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Global cognitive functioning and physical mobility in older adults with and without mild cognitive impairment: evidence and implications

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Abstract: **Introduction:** Co-occurrence of physical and cognitive dysfunctions contribute to functional decline and a gradual loss of independence.

Objectives: The purpose of this study was to evaluate the association between global cognitive impairment and physical mobility in older adults with and without mild cognitive impairment (MCI).

Material and Methods: A total of 800 older adults were recruited (653 with normal cognitive functioning and 147 participants with MCI). Motor performance was measured with the Timed Up and Go test (TUG) and the 6 Minute Walk Test (6MWT). Cognitive functions were evaluated using Mini-Mental State Examination (MMSE) and Addenbrooke's Cognitive Examination (ACE-III).

Results: ACE-III scores were associated with the TUG test performance in older adults (with and without MCI), but not with 6MWT results. The overall score in ACE-III and its subscales, i.e. a) memory and fluency in the MCI group and in the total group, and b) fluency in the control group, were associated with TUG after adjusting for age, sex, body mass index, medication use, depressive symptoms, hypertension, coronary artery disease and diabetes. In the case of the 6MWT test results, only the ACE-III fluency subscale scores and not the overall ACE-III score were associated with them.

Conclusions: Global cognitive function, verbal fluency and memory were independently associated with the TUG. ACE-III, being a more extensive testing tool than MMSE, made it possible to show the relationship between global cognition and motor skills.

Key words: mild cognitive impairment, ACE-III, TUG, 6MWT.

Introduction

The limitations of physical and cognitive performance are common health problems among older adults. Functional mobility decline limits the ability to perform everyday activities, leads to the loss of independence, as well as to disability and death [1, 2]. Mild cognitive impairment (MCI) is the intermediate stage between normal cognitive aging and dementia [3]. In European studies the prevalence of cognitive impairments is estimated between 10.7% and 14.5% [4–6]. Moreover, several longitudinal studies have found that gait abnormalities tend to be associated with a higher risk of cognitive decline and dementia [7–11]. Alternatively, few studies also suggest that cognitive changes precede or co-occur with slowing gait [12, 13] and that the impairment of cognitive functions is an independent risk factor for falls [14, 15]. It is also recognized that gait disturbances co-occur with injury to specific brain networks which are also important for specific cognitive functions [16]. Mobility requires maintaining postural control and coordinated work of different muscle activation patterns [17]. Changing the requirements of the internal and external environment needs planning and monitoring of motor performance and a continuous modification of motor programs.

It is important to identify the problem regarding mobility and cognitive functions at an early stage to limit the development of disability in older people. There is abundant evidence of the relationship between gait and specific cognitive functions including attention, executive function and processing speed in both healthy adults [18–20] and adults with MCI [21, 22]. Executive functions are engaged in controlling, organizing and integrating various processes as well as in maintaining information [23]. It would also be helpful to identify whether there is a relationship between physical mobility and global cognitive functions. In clinical practice, screening scales of cognitive function and motor mobility are more frequently used. If global cognitive functions are also associated with functional mobility, this may allow further diagnostic and therapeutic processes. It would also help to identify relevant tests for global assessment of cognition which are more widely available than specialist neuropsychological tests, allowing to capture people with limitations in the physical mobility.

Therefore, the aim of our research was to assess the relationship between two popular tests to evaluate motor performance and global cognitive functions in the group of older adults with and without MCI. We also examined whether the relationship between cognition and motor skills differs in the profiled assessment of individual domains of global cognition. We chose two common tests of functional mobility: the Timed Up and Go test (TUG) and the 6 Minute Walk Test. For the

global assessment of cognitive functions, we chose the Mini-Mental State Examination (MMSE) and Addenbrooke's Cognitive Examination (ACE-III).

In this study, we tested the hypothesis that the higher level of global cognition and five global cognitive subscales were related to the better physical mobility performance measured with two different tools in a group of participants aged 60 and over with and without MCI.

