produce any cognitive response during dual-task walking were associated with decline in Mini-Mental State Examination scores over 3 years, with findings being stronger for fast-paced walking [26].

Neuroimaging studies provide evidence of a mechanistic link between poor performance on complex walking tasks and cognitive outcomes. Greater dual-task cost in gait speed has been associated with higher amyloid deposition [27], a well-known biomarker of Alzheimer's disease pathology. Slower dual-task speed has been associated with smaller volumes of several cognitive control-related regions in the brain, including portions of the frontal lobe, cingulate, and the hippocampus [28]. Slower fast-pace gait speed has been related with smaller total brain volume [25] and basal ganglia volumes [28] and with lower glucose metabolism in the posterior cingulate cortex [29]. Gait speed has multifactorial contributions from many body systems [30] and may not arise from neurologic pathology in all individuals [31]. Therefore, tests that target gait changes specific to neurologic impairments could be critical screening tools for early detection of increased risk for cognitive impairment. Complex walking tasks such as fast-pace and cognitive dual-task may challenge walking enough to uncover subtle and early neurologic changes that signal increased risk for future cognitive decline, whereas usual pace gait speed may not. Increasing one's walking speed requires faster processing and integration of multiple inputs with similarly faster preparation and implementation of a complex motor response. Our cognitive dual-task paradigm challenged the visuospatial and processing speed networks; during the task, the participant converts verbal information into spatial information, requiring internal rehearsal of the spatial distribution of the hands of a clock and then converting back to a verbal response. Both of these tasks likely have direct input from higher order cognitive processes that are related to dementia risk.

In contrast to fast-pace and cognitive dual-task walking, we found no association of usual pace or narrow walk speed with cognitive decline after adjustments. No prior studies to our knowledge have reported the longitudinal association of narrow-path walk speed with cognitive outcomes. One study found no association between stepping outside of the lines during narrow-path walking and decline in Mini-Mental State Examination scores over 3 years [26]. It is possible that non-neurologic characteristics (e.g., anthropomorphic characteristics, joint pain) are stronger determinants of speed during narrow walk. Neuroimaging studies of narrow walk performance have not been published, so we do not yet know what the neurologic drivers of this task are and whether they align with regions related to dementia risk.

The cognitive maintainer variable does not distinguish between subtypes of dementia and the number of individuals with adjudicated outcomes was too small to allow for assessment

of associations with subtypes. Therefore, we cannot determine whether these associations apply to all dementia types or are specific. A recent study indicated that dual-task gait is more strongly associated with vascular dementia than with Alzheimer's disease [32]. In

contrast, dual-task gait has been associated with Alzheimer's disease pathology, as described earlier [27, 28]. These discrepancies may arise from differences in walking tasks, the specific gait characteristic assessed, and/or the cognitive status and underlying pathology prevalent in the assessed sample. The effect of these differences on the screening potential of complex walking tasks for cognitive outcomes is yet to be determined.

There were several limitations to our analysis. We did not have cognitive adjudication at the time that the complex walking tasks were conducted. However, we used a conservative cutoff of 85 on the 3MS to exclude those with possible cognitive impairment at baseline. Results for our cognitive maintainer and the adjudicated outcome were remarkably similar, but we may have underestimated the true association with clinical MCI/dementia outcomes since participants had to survive and remain in the study 8–9 years past baseline to receive an adjudication. We also had data on only one type of cognitive dual-task. Therefore, we were unable to compare findings for our visuospatial task with performance during a working memory [33] or verbal fluency task [34], for example. We also did not have data utilizing non-walking motor tasks; tasks involving the upper limbs could be critical for individual who are unable to walk or have great difficulty walking. Finally, we only had gait speed measured during complex walking tasks. Other aspects of gait (for example, variability) may be more sensitive to subtle brain changes [7, 34]. However, assessment of variability requires more instrumentation than gait speed and, therefore, may have more limited clinical utility.

Our study also has several strengths. The cohort was very well characterized, allowing us to assess a number of potential confounders. There were up to 9 years of follow-up for cognitive function, allowing for detection of change in initially cognitively normal older individuals. The long follow-up allowed us to calculate a cognitive maintainer variable that has previously been validated with regards to predictors, neuroimaging correlates, and clinically relevant outcomes in this cohort [17, 18, 35]. Further, we had gait speed measured under several different conditions, allowing us to compare the associations of each with our cognitive outcomes.

Our results indicate that among cognitively normal older adults, fast-pace and cognitive dual-task walking may provide early screening tools for risk of cognitive decline and cognitive impairment. While the associations were slightly stronger for dual-task walking, there are several reasons why fast-pace walking may be more appealing for widespread clinical use. Fast-pace walking is simple to administer, requires minimal equipment (a 20-m hallway and a stopwatch), and can be administered in under 4 minutes, with results immediately available. In contrast, dual-task walking requires a secondary task which can be difficult to standardize. There is a wide range of secondary tasks available which have different psychometric properties and may be related to different functional outcomes [9]; even something as simple as which letter is used to start an alphabet task can change the properties of dual-task walking [36]. An additional concern is the inability to account for task prioritization [10]. Therefore, it may be more difficult to standardize administration of

dual-tasks on a large scale. Fast-pace walking may provide an effective, easy, and costeffective way to screen cognitively healthy older adults for risk of future cognitive decline.

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Demographic, health, and gait characteristics of cognitive maintainers and cognitive decliners aged 74–85 at baseline (Demographic, health, and gait characteristics of cognitive maintainers and cognitive decliners aged 74-85 at baseline ($n = 223$)

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CHD, coronary heart disease; CES-D, Center for Epidemiologic Studies Depression Scale; 3MS, Modified Mini-Mental State; DSST, Digit Symbol Substitution Test; m/s, meters/second.

CHD, coronary heart disease; CES-D, Center for Epidemiologic Studies Depression Scale; 3MS, Modified Mini-Mental State; DSST, Digit Symbol Substitution Test; m/s, meters/second.

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Associations of gait measures with being a cognitive decliner compared to being a cognitive maintainer (Associations of gait measures with being a cognitive decliner compared to being a cognitive maintainer ($n = 223$)

∗ Adjusted for race, coronary heart disease, and Digit Symbol Substitution Test. Associations in bold are significant at $\alpha = 0.05$. Adjusted for race, coronary heart disease, and Digit Symbol Substitution Test. Associations in bold are significant at α = 0.05.

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Associations of gait measures with developing MCI or dementia compared to remaining cognitively normal (Associations of gait measures with developing MCI or dementia compared to remaining cognitively normal ($n = 66$)

f,

∗ Adjusted for race, coronary heart disease, and Digit Symbol Substitution Test. Associations in bold are significant at α = 0.05.