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Gait speed, executive functions, and memory in older adults with and without dementia

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Submitted



Abstract

Background: Older adults with dementia show a decline in cognitive and physical functioning. An association between executive functioning and gait speed has been found in healthy older adults and older adults with mild cognitive impairment. This relationship is not properly assessed in older adults with dementia. We analyzed if an association between gait speed, executive functions and memory exists and if this association differs between healthy controls and patients with dementia.

Design: Descriptive, cross-sectional.

Setting: Nursing homes

Participants: 116 patients with dementia (age 84.18 ± 6.15 ; Mini Mental State Examination 19.16 ± 3.45) and 90 cognitive healthy controls (age 82.20 ± 6.54 ; Mini Mental State Examination 28.49 ± 1.03) were included in this study.

Measurements: Four different aspects of executive functions, i.e. set-shifting and inhibition, working memory, fluency, and planning as well as visual and verbal memory were assessed. Gait speed was measured with the six meter walk test.

Results: Mixed-effects regression showed that gait speed was a significant predictor for all cognitive tests in patients with dementia and in cognitive healthy controls. Moreover, model comparison revealed that the effect of gait speed did not significantly differ between both groups and across the various cognitive tests.

Discussion: Gait speed is a significant predictor of executive functions and memory in older adults with and without dementia. Gait speed might be an indicator of overall cognitive performance and not of specific cognitive subdomains. Consequently, if a decline in gait speed is observed, cognition might be declined as well, and should be monitored.

5.1 Introduction

There is great interest in studies assessing the relationship between physical and cognitive performance in healthy older adults (Snowden, Steinman et al. 2011, Littbrand, Stenvall et al. 2011, Gates, Fiatarone Singh et al. 2013). Physical performance and physical exercise are seen as possible mechanisms to deal with age-related cognitive decline (Erickson, Weinstein et al. 2012), or even as means to influence the process of dementia (McLaren, Lamantia et al. 2013). Most studies among healthy older adults found a positive association between physical and cognitive performance (Brown, Peiffer et al. 2012, Miller, Taler et al. 2012). In addition, physical intervention studies with healthy older adults confirmed the existence of a causal relationship between exercise and cognitive performance (Colcombe, Kramer 2003, Erickson, Voss et al. 2011, Kramer, Hahn et al. 1999), in particular when people were sedentary (Scherder, Scherder et al. 2013). In contrast, findings are inconsistent concerning the causal relationship in patients with dementia and in persons with mild cognitive impairment (Eggermont, Swaab et al. 2009, McLaren, Lamantia et al. 2013, Snowden, Steinman et al. 2011).

Important and often used variables in studies assessing the relationship between physical and cognitive performance are gait speed (Nadkarni, Studenski et al. 2013, Callisaya, Beare et al. 2013, Hausdorff, Buchman 2013), executive functions, and memory (Mielke, Roberts et al. 2012, Martin, Blizzard et al. 2012). Executive functions consist of multiple domains, including planning, set-shifting, inhibition, working memory, and fluency (Wilson, Alderman et al. 1997, Pennington, Ozonoff 1996). Of note is that gait speed is associated with both executive functioning (Watson, Rosano et al. 2010, Martin, Blizzard et al. 2012) and memory in healthy older adults (Watson, Rosano et al. 2010). However, the association between gait speed, executive functions, and memory has almost exclusively been studied in healthy older adults (de Bruin, Schmidt 2010, Fitzpatrick, Buchanan et al. 2007, Holtzer, Wang et al. 2012, Liu-Ambrose, Davis et al. 2010, Martin, Blizzard et al. 2013, Mielke, Roberts et al. 2012, Watson, Rosano et al. 2010) and adults with mild cognitive impairment (MCI; McGough, Kelly et al. 2011, Persad, Jones et al. 2008) but hardly in older adults with dementia (Hausdorff, Buchman 2013, Amboni, Barone et al. 2013). As far as we know, only one study investigated the relationship between some aspects of executive functions and gait speed in older adults with dementia (Bruce-Keller, Brouillette et al. 2012). They found that animal naming (fluency) and clock drawing were significantly correlated with gait speed in patients with dementia. However, the

relationship with memory or other executive functions such as inhibition, planning, and set-shifting was not assessed. Even though they included a healthy control group, Bruce-Keller and colleagues (Bruce-Keller, Brouillette et al. 2012) only provided the correlation between gait speed and the cognitive task. They did not investigate if the correlation significantly differed between animal naming and clock drawing.