Material and Methods

Subjects eligible for this study were participants of a population participating in the Project entitled "The implementation of the project of diagnostics, geriatric prevention, with the application of elements of Telecare as a method of better adjustment of the healthcare system to the needs of the rapidly growing population of persons over 60", implemented by Nowa Rehabilitacja Sp. z o.o. at the Medical and Rehabilitation Centre in Kraków. It was a cross-sectional study conducted from September 2015 to April 2017. The total number of subjects amounted to 1001. The inclusion criteria for the study discussed here allowed enrolment of subjects aged 60 and above. The exclusion criteria included: inability to walk 10 meters unassisted, neurological and psychiatric diseases (cerebrovascular disease, Parkinson's disease, depression and dementia), deafness and blindness, alcohol and/or medication addiction, impairment of general cognitive function (individuals who scored 23 or lower on the MMSE), ($n = 877$). Clinical and demographic data were collected during a face-to-face interview. Medical histories were collected by a physician during a face-to-face semi-structured interview as well as on the basis of medical records presented by the subject.

Finally, 800 participants who completed all assessments (medical, psychological and physiotherapeutic assessment) qualified for the study (see Fig. 1). Clinical diagnoses were established at consensus meetings by a multidisciplinary team including physicians (geriatrician, neurologist, internist and cardiologist), neuropsychologists, physical therapists, nurses and occupational therapists. Independence in the activities of daily living (ADL) [24] and the instrumental activities of daily living [25] were used as a measurement of functional status of each participant. The body mass index (BMI) was calculated according to the following formula: $BMI = \text{body mass [kg]} / (\text{height [m]})^2$. The evaluation of the level of depressive symptoms was measured by the Short Form Geriatric Depression Scale (GDS-S). The Scale consists of 15 brief yes/no questions. GDS-S is used as a screening tool enabling the evaluation of depressive symptoms severity in elderly persons [26]. The quantitative measure of depressive symptoms was used in this study.

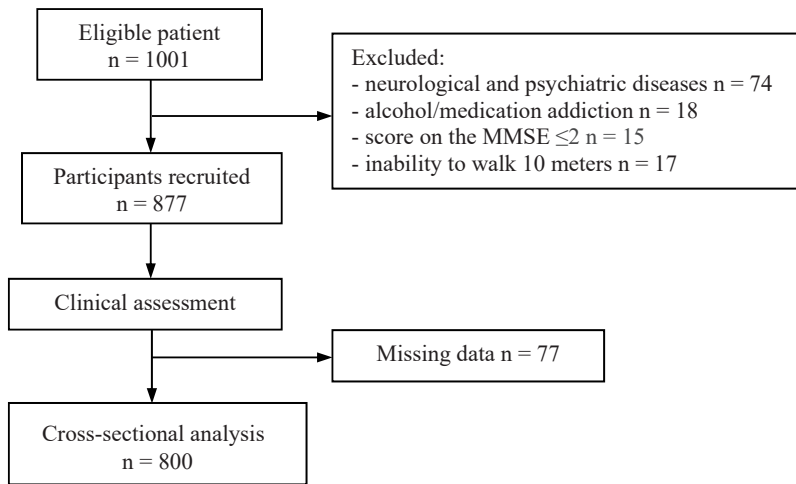


Fig. 1. Flow chart of participant recruitment.

Neuropsychological assessment

Each participant underwent a cognitive assessment during a face-to-face examination by a clinical neuropsychologist. The following standardized tests were used to assess the participants' global cognitive functioning: the Mini-Mental State Examination (MMSE) [27] and Addenbrooke's Cognitive Examination (ACE-III) [28, 29]. Furthermore, in order to identify people with MCI several neuropsychological tests were selected. The Rey Auditory Verbal Learning Test (AVLT) was used to evaluate episodic memory [30]. The Verbal Fluency Test (category and letter fluency) was used to assess verbal functioning [31]. The Clock Drawing Test (CDT) was used to assess visual spatial functions [32]. Digit Span Forward and Backward Test was used to evaluate attention and working memory [31]. Trail Making Test (TMT) Parts A and B was selected for the evaluation of executive functions [33].

