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The Trail Walking Test to predict probable mild cognitive impairment in older adults

Trail Walking Test k detekci pravděpodobné mírné kognitivní poruchy u starších jedinců

Abstract

Background: Early detection of mild cognitive impairment (MCI) as a risk factor for dementia using valid screening tools can present an opportunity for timely intervention to slow the progression of cognitive decline in older adults. *Aim:* The aim of this study was to evaluate the Trail Walking Test (TWT) that includes a dual task to predict probable MCI (pMCI) in older adults and to evaluate its usability as a screening tool. *Methods:* The study was conducted on a sample of 61 subjects categorized using the Montreal Cognitive Assessment (MoCA) into three groups: older adults with intact cognitive ability (ICA, MoCA > 25); older adults with pMCI (MoCA ≤ 25); and "healthy young adults (HYA)". All participants completed the Trail Making Test (TMT) and three variants of the TWT with increasing complexity. Area under the receiver operating curve (AUC), sensitivity, specificity and Youden indices were used to evaluate the capacity of each test to predict pMCI in older adults. Internal validation was performed to calculate AUCs corrected for optimism (AUC_{VAL}). *Results:* The pMCI group performed significantly worse in all evaluated variations of the TMT and TWT than the ICA and HYA groups ($P < 0.001$). We found that all versions of the TMT (e.g., TMT-A and TMT-B) and TWT tests (e.g., TWT-1, 2, 3) have very good ability to discriminate between people with pMCI and all controls (e.g., ICA and HYA combined) with AUCs ranging from 0.81 to 0.876, generally increasing with increasing complexity of the dual task. Best performance was achieved when only HYA were used as a control group (AUCs: 0.894–0.975). The validity of these tools to predict pMCI remained very good after corrections using bootstrapping (AUCs: 0.829–0.839). While TWT-2 showed more benefits over TWT-1, the added value of TWT-3 over TWT-2 has been limited in this study. *Conclusions:* The dual component TWT is a valid screening tool for pMCI in older adults. Its use may improve early detection of pMCI in clinical and non-clinical settings. While increasing complexity of the test increases its predicting performance, based on our findings there seems to be a cutoff beyond which the added value of more complex dual tasks diminishes.

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I. Hereitová[1,2], A. M. Hašková[1], M. Majdan[3]

[1] Department of Rehabilitation Fields, Faculty of Health Care Studies, University of West Bohemia, Pilsen, Czech Republic
[2] Department of Neurology, Faculty of Medicine, Palacký University Olomouc, Czech Republic
[3] Institute for Global Health and Epidemiology, Department of Public Health, Faculty of Health Sciences and Social Work, Trnava University, Trnava, Slovakia

✉
Prof. Marek Majdan, PhD
Institute for Global Health and Epidemiology
Department of Public Health
Faculty of Health Sciences and Social Work
Trnava University
Hornopotocna 23
918 43 Trnava
Slovakia
e-mail: mmajdan@truni.sk

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Souhrn

Úvod: Včasná detekce pomocí platných screeningových nástrojů může představovat příležitost k odhalení mírné kognitivní poruchy (mild cognitive impairment; MCI) jako rizikového faktoru demence a tím zpomalit progresi kognitivního poklesu u starších dopělích. *Cíl:* Cílem této studie bylo vyhodnotit Trail Walking Test (TWT) k detekci pravděpodobné MCI (probable MCI; pMCI) u starších jedinců a zhodnotit jeho použitelnost jako screeningového nástroje. *Metodika:* Studie se zúčastnilo 61 osob rozdělených pomocí Montrealského kognitivního testu (Montreal Cognitive Assessment; MoCA) do tří skupin: starší dospělí s intaktními kognitivními funkcemi (ICA, MoCA > 25); starší dospělí s pMCI (MoCA ≤ 25); a kontrolní skupina mladých jedinců (healthy young adults; HYA). Všichni účastníci absolvovali Trail Making Test a tři varianty TWT se zvyšující se složitostí. Plocha pod křivkou (area under the curve; AUC), senzitivita, specificita a Youdenovy indexy byly použity k vyhodnocení schopnosti každého testu předpovídat projev pravděpodobné mírné kognitivní poruchy u starších jedinců. Na korekciu optimizmu predikcie bola vykonaná interná validácia AUC a vypočítala sa príslušná korigovaná AUC (AUC_{VAL}). *Výsledky:* Skupina pMCI dosáhla významně horších výsledků ve všech hodnocených variantách TMT a TWT než skupiny ICA a HYA ($p < 0,001$). Zjistili jsme, že všechny verze testů TMT (např. TMT-A a TMT-B) a TWT (např. TWT-1,2,3) mají velmi dobrou detekční schopnost rozlišení osob s pMCI od kontrolních skupin ICA a HYA hodnocené dohromady s hodnotami AUC v rozmezí od 0,81 do 0,876, které se obecně zvyšují s rostoucí složitostí duálního úkolu. Nejlepší detekční schopnosti však bylo dosaženo, když byla jako kontrolní skupina použita pouze HYA (AUC: 0,894–0,975). Screeningové testy TMT pro detekci pMCI zůstaly validní i po korekcích pomocí bootstrappingu (AUCs: 0,829–0,839). Zatímco varianta testu TWT-2 vykazovala přínos oproti TWT-1, přidaná hodnota TWT-3 oproti TWT-2 byla v naší studii omezená. *Závěr:* TWT je platným nástrojem pro screening pMCI u starších dospělých. Jeho použití může zlepšit včasnou detekci pMCI v klinických i neklinických podmínkách. Zatímco zvyšující se složitost testu zvyšuje jeho prediktivní výkonnost, na základě našich zjištění se zdá, že existuje hranice, za kterou se přidaná hodnota složitějších duálních úloh snižuje.