To support future intervention studies, it is useful to know whether the possible effect of gait speed on cognitive performance is similar for people with and without dementia and if the association is similar for different cognitive (sub)domains. Therefore, the goal of the present study is to examine the association between gait speed, different executive functions and verbal and visual memory in older adults with and without dementia.

5.2 Methods

Subjects

The participants were patients with dementia who lived in a nursing home in the north of the Netherlands. The healthy controls mostly consisted of spouses of the participants with dementia. Each participant had to be at least 65 years old and able to walk short distances with or without a walking aid. Further inclusion criteria were a diagnosis of dementia and a score between 13 and 24 on the Mini Mental State Examination (MMSE, range between 0 and 30 with higher scores indicating better performance; Folstein, Folstein et al. 1975). Healthy controls required a score on the MMSE of 27 or higher. Exclusion criteria were vision problems hampering mobility and test performance, a history of psychiatric illness (e.g., schizophrenia or bipolar disorder) or neurological illness (e.g., epilepsy), suffering from alcoholism, having other brain diseases that could account for the cognitive impairment, or having performance-affecting physical problems (e.g., being in a wheelchair, having musculoskeletal disorders, or having a sprained ankle). Our study was approved by the local medical ethics committee and is in accordance with the declaration of Helsinki (59th Amendment). Participants or their legal representatives gave informed consent.

Assessment of gait

Gait speed was assessed with the six meter walk test (6MWT), which requires subjects to walk six meters in a straight line at their normal pace. The use of a walking aid was allowed. The outcome measure was the mean duration of two attempts, converted to walking speed

(m/s), with higher scores indicating better performance. The reliability of the 6MWT is good in patients with dementia (Blankevoort, van Heuvelen et al. 2013).

Assessment of cognitive functioning

Executive functions and memory were assessed by means of neuropsychological tests. For all neuropsychological tests a higher score indicates a better performance.

Memory

Verbal Memory was assessed with the Eight Word Task (Lindeboom, Jonker 1989). This test was used to examine the verbal episodic memory in direct recall, delayed recall and recognition. First, eight words are presented five times and after each session of eight words participants have to recall as many words as they can (total score ranging between 0 and 40). After 10 to 15 minutes the participant have to perform the delayed recall test in which they have to recall all eight words (score ranging from 0 to 8). Finally, the recognition test measures how many of 16 words can be correctly identified as being part (or not) of the original set of eight words (score ranging from 0 to 16). The total verbal memory score is calculated by averaging the *z*-transformed scores for the three tests.

Visual Memory was assessed with the Faces and Pictures test of the Rivermead Behavioral Memory Test (RBMT; Wilson, Cockburn et al. 1987). Cards of faces and pictures have to be remembered and recognized (score range faces: 0-10; score range pictures: 0-20). The total visual memory score is calculated by averaging the *z*-transformed scores of both tests.

Executive functions

Working memory was assessed with the Digit Span Backwards Test (Wechsler 2008). Participants had to repeat digits in reversed order. The sequence was increased by one digit after three trials. If two consecutive errors were made the test was terminated. The score was equal to the number of successful trials (ranging from 0 to 27).

Fluency was assessed with the animal and professions naming task from the Groninger intelligence test (GIT; Luteijn, Vanderploeg 1983). The number of named animals (or professions) within 60 seconds was recorded. The fluency score was calculated by averaging the *z*-transformed scores of both tests.

Set-shifting and inhibition were assessed with the Rule-Shift cards from the Behavioral Assessment of the Dysexecutive Syndrome (BADS; Wilson, Alderman et al. 1997) This test examines the ability to shift from a simple (i.e. respond 'yes' to a red card and 'no' to a black card) to a more complex rule (i.e. respond 'yes' if the card has the same color as the previous card), and inhibit the 'automated' response. The final score consisted of the number of correct answers using the more complex rule (between 0 and 19).

Planning was measured with the Key Search Test of the BADS (Wilson, Alderman et al. 1997). Participants had to imagine that they had lost their keys on a field and were asked to draw their search path. Based on their path a maximum score of 16 points could be obtained.