Having reviewed the results of the clinical evaluation and neuropsychological examination, the team of experts classified both fully functioning persons and participants with MCI. The following MCI criteria were adopted: absence of dementia according to Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), evidence of cognitive deterioration shown by self-reported cognitive complaints, and they presented an objective impairment on at least one of the neuropsychological tests (defined as a score 1.5 SD or more below the age-appropriate mean, derived from baseline assessments in the cohort), and independence in the activities of daily living [34]. From the group of 800 participants, 147 people met the criteria of MCI. Bioethics Commission at the Regional Medical Chamber in Kraków approved the study and all participants signed the information consent form.

Physical mobility assessment

The Timed Up and Go test (TUG) was used to evaluate functional capability [35]. This test was carried out by experienced and trained physiotherapists. The TUG is a test that involves performing a sequence of functional tasks: rising from a chair (46 cm), walking 3 metres, turning around at a cone placement, walking back to the chair, and sitting down again. An armless chair was used [36]. The assessment in this test is based on the measuring of execution time using a stopwatch. The participants were asked to move at a normal walking pace. Both verbal and visual instructions were used to make all participants understand the test procedure. One practice trial before actual testing was performed. The test was performed twice and the average time was used for analysis.

The 6MWT is a submaximal exercise test used mainly to assess exercise tolerance and endurance in various diseases such as chronic respiratory disease and heart failure (a global test to evaluate submaximal level of functional performance) [37]. It is the test used widely to evaluate patients who suffer from various diseases common in elderly population [38]. It was found that the level of performance during 6MWT is similar for daily physical activities more than in the case of other walk tests [39]. In this study a standard procedure according to American Thoracic Society Guidelines for 6MWT was used [37]. The test was held inside a building. The participants were instructed to walk as quickly as possible to make the longest distance within 6 minutes.

Statistical analysis

Elements of descriptive statistics were applied in the analysis. The results were presented as the average values for groups with a standard deviation (SD) or as a percentage. Multiple linear regression analyses were performed to specify the association between physical mobility used as a dependent variable and cognitive functioning used as an independent variable adjusted for baseline characteristics, i.e., age, sex, BMI, medication use, depressive symptoms and chronic conditions (hypertension, coronary artery disease and diabetes). P-values below 0.05 were considered statistically significant. The statistical analysis was performed with the application of Statistica 13 PL.

Results

From among 1001 people taking part in the project carried out by Nowa Rehabilitacja the results of 800 participants were included in the analyzes. The average age of the study participants was 69.3 years (SD, 5.19), 71% were female, with a minimum of

seven years of education. Table 1 presents demographic and clinical characteristics of the participants. The analysis of the relationship between global cognitive functions and motor performance was carried out in two stages (1st stage for the TUG and the second stage for the 6MWT), each comprised six models (1A, 2A and 3A are univariate models and 1B, 2B and 3B are multivariable models). In multivariable models the relationship between motor and cognitive performance was adjusted for age, sex, body mass index, medication use, depressive symptoms, hypertension, coronary artery disease and diabetes.

Table 1. Sample characteristics of participants.