Introduction

Neurodegenerative disorders are a major public health and societal challenge in need of robust preventive measures and disease-modifying treatments [1], and the situation is projected to become even worse in the coming decades: the Global Burden of Diseases (GBD) study estimated that the number of people with dementia will nearly triple from about 57 million cases in 2019 to over 152 million cases in 2050 – the increase caused especially by population growth and population aging [2].

While truly effective treatment for dementia is not readily available, the progression of the disease can be slowed down with timely and effective interventions and prevention measures [3]. An example of such interventions is aerobic or resistance training showing promise in some earlier studies [4] (however, in more recent studies the results of the association between aerobic exercise and mild cognitive impairment [MCI] were not shown [5,6]). Nevertheless, early detection of the signs of cognitive impairment that would allow for early interventions is a crucial component of the overall strategy to improve the quality of life and outcome of people with dementia. MCI has been shown to be a risk factor for dementia [7] and its early detection can present an opportunity for timely intervention that could alter the progression of cognitive decline in seniors [8], while releasing the burdens that cognitive impairment poses for the patient (such as loss of function and relationships, financial misjudgments, and nonadherence with recommended therapies, caregivers, and society) [9]. Ultimately, the ability to identify individuals who are asymptomatic but at risk for developing the disease at an early stage appears to be a strong tool in fighting dementia; MCI represents an intermediate clinical state between the cognitive changes of aging and the very earliest features of Alzheimer's disease [10].

Research efforts have therefore been focused on identification of tools and methods for fast and reliable screening for persons with probable MCI (pMCI). One of the promising sets of tools for that purpose includes dual task tests. These tests arise from the dual task gait paradigm [11], in which the association between gait and cognition is evident [12]. A dual task gait paradigm is a procedure in experimental neuropsychology, which compares the performance under routine conditions (i.e., walking without distractions) with performance under a dual task condition (i.e., simultaneously executing an attention-demanding task or motor task) [13]. The relative changes in dual task walking performance are referred to as dual task interference or dual task effect (DTE) due to competing demands on cognitive resources required by the two tasks [14]. While tasks based on these principles have been widely documented to be used in neurorehabilitation, few studies demonstrated the utility of this tool as a clinical marker of cognitive decline in the elderly [15].

Dual-task-related changes in gait are considered as a sensitive marker of adverse effects of cognitive impairment on the highest levels of gait control. Individuals with early cognitive decline demonstrated reduced gait speed, particularly under dual task conditions [16]. These findings provide new perspectives and potential in the field of secondary prevention of dementia, which is key to developing public health-related policies to counter the global increase of the prevalence of dementia [17]. Furthermore, cognitive decline accompanied by slow gait speed is a more significant risk factor for dementia than slow gait speed or cognitive impairment alone, which supports the increased diagnostic value of dual task assessment over the evaluation of a single task [18].

One of the potential tools for rapid screening for pMCI among older adults is the Trail Walking Test (TWT). TWT is a cognitive-motor variant of the original Trail Making Test (TMT) [19] that has been routinely used in neuropsychology to predict the risk of falls among the elderly [20–22]. A previous study showed that it was a feasible, valid and reliable tool for assessment of the relationship between cognitive function and locomotion in persons with MCI, and with the potential to be used as a screening tool for pMCI [23]. Based on this evidence, we aimed to evaluate three variations of the TWT test of increasing complexity to predict pMCI in older adults, while thoroughly evaluating their discriminative abilities, sensitivity and specificity under various case-mix scenarios.

Materials and methods

Study design

A cross-sectional study has been conducted to evaluate the performance of the TMT and TWT tests to predict pMCI in older persons from among healthy adults of varying age.