Possible confounders

Depression was assessed with the 30-point Geriatric depression scale (GDS; Yesavage 1988) No depression was indicated by a score between 0 and 10, while a score between 10 and 20 indicated mild depression. Finally, a score between 20 and 30 indicated severe depression (Yesavage 1988). The number of comorbidities was retrieved from the medical records of the participants. They were categorized according to the International Classifications of Disease and the number of comorbidities was summed. Education was measured with a seven-point scale suitable for the Dutch educational system (ranging from 1: less than elementary school to 7: Master's degree or higher). Age and gender were also included as possible confounders.

Missing values

Less than two percent of the data was missing, and this is considered 'trivial' (Acuna, Rodriguez 2004). As none of the individual variables had more than four percent of missing data, and there was no significant correlation between the MMSE (i.e. a general indicator of cognitive performance) and the number of missing values, we used regression substitution to replace the missing values.

Data analyses

SPSS statistics 20 and R 2.10.1 were used for the data analyses. Means, standard deviations, and correlations were calculated for neuropsychological scores and gait speed. For the correlation table the Bonferroni-Holm correction was applied (Aickin, Gensler 1996, Holm 1979). The Student's *t*-test and the chi-square test were used to determine differences

between men and women. To assess the effect of normal gait speed on the different cognitive functions, we analyzed the data using linear mixed-effects regression (Pinheiro, Bates 2000) with participant as a random-effect factor. In this way, the structural variation linked to each participant is taken into account (i.e. participants who scored high on one cognitive test are more likely to score high on another cognitive test). Importantly, this method enabled us to analyze if the effect of gait speed is significantly different for different aspects of cognitive performance and if the effect of gait speed on cognitive performance differs between healthy controls and patients with dementia. In the analysis, the cognitive score was used as the dependent variable. By including the type of cognitive test in our model, we were able to assess the precise effect of gait speed for each individual cognitive test (i.e. we assessed the possible interaction between cognitive test and gait speed) and between the two groups of participants. Besides the variable of interest, gait speed, six covariates were added to the model (i.e. age, gender, education, comorbidity, depression, and the use of a walking aid). The score of gait speed was normalized for gender, due to the large sex differences (i.e. new score men = (mean women / mean men) * old score men).

The significance of gait speed and the six covariates or interaction between those variables were evaluated by means of the *t*-test for the coefficients, in addition to model comparison likelihood ratio tests and Akaike Information Criterion (AIC; Akaike 1974). The model comparison likelihood ratio test and AIC make it possible to test whether the addition of variables or interactions improve the model significantly. This approach is similar to the one previously reported (Blankevoort, Scherder et al. 2013).

5.3 Results

Table 5.1 shows the demographics and the summary statistics of the test scores of the participants. The healthy controls had significantly higher cognitive test scores and gait speed than the patients with dementia. In addition, patients with dementia were significantly older, had less education, and made more frequently use of a walking aid.

Table 5.2 shows the correlations between gait speed and cognitive function for older adults with and without dementia. In patients with dementia no significant correlations are detected between gait speed and cognitive functions. In healthy controls gait speed is significantly associated with set-shifting, planning, and verbal memory. When combined all correlations are significant.

Table 5.1. Demographics and Summary Statistics of the Test Scores of the Patients with Dementia ($n = 116$) and Healthy Controls ($n = 90$).

	Dementia	Controls	Group differences
	Mean (SD)	Mean (SD)	<i>p</i> -value
Age	84.18(6.15)	82.2 (6.54)	.027
Gender	29.3 % ♂	33.0% ♂	.538
Education	3.50 (1.39)	4.28 (1.32)	< .001
Comorbidity	1.48 (1.53)	1.21 (1.50)	.897
Walking aid	36.2%	22.2%	.027
GDS	5.59 (4.68)	6.82 (5.36)	.079
MMSE	19.16 (3.45)	28.49 (1.03)	< .001
Memory Direct	16.60 (6.29)	29.39 (5.50)	< .001
Memory Delayed	0.65 (1.51)	4.49 (2.39)	< .001
Memory Recognition	11.41 (3.17)	15.17 (1.47)	< .001
RBMT Faces	5.06 (3.22)	9.08 (1.56)	< .001
RBMT Pictures	12.10 (7.24)	19.77 (0.82)	< .001
Working memory	5.34 (2.44)	7.84 (2.61)	< .001
Fluency animals	9.31 (4.17)	18.94 (4.94)	< .001
Fluency professions	6.44 (3.30)	15.17 (4.53)	< .001
Set-shifting	10.88 (3.93)	15.08 (4.24)	< .001
Planning	5.08 (3.40)	8.86 (4.96)	< .001
Gait speed (6MWT m/s)	0.74 (0.24)	0.93 (0.34)	< .001

GDS: geriatric depression scale; MMSE: mini mental-state examination; RBMT: Rivermead Behavioral Memory Test; 6MWT: six meter walk test

Table 5.2. Correlations Between Cognitive Functions and Gait Speed (Normalized for Gender) in Patients with Dementia ($n = 116$) and Healthy Controls ($n = 90$).