Variables	Values		
	MCI (n = 147)	Control (n = 653)	Total (n = 800)
<i>Demographic and clinical characteristics</i>			
Age ²	71.3 (5.95)	68.9 (4.91)	69.3 (5.19)
Education level ²	12.1 (3.22)	15.1 (3.13)	14.5 (3.37)
Body mass index (kg/m ²) ²	28.6 (4.29)	28.3 (5.2)	28.3 (5.04)
Geriatric Depression Scale ²	2.9 (3.02)	2.1 (2.41)	2.2 (2.55)
Women ¹	99 (67)	470 (72)	569 (71)
Hypertension ¹	96 (66)	404 (62)	500 (62)
Coronary artery disease ¹	19 (12)	81 (13)	100 (12)
Diabetes ¹	23 (16)	81 (13)	109 (14)
Medications ²	4.9 (3.17)	4.46 (2.99)	4.6 (3.03)
<i>Physical performance</i>			
Timed Up and Go test (s) ²	9.97 (2.23)	8.86 (1.86)	9.1 (1.97)
6 Minute walk test (m) ²	440.09 (92.09)	441.23 (87.54)	441 (88.36)
<i>Global cognitive performance</i>			
MMSE ²	26.97 (1.22)	28.9 (1.02)	28.5 (1.29)
ACE-III ²	82.8 (6.04)	94.7 (3.13)	92.5 (5.99)
Attention (ACE-III) ²	16.7 (1.27)	17.5 (0.88)	17.4 (1.02)
Memory (ACE-III) ²	19.1 (3.73)	24.1 (1.7)	23.2 (2.95)
Fluency (ACE-III) ²	9.6 (2.01)	12.1 (1.65)	11.7 (1.97)
Language (ACE-III) ²	23.6 (2.62)	25.5 (0.86)	25.1 (1.56)
Visuospatial (ACE-III) ²	14.4 (1.57)	15.6 (0.76)	15.4 (1.07)

n — sample size, ¹sample size (%), ²mean (standard deviation)

MMSE, Mini-Mental State Examination; ACE-III, Addenbrooke's Cognitive Examination-III.

Table 2. Analysis of multiple linear regression to Timed Up and Go test.

Variables	Univariate Models			Multivariable Models		
	MCI	Control	Total	MCI	Control	Total
	β (CI)	β (CI)	β (CI)	β (CI)	β (CI)	β (CI)
Global Cognitive		Model 1A		Model 1B		
MMSE	-0.08 (-0.25; 0.09)	0.05 (-0.03; 0.14)	0.01 (-0.06; 0.08)	0.03 (-0.17; 0.24)	0.05 (-0.03; 0.14)	0.01 (-0.07; 0.08)
ACE-III	-0.18 (-0.33; -0.06) ^a	-0.14 (-0.21; -0.03) ^c	-0.26 (-0.33; -0.19) ^a	-0.09 (-0.26; -0.05) ^c	-0.06 (-0.17; 0.13)	-0.16 (-0.25; -0.09) ^a
ACE-III (domains)		Model 3A		Model 3B		
Attention	0.07 (-0.09; 0.23)	0.07 (-0.02; 0.14)	0.06 (-0.02; 0.14)	0.07 (-0.13; 0.26)	0.03 (-0.05; 0.12)	0.06 (-0.05; 0.11)
Memory	-0.25 (-0.41; -0.08) ^b	-0.03 (-0.11; 0.05)	-0.13 (-0.21; -0.06) ^b	-0.21 (-0.39; -0.03) ^c	-0.03 (-0.11; 0.06)	-0.11 (-0.18; -0.04) ^b
Fluency	-0.29 (-0.45; -0.14) ^a	-0.14 (-0.22; -0.06) ^a	-0.18 (-0.25; -0.09) ^a	-0.29 (-0.47; -0.09) ^b	-0.11 (-0.19; -0.02) ^c	-0.15 (-0.24; -0.07) ^a
Language	0.01 (-0.17; 0.18)	-0.06 (-0.15; 0.02)	-0.07 (-0.14; 0.02)	0.02 (-0.18; 0.22)	-0.05 (-0.14; 0.04)	-0.05 (-0.13; 0.04)
Visuospatial	0.05 (-0.12; 0.22)	-0.03 (-0.11; 0.05)	-0.01 (-0.08; 0.07)	0.09 (-0.09; 0.29)	-0.03 (-0.05; 0.11)	0.04 (-0.03; 0.15)

MCI, mild cognitive impairment; CI, confidence interval; MMSE, Mini-Mental State Examination; ACE-III, Addenbrooke's Cognitive Examination-III.