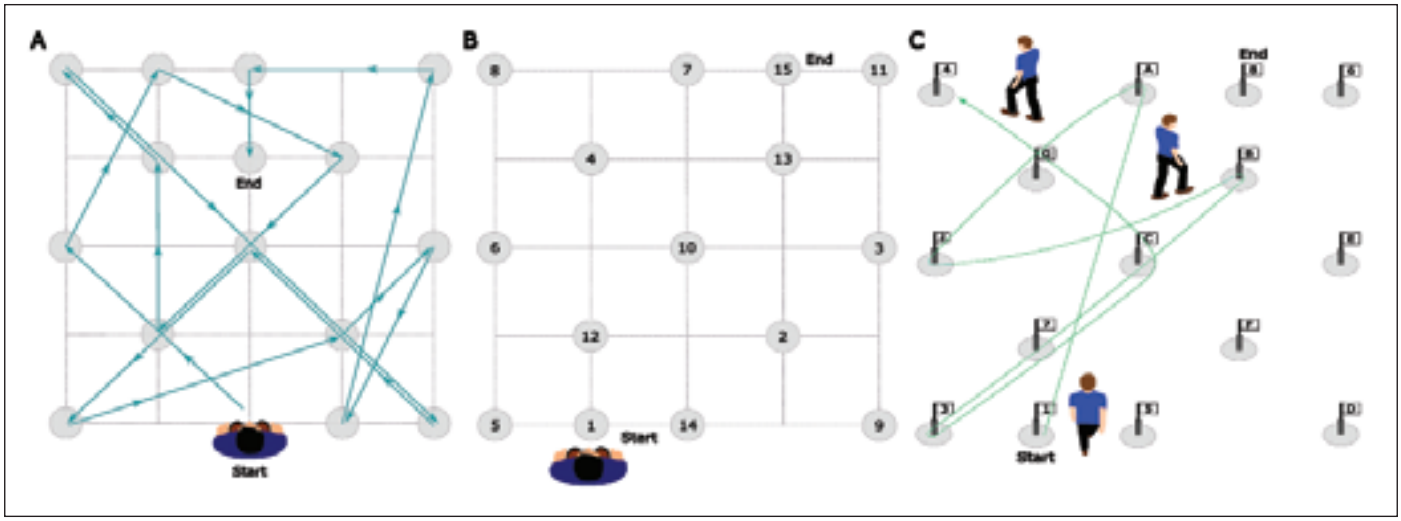

Fig. 1. Layouts of the TWT-1 (A), TWT-2 (B) and TWT-3 (C) used in the study. Adopted from [23].
Obr. 1. Schéma variant testů TWT-1 (A), TWT-2 (B) a TWT-3 (C) použitých ve studii. Převzato z [23].

Participants and setting

Participants in the "healthy young adults (HYA)" cohort were selected from among graduate students at the Faculty of Health Sciences at the University of West Bohemia. The inclusion criteria were defined as: age between 20 and 27 years, normal or corrected-to-normal vision, and being fully enrolled in a graduate university program. Those with known cognitive impairments, neurological disease, or physical gait restrictions were excluded.

Participants in the "older adults" cohort were selected from among the visitors of a sports center in a senior home in Prague. Inclusion criteria for this group were set following previous similar investigations [24] as: age 45 years and over, no eye or hearing impairment (including corrected impairments), ability to walk on his/her own without locomotion aids and ability to understand and obey instructions during testing. Those with musculo-skeletal impairments (such as osteoarthritis that influences the posture during walking), those with central and/or peripheral neurological diseases, those with recent or undergoing surgical procedures, and those with psychiatric diagnoses or those using psychiatric medication potentially influencing the cognitive abilities were excluded.

Participants recruited in the "older adults" group underwent a test of the level of their cognitive abilities using the Montreal Cognitive Assessment tool (MoCA). MoCA has been shown to have high sensitivity and specificity for detecting MCI [25]. Based on the achieved score, the group was divided into two subgroups: older adults with intact cognitive ability (ICA), which included scores > 25 (out of the maximum possible 30 points) in the MoCA; and older adults with pMCI which included those achieving a score ≤ 25 in the MoCA. The cut-off of 25 points for pMCI has been previously shown as optimal and having high specificity and sensitivity [26]. Overall, 61 participants were recruited for the study. The existence of two control groups allowed exploration of the differences in performance between the pMCA group, (N = 21), compared to healthy younger adults (N = 21) and healthy older adults (N = 19). Furthermore, the existence of two control groups (younger and older) allowed us to explore the association of age and performance in dual tasks in adults with ICA. For this reason, we used TWT as a feasible, reliable and ecological valid dual task to better understand the relationship between cognitive and gross motor functions in the preclinical stage of mild cognitive impairment, including healthy young individuals [27]. The study has been implemented between June 2021 and March 2022.

Measures

The Trail Making Test

In order to assess the executive functioning in the single task domain, TMT was used [19], which consists of two parts. During the first part (TMT-A), the tested persons are asked to join the randomly placed numeric targets printed in circles on the test sheet in order from 1 to 25 as fast as they can. During the second part (TMT-B), the tested persons are asked to join the numerical (1 to 13) and letter (A to L) targets printed in circles on the test sheet in order (e.g., 1–A–2–B etc.), as fast as they can. TMT-A and TMT-B present a task of cognitive-motor interference using fine motor skills. TMT evaluates visual perception abilities, perceptual/motor speed, and speed processing in Part A, and mental flexibility in Part B.

As part of the TMT, a test of motor speed (TMT-MS) was performed in all participants in which they were asked to connect the targets with dotted lines in the direction shown by arrows. The aim of this test was to assess the ability to adjust the precision of movement based on spatio-temporal limitations [27].

A practical demonstration of the task was presented to all participants before the actual testing. Participants were asked to correct all errors made during the test, which increased the time needed for completing it. All tests were conducted in a randomized manner (order of subjects to be tested was determined using a random draw); the time was measured using a stopwatch with a precision of 0.01 s. Due to the longer time needed to complete TMT-B, compared to TMT-A and TMT-MS, we provide a measure of speed in centimeters per second (cm/s) instead of time.

The Trail Walking Test

The Trail Walking Test [21,27] is an adaptation to walking of the TMT – a traditional neuropsychological test. TWT has been designed to assess the walking speed under dual task conditions. Three variants of the TWT were used in this study (TWT-1, TWT-2,

Tab. 1. Demographic characteristics, exercise profile of the tested subjects by study group and their performance in the Montreal Cognitive Assessment test.

Parameter	Study Group			Total (N = 61)	P-value
	pMCI (N = 21)	ICA (N = 19)	HYA (N = 21)		
age (mean, SD)	70 (8.6)	62.8 (10.1)	22.6 (2.7)	51.5 (22.6)	< 0.001
female sex (N, %)	12 (57%)	13 (68%)	17 (81%)	42 (69%)	0.249
height (mean, SD)	168.6 (11.1)	167.4 (10.4)	171.1 (9.8)	169.1 (9.8)	0.479
weight (mean, SD)	77 (13.8)	74.3 (18.2)	67.4 (12.8)	72.9 (15.3)	0.114
BMI (mean, SD)	27.1 (4.3)	26.5 (6.2)	22.9 (3.3)	25.5 (5)	0.012
education time (mean, SD)	13.8 (1.7)	14.4 (2.4)	15.9 (1.9)	14.7 (2.1)	< 0.01
weekly activity (days; mean, SD)	2.5 (1.8)	2.8 (1.6)	1.7 (1.7)	2.3 (1.8)	0.104
weekly physical activity (hours; mean, SD)	2.6 (2.5)	3.7 (3.4)	2 (3.4)	2.7 (2.4)	0.154
MoCA Score (mean, SD)	22.9 (1.9)	27.6 (1.1)	28.7 (1.2)	26.4 (1.1)	< 0.001

BMI – body mass index; HYA – healthy young adults; ICA – older adults with intact cognitive ability; MoCA – Montreal Cognitive Assessment; N – number; pMCI – probable mild cognitive impairment; SD – standard deviation

and TWT-3) in a randomized order. Test areas of the three TWT variants were prepared separately side by side. Each test was laid out on a surface of 16 m^2 (4 × 4 m) with 15 flags one meter apart on cones placed in 30-cm circles. Both start and finish of the trail were marked.

For the TWT-1 test with shown indicators of walking direction, the path between the flags was marked with arrows (Fig. 1A). The tested persons were asked to follow the route marked with arrows. They were instructed to follow the required direction as fast as possible (while still walking, not running) and as precisely as possible. Time to complete the task was measured using a stopwatch with a precision of 0.01 s.

For TWT-2, 15 flags with numbers 1–15 were selected and randomly placed in the test area (Fig. 1B). The tested persons were asked to proceed to the marks with increasing order of numbers 1–15. They were instructed to follow the required direction as fast as possible (while still walking, not running) and as precisely as possible. Time to complete the task was measured using a stopwatch with a precision of 0.01 s.

For TWT-3, targets were prepared in the same manner as for the previous test, but with increasing sequential numbers and letters. The tested persons were asked to follow the increasing order of numbers combined with letters (i.e., 1–A–2–B–3–C) (Fig. 1C). The numbers ranged from 1–8 and the letters ranged from A–G. The test ended with the last number, namely number 8. The tested persons were instructed to follow the required direction as fast as possible (while still walking, not running) and as precisely as possible. Time to complete the task was measured using a stopwatch with a precision of 0.01 s.

A test was considered completed successfully if the tested person completed the trail by stepping into each of the circles without moving and flipping the cones. Failing to contact the required field or failing to maintain the required direction of walking were both considered errors. All errors were noted and corrected – after which the tested person was allowed to continue, but the time to correct the error was added to the final time.

10 Meter Walking Test

All participants were also asked to complete the 10 Meter Walking Test (10-MWT) where they were asked to complete a 10-m trail marked with a colored tape (with additional 2 m before the start and after the end of the 10-m section) by walking at a constant maximum speed. The time to complete the trail was timed to a precision of 0.01 s. The test was repeated three times and the average speed has been calculated.

Analysis and Statistical Methods

Two strategies were applied during the analyses. First, univariate comparisons were performed between the three groups of participants (e.g., HYA, ICA and pMCI) in all obtained characteristics and measures (e.g., demographic characteristics and performance measures for each test applied). One way analysis of variance (ANOVA) was used to compare numerical variables, and the chi-square test was used to test for differences among the groups in case of categorical variables.