	Dementia Gait speed	Controls Gait speed	Total group Gait speed
Verbal memory	-.014	.290*	.322*
Visual memory	.077	.015	.238*
Working memory	.221	.146	.289*
Fluency	.252	.281	.401*
Set-shifting	.122	.302*	.325*
Planning	.154	.394*	.388*

* significant at .05 with bonferroni-holm correction applied.

Table 5.3 shows the best mixed-effects regression model (explained variance 50.2%). This model shows that education ($\beta = .13$, $t = 4.50$) and being an older adult without dementia ($\beta = 1.01$, $t = 16.42$) has a positive effect on all cognitive measures. The other potentially confounding variables (i.e. gender, comorbidity, walking aid, and age) did not reach significance by itself or in interaction with any other variables and were therefore not included in the model. Gait speed appeared to be a significant predictor of cognitive performance by itself ($\beta = .16$, $t = 5.31$). The model did not significantly improve by adding an interaction with group ($p = .71$), or differentiating between cognitive tests ($p = .21$), or by including any other interaction, involving gender, age, comorbidity, or walking aid.

Table 5.3. The Linear Mixed-Effects Regression Model Predicting Cognitive Performance.

Fixed effects	Estimate	Std. Error	<i>t</i> -value	<i>p</i> -value (approx.)
Intercept	-.44208	.03904	-11.325	< .001
Education	.13202	.02933	4.502	< .001
Healthy control	1.01330	.06171	16.421	< .001
Gait speed ^a	.15746	.02965	5.310	< .001

^a Gait speed is gender-normalized (see text for details).

5.4 Discussion

The goal of this study was twofold. The first goal was to analyze the association between gait speed, executive functions, and memory in older adults with and without dementia. The second goal was to determine if this association varied depending on cognitive domain or group.

Our results show that gait speed is a significant predictor for all aspects of executive functions and memory in older adults with dementia and without dementia. The linear mixed effect regression model showed, despite the fact of some minor differences in the correlation table, that the predictive effect of gait speed did not significantly vary per group (i.e. dementia patients or healthy controls) or cognitive task. Consequently, we propose that the association between gait speed and cognitive performance is a general phenomenon, rather than a specific association for individual groups or cognitive (sub) domains (i.e. planning, fluency, working memory, inhibition and set-shifting, and verbal end visual memory). This is important, because all aspects of executive functions are vital to function independently, and independence is especially at risk in older adults

with dementia. Previous research showed that gait speed is trainable in older adults with dementia (Blankevoort, van Heuvelen et al. 2010) and in healthy older adults (Agmon, Perry et al. 2011). However, the improvements in gait speed have not been linked to cognitive improvement. Intervention studies, therefore, are needed to assess if improving gait speed also results in improved executive functions and memory.

The association between gait speed and cognitive performance has also been addressed in neuroimaging studies. White matter hyper-intensities were associated with a reduced gait speed (Soumare, Elbaz et al. 2009) and with a decline in executive functions and memory (Maillard, Carmichael et al. 2012). In line with our finding (gait speed has a general predictive effect) an MRI study in cognitive healthy older adults showed that gait velocity was not associated with white matter hyper-intensities in specific areas (e.g. periventricular, subcortical or lobar), but with the amount of white matter hyper-intensities in general, which indicate a more global involvement of neural networks in gait velocity (Murray, Senjem et al. 2010). Our findings add to the evidence of the more general relationship between gait speed and executive functions and memory.

Limitations

This study has several limitations. First, as the study is cross-sectional, it cannot reveal a causal relationship. Second, we used a specific patient and control population, which might hamper the generalizability of our findings to other patients groups or age categories.

5.5 Conclusions

This study shows that gait speed is a significant predictor of executive functions and aspects of memory in healthy older adults and older adults with dementia. This association is not different for patients with dementia compared to cognitive healthy controls and does not differ between various cognitive functions. Intervention studies are necessary to examine a possible causal relationship between gait speed, executive functions, and memory in older adults with dementia.