^a Significant at $P < .001$; ^b Significant at $P < .01$; ^c Significant at $P < .05$.

Multivariable regression was adjusted for age, sex, body mass index, medication use, depressive symptoms, hypertension, coronary artery disease, diabetes.

Table 3. Analysis of multiple linear regression to 6 Minute walk test.

Variables	Univariate Models			Multivariable Models		
	MCI	Control	Total	MCI	Control	Total
Global Cognitive						
MMSE	0.04 (-0.14; 0.20)	-0.06 (-0.15; 0.03)	-0.04 (-0.11; 0.04)	0.01 (-0.17; 0.19)	-0.06 (-0.15; 0.03)	-0.04 (-0.13; 0.04)
ACE-III						
ACE-III (domains)						
Attention	0.06 (-0.12; 0.23)	-0.02 (-0.11; 0.05)	-0.02 (-0.08; 0.08)	0.07 (-0.12; 0.26)	-0.05 (-0.13; 0.04)	-0.02 (-0.11; 0.07)
Memory	-0.12 (-0.29; 0.06)	-0.05 (-0.13; 0.03)	-0.07 (-0.17; 0.01)	-0.14 (-0.33; 0.05)	-0.03 (-0.12; 0.07)	-0.06 (-0.15; 0.05)
Fluency	0.19 (0.03; 0.36) ^c	-0.05 (-0.12; 0.04)	-0.02 (-0.09; 0.07)	0.23 (0.05; 0.42) ^c	-0.06 (-0.15; 0.03)	-0.01 (-0.09; 0.07)
Language	0.11 (-0.07; 0.29)	0.07 (-0.02; 0.17)	0.12 (-0.04; 0.22)	0.02 (-0.18; 0.22)	0.07 (-0.03; 0.16)	0.07 (-0.02; 0.17)
Visuospatial	-0.05 (-0.22; 0.14)	0.01 (-0.08; 0.09)	-0.02 (-0.09; 0.08)	-0.08 (-0.27; 0.13)	0.03 (-0.07; 0.12)	0.01 (-0.09; 0.08)

MCI, mild cognitive impairment; CI, confidence interval; MMSE, Mini-Mental State Examination; ACE-III, Addenbrooke's Cognitive Examination-III.

^cSignificant at $P < .05$.

Multivariable regression was adjusted for age, sex, body mass index, medication use, depressive symptoms, hypertension, coronary artery disease, diabetes.

The global cognitive score was associated with the TUG as measured by the ACE-III test and not by the MMSE. In univariate analyses, ACE-III and ACE-III domains (memory and fluency) were associated with the TUG in MCI and total group. These relationships were unchanged after adjusting for age, sex, body mass index, medication use, depressive symptoms, hypertension, coronary artery disease or diabetes. In control group ACE-III and fluency were associated with the TUG in unadjusted analyses. In the adjusted model, fluency was the only independent factor associated with the TUG (see Table 2). At the second stage of the analysis, fluency was the only independent factor associated with 6MWT (see Table 3).

Discussion

To our knowledge, this is the first study in which the ACE-III scale was used to evaluate the association of global efficiency of cognitive functions with the motor performance (measured by TUG and 6MWT) of the cognitively normal aging adults and participants with mild cognitive impairment. The major findings of this study indicate a relationship between global cognitive functioning and physical mobility in older adults with and without MCI. The results we obtained support the hypothesis assumed, revealing that higher levels of global cognition were related to the better physical mobility performance. This study supports the strong relationship between cognition and physical performance in healthy older adults [18–20, 40–44] and older adults with MCI [21, 22, 45–47].

Our study showed that global cognition and global cognitive domains including memory and fluency were associated with the TUG performance. Independent associations were revealed by a multivariable analysis adjusting for age, sex, body mass index, medication use, depressive symptoms, and health characteristics. Slower TUG test performance was associated with worse results in global cognitive assessment. Interestingly, no such association was found between the 6MWT results and global cognitive performance. Fluency as the ACE-III subscale was the only significant cognitive factor associated with 6MWT. The relationship between the TUG test performance and global cognition was also observed in another study that included healthy older participants [48]. What is more, other authors also reported associations between a slower performance of the TUG test and a lower level of specific cognitive performance [21, 41, 44, 49]. Our findings showed that both verbal fluency [49] and memory [44] were associated with the TUG test results. In our study, we did not observe any relationship between the TUG test results and other ACE-III subscales scoring (attention, language and visuospatial function). Presumably, the degree of cognitive functions involvement in gait depends on many factors. Perhaps this explains why the TUG test results, unlike the ones obtained in 6MWT, were associated with global cognitive performance. The TUG consists of

a sequence of many complex tasks that involve various aspects of muscle strength, coordination, balance, and mobility [50]. The ability to perform such different complex tasks requires the involvement of higher cognitive functions. The necessity of undertaking emergency activities or a modification of previously learned motor programs undoubtedly require the involvement of memory and executive functions. This explains the TUG test relationship with verbal fluency and memory subtests. The need for flexible modification of previously learned movement patterns may occur in situations of internal or external environment change.

Performing the TUG test requires an interaction between environmental stimuli (test requirements, variability of the environment), the cognitive adaptation capability and the completion of a complex task. Cognitive functions impairment may result in an inability to coordinate parallel processes, plan, remember and execute the task. Therefore, executive dysfunctions may be particularly important to explain why gait slows with age [40, 43]. Another issue to be noted are imaging studies which show that the activity of frontal-subcortical neuronal circuits modulates a number of cognitive processes and motor activities [51, 52]. Furthermore, the level of hippocampal metabolism, which is crucial for the functioning of memory, was also found to be important for gait [53].

In the light of the studies conducted as well as conclusions presented by other authors, it can be argued that the decrease in physical mobility is related to the impairment of cognitive functions. Analysing the relationship between cognition and physical performance in older adults has significant public health implications. Prevention of disability among the elderly is a challenge for the whole society. Effective prevention of disability requires the identification of persons who are at risk of disability. The ACE-III scale is a powerful tool for global assessment of cognitive functions including such domains as: attention, memory, fluency, language and visual-spatial functions. The wide range of cognitive functions assessed with the ACE-III scale allowed to show the relationship between cognition and motor skills as early as at the screening stage. In clinical practice, screening scales are much more frequently used than specialist neuropsychological tests. The TUG is a quick and simple test used to assess mobility in older adults. It is worth emphasizing here that the TUG can be a useful screening tool for functional mobility with regard to both physical and cognitive abilities. Therefore, it is recommended to use both the TUG and the ACE-III scale in the overall geriatric evaluation. Taking into account the prevention of old-age diseases, it is also worthwhile to encourage physical activity because, as research shows, physical activity may positively affect cognitive functions [54]. The relationship between cognitive functions and physical mobility indicates a number of clinical implications, from the use of multimodal screening tools to the application of diagnostic and therapeutic intervention strategies.

Our study had several strengths and limitations. The main strengths of this study are the sample size, the application of the ACE-III test for global cognition assessment (with the analysis of individual domains), and the use of two tests that are popular in clinical practice to assess physical mobility. Additionally, in our analyses we have included adjustments for several potential covariates such as the number of medicines, chronic diseases and the level of depression. Finally, the cross-sectional design of our study limited the ability to draw a valid conclusion such as the relationship between cognition and motor skills. Future prospective studies should determine the biological mechanisms and establish an early intervention strategy to optimize the functioning of older people.

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Conflict of interest

None declared.

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