Secondly, the performance of the respective variants of the TMT and TWT used in the study to discriminate participants with pMCI (as determined by MoCA used as a reference in these analyses) were tested by fitting a logistic regression model. The area under the receiver operating characteristics curve (AUC) was used as a primary measure of discrimination ability. Optimal cut-off points were calculated, along with sensitivities and specificities under each respective scenario. In addition to these parameters, the Youden index as a summary measure of sensitivity and specificity was obtained. To correct for optimism of the predictions, an internal validation procedure was performed using bootstrapping (1,000 iterations) and optimism corrected AUCs (AUC_{VAL}) were calculated. P-value < 0.05 was considered as statistically significant. The R statistical software (R Cote Team, Auckland, New Zealand) was used for all analyses presented in this paper [28].

Results

Characteristics of participants

Table 1 presents an overview of the characteristics of the study participants. Overall, 61 participants were recruited for the study and were categorized as HYA (21; 34%), ICA (19; 32%) and pMCI (19; 34%). The mean

Tab. 2. Performance in the Trail Making test, Trail Walking Test and 10 Meter Gait test of the tested subjects by study group.

Parameter	Study Group			Total	P-value
	pMCI (N = 21)	ICA (N = 19)	HYA (N = 21)	(N = 61)	
TMT-MS (s; mean, SD)	24.9 (11.9)	18.7 (8.3)	15.6 (6.5)	19.8 (9.9)	< 0.001
TMT-MS (cm/s; mean, SD)	6.1 (2.5)	7.7 (2.6)	9.5 (3.6)	7.8 (3.2)	< 0.01
TMT-A time (s; mean, SD)	34.6 (12.2)	26.6 (9.7)	19.1 (5.2)	26.7 (11.3)	< 0.001
TMT-A speed (cm/s; mean, SD)	4.1 (1.3)	5.3 (1.6)	7.1 (2)	5.5 (2.1)	< 0.001
TMT-B time (s; mean, SD)	99.6 (47.6)	73.7 (22.1)	44.6 (11.3)	72.6 (38.4)	< 0.001
TMT-B speed (cm/s; mean, SD)	2.1 (0.9)	2.5 (0.8)	4.1 (0.9)	2.9 (1.2)	< 0.001
average 10-MWT (mean; SD)	1.9 (0.9)	2.3 (0.8)	2 (0.2)	2 (0.7)	0.145
average TWT-1 (s; mean, SD)	28.5 (8.3)	22.6 (5.1)	17.6 (2.6)	22.9 (7.4)	< 0.001
average TWT-2 (s; mean, SD)	49.8 (15.2)	38.4 (8.3)	28.8 (2.6)	39 (13.3)	< 0.001
average TWT-3 (s; mean, SD)	63.8 18.9)	45.7 (11.3)	38.7 (6.9)	49.5 (17)	< 0.001

10-MWT – 10 Meter Walking Test; HYA – healthy young adults; ICA – older adults with intact cognitive ability; MS – motoric speed; N – number; pMCI – older adults with probable mild cognitive impairment; SD – standard deviation; TMT – Trail Making Test; TWT – Trail Walking Test

age in the pMCI group was the highest – 7.2 years higher than the ICA group. The most balanced sex ratio was observed in the pMCI group, while female sex was observed in over 2/3 of the participants in the ICA and HYA groups. The mean body mass index (BMI) of the whole group was 25.5 points (standard deviation [SD] = 5), with a significantly lowest mean value observed in the HYA group. On average, the participants reported 14.7 years of attained education, with a significantly higher average number of years in the HYA group. No significant differences were observed in the weekly reported physical activity hours or days.

Univariate comparisons in the selected performance measures of the used tests are summarized in Tab. 2. Statistically significant differences in average performances were observed between the three compared groups in all cases except in the 10-MWT. A general trend can be seen in the tabulated results, where clearly the pMCI group on average showed the worst performance in all tests (highest mean times were observed in this group needed to complete all used versions of the TMT and TWT, while lowest average speed was observed in participants in this group to complete the TMT-MS). On the other hand, the HYA group displayed the best results related to time and speed needed to complete the tests.

In addition to this, a clear increasing time needed for completion can be observed between the TMT and TWT test versions of increasing complexity of the dual task (e.g., the average time to complete the TWT-3 was the highest among all three compared groups followed by TWT-2 and TWT-1; a similar gradient was seen when comparing the more complex TMT-B to the TMT-A version). This points to the sensitivity of the used versions of the test to put increasing demand on the participant's cognitive function while being tested using tests of increasing intended complexity.

Table 3 presents a summary of the analyses of the ability of the used test to discriminate between persons with pMCI (as assessed by MoCA as a reference tool) and no cognitive impairment in three different comparison scenarios: pMCI vs. all controls (e.g., ICA + HYA combined in one control group), pMCI vs. ICA, and pMCI vs HYA. When pMCI was compared to all controls combined, the models showed very good discriminative ability in all instances (AUC > 0.8), with the best performance (as measured by the AUC) observed when using the TWT-2 test (AUC = 0.876), and the worst in case of the TMT-A and TMT-B tests. Models only including HYA as controls showed even higher performance, with AUCs nearing or exceeding 0.9 (the overall best performance was seen in TWT-2 when discriminating between pMCI and HYA participants, AUC = 0.975). Of all three comparison scenarios, the worst discriminating performance was observed when comparing pMCI with the ICA group (AUCs ranging from 0.67 to 0.77). Tab. 3 also shows the values of AUC that were corrected for optimism using a validation procedure with bootstrapping. Values of the corrected AUCs (AUC_{VAL}) were very similar to the uncorrected ones, pointing towards high internal validity of all evaluated tests in our setting. Summary comparisons of AUCs in various scenarios are presented in Fig. 2.

Similar results were obtained when analyzing the ability of the test to correctly identify patients with pMCI (e.g., sensitivity), and the ability of the tests to correctly identify people without pMCI (e.g., specificity). Highest values in general were observed under the scenario comparing the pMCI and ICA groups, followed by the scenario using all controls combined, and only ICA. The Youden index, as a summary measure of sensitivity and specificity, showed the best performance in TWT-2 when comparing pMCI vs. HYA. In general, TMT-B showed increased performance measured by both AUC and sensitivity/specificity over TMT-A. Similarly, TWT-2 performed better when compared to TWT-1 in all parameters, but TWT-3 did not show added value over TMT-2.

Discussion

Main findings

We conducted a cross-sectional study to analyze the ability of the TMT and TWT tests with a dual task component of increasing complexity to discriminate between older adults with pMCI and between adults with intact cognitive abilities. We found that all

Tab. 3. Performance of the applied tests in discriminating older adults with probable cognitive impairment, healthy older adults and healthy young adults.

Test	Groups compared	AUC	AUC_{VAL}	Sensitivity	Specificity	Optimal Cut-off point	Youden index	P-value
TMT-A	pMCI vs. all controls	0.81	0.809	78%	71%	4.8	0.49	< 0.001
	pMCI vs. HYA	0.717	0.716	89%	48%	3.5	0.37	0.023
	pMCI vs. ICA	0.894	0.894	90%	71%	4.8	0.62	< 0.01
TMT-B	pMCI vs. all controls	0.81	0.805	75%	76%	2.5	0.52	< 0.001
	pMCI vs. HYA	0.67	0.66	100%	33%	1.5	0.33	0.103
	pMCI vs. ICA	0.927	0.927	95%	81%	2.9	0.76	< 0.001
TWT-1	pMCI vs. all controls	0.832	0.829	76%	83%	24	0.59	< 0.001
	pMCI vs. HYA	0.734	0.736	52%	95%	29.1	0.47	0.021
	pMCI vs. ICA	0.918	0.917	76%	100%	24	0.76	< 0.01
TWT-2	pMCI vs. all controls	0.876	0.875	71%	95%	41.6	0.66	< 0.001
	pMCI vs. HYA	0.767	0.765	71%	89%	41.6	0.61	0.019
	pMCI vs. ICA	0.975	0.977	90%	95%	34.1	0.86	< 0.01
TWT-3	pMCI vs. all controls	0.837	0.839	71%	93%	56.3	0.64	< 0.001
	pMCI vs. HYA	0.77	0.77	71%	84%	56.3	0.56	< 0.01
	pMIC vs. ICA	0.896	0.895	71%	100%	56.3	0.71	< 0.01

AUC – area under the receiver operating curve; AUC_{VAL} – AUC corrected for optimism using internal validation; HYA – healthy young adults; ICA – older adults with intact cognitive ability; pMCI – older adults with probable mild cognitive impairment; TMT – Trail Making Test; TWT – Trail Walking Test

versions of the TMT (e.g., TMT-A and TMT-B) and TWT tests (e.g., TWT-1, 2 & 3) have very good ability to discriminate between persons with pMCI and those with ICA, and to correctly identify those with and without pMCI (using MoCA as a reference). Gait disturbances are among the main symptoms of MCI, along with memory impairments and executive dysfunction, but have not been examined in combination through clinical practice. Persons with MCI have poor gait performance under dual tasking, especially in the prodromal stage. These clinical differences without the benefit of interference effects may remain otherwise undetected in the early stages of cognitive decline. The TWT, which includes walking, should help to better understand the relationship between cognitive function and gait in people with MCI. Thus, TWT can help to differentiate between different subtypes of MCI, describing dual task results as a motor signature in MCI, which may be considered as an added value.

There was a clear benefit using TMT-B over TMT-A with regard to performance. While TWT-2 showed benefit over TWT-1, the added value of TWT-3 over TWT-2 has not been shown in the study. All tests showed very good predictive performance even after correction for optimism, suggesting their robustness to be used as screening tools for pMCI in older adults.

Comparison with literature and interpretation

Previous studies have investigated the effect of dual tasks, e.g., the effect of a concurrent task on a complex walking task in persons with pMCI. Most notably, the study Klotzbier et al. [23] evaluated the performance of older adults with probable pMCI in such tests, compared to older adults without pMCI, and healthy young adults. As this study used the same methodology for stratification of subjects, and the same battery of dual task tests, their results are directly comparable to our findings. In all comparisons, similar results are presented by both studies: the pMCI group achieved the lowest average speed in the TMT-MS test (6.1 m/s in our study vs. 8.65 m/s); in the TMT-A test (4.1 m/s in our study vs. 4.38 m/s); and in the TMT-B test (2.1 m/s in our study vs. 1.97 m/s in the study by Klotzbier et al. [23]), when compared to ICA and HYA. Thus, our study confirms that people with pMCI perform significantly worse in these tests.

Both our study and the study by Klotzbier et al. [23] used the TWT for assessment of performance in a dual task, as designed by previous studies [21,29,30]. As with the TMT, both studies yielded very similar results: e.g., that older adults with pMCI performed significantly worse in all comparisons against the ICA and HYA groups, and that increasing complexity of the dual task led to significantly worse performance (all groups performed worse in TWT-3 and best in TWT-1). Thus, our findings also confirm that persons with pMCI as measured by MoCA perform significantly worst in all iterations of the TWT as a dual task test, when compared to healthy older and healthy young adults. This pattern of performance was confirmed also in the study by Perrochon et al. [29], albeit using a slightly different variation of the TWT.

Our study showed a clear gradation of the performance in TWT between older adults with and without cognitive impairment (in our study the pMCI and ICA groups). In addition, other studies (while reporting similar findings) showed that both age and degree of cognitive impairment play an important role – performance in TWT and its variations decreased by age and degree of cognitive impairment [3,20,31].

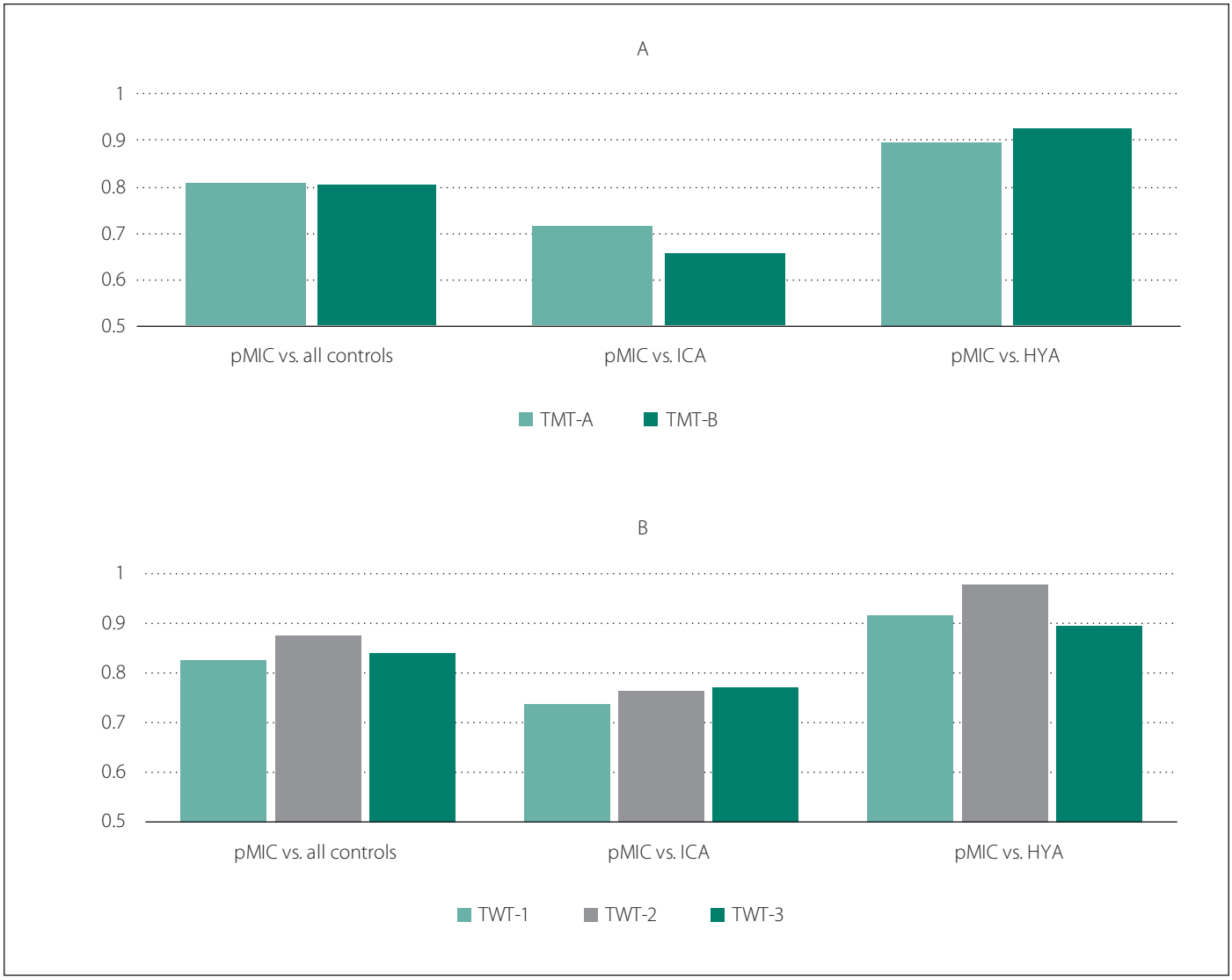

Fig. 2. Comparison of the discrimination ability (AUC) of the tested versions of the TMT (A) and TWT (B) tests in various comparison scenarios.

AUC – area under the receiver operating characteristic curve; HYA – healthy young adults; ICA – older adults with intact cognitive ability; pMCI – older adults with probable mild cognitive impairment; TMT – Trail Making Test; TWT – Trail Walking Test

Obr. 2. Srovnání diskriminační schopnosti (AUC) testovaných verzí testů TMT (panel A) a TWT (panel B) v různých případech sledování.

AUC – plocha pod křivkou; HYA – kontrolní skupina mladých jedinců; ICA – starší dospělí s intaktními kognitivními funkcemi; pMCI – starší dospělí s pravděpodobnou mírnou kognitivní poruchou; TMT – Trail Making Test; TWT – Trail Walking Test

Our results complement the motor cognitive risk syndrome, where participants with cognitive decline and slower walking speed had a higher risk of dementia, by demonstrating that dual task walking can predict dementia in participants with MCI, whereas single-task walking speed does not. Previous studies in the general population have suggested that dual task walking slowly is most probably associated with the incidence of vascular dementia [32]. This interplay is further supported by a common neural substrate, as the prefrontal cortex is involved in neural control of gait and cognitive function. In particular, executive functions are involved in the control of gait. Evidence from functional MRI studies suggests a different pattern of prefrontal cortex oxygenation in older adults with MCI during walking under challenging circumstances compared to cognitively healthy controls [33]. In our study, gait changes during dual task were primarily associated with Alzheimer's disease, which may be explained by the fact that our study focused only on individuals with MCI.

In addition to previous studies, our study is the first to provide indicators of predictive performance that are corrected for optimism using an internal validation procedure based on bootstrapping. Even after correction, the very good performance of all evaluated tests remained, which further confirms that they can potentially be used as a robust screening tool for pMCI in older adults. Previous studies have only assessed cognitive-motor behavior in older and younger groups and have not focused on validating the TWT.

This form of validation procedure has not been previously investigated, allowing them to confirm the stratification factor of detecting MCI using dual task interference, which

could not be validated with confidence compared to previous studies.

Other tests, such as the Stroop walking test [34], the Walking Stroop carpet [35], or the Floor maize test [36] were designed following the dual task paradigm to be used for the assessment of various aspects of cognitive impairment in older adults. General studies reporting results using these tests confirmed our findings that dual task tests could be used to detect cognitive impairment in older adults, but due to different tests, study set-ups, and populations, we are not able to provide a more comprehensive comparison.

Our study also evaluated the potential of TWT and its variants as dual task tests to predict pMCI in older adults. We found that all evaluated variants of TWT (TWT-1, TWT-2 and TWT-3) showed very good ability to discriminate between older adults where pMCI was suggested by MoCA, and between healthy older and younger adults - with better performance in discriminating between pMCI vs. HYA than between pMCI and ICA. Our results confirmed the findings of a previous study reporting on this: the AUC (as the primary measure of discriminating ability) in our study was ≥ 0.9 in all iterations of the TWT (vs. ≥ 0.96) when the pMCI and HYA were compared; it was ≥ 0.7 vs. > 0.6 in the study by Klotzbier et al. [23].

We have also evaluated predictive performance of all tested TWT versions when the pMCI group was compared against all controls combined (e. g., ICA and HYA) – with AUCs observed for the TWT-2 version. These comparisons have important practical implications, as they show that TWT (especially TWT-2) as a dual task test can be used to identify older adults with pMCI from among a mix of healthy younger and older persons with a very good discriminative ability. Further research is needed to confirm these findings, and as to our knowledge, this is the first evaluation of its kind.

In addition, our study showed that there was no added value of the TWT-3 over the TWT-2 version to discriminate older adults with pMCI from healthy persons (AUC 0.876 vs. 0.837). The difference in stratification between TWT-2 and TWT-3 has not yet been addressed stratification-wise and also provides an opportunity to provide insights into the use of all test variants. In the study by Klotzbier et al. [23], the difference was relatively small (AUC 0.986 vs. 0.999). We suggest that further research should be done to elucidate the increasing/diminishing added value of using tests of increasing complexity - based on our results, TWT-2 seems to be the best compromise between complexity and performance.

Other neuropsychological tests are readily available for the diagnosis of MCI such as the Mini Mental State Examination (MMSE) or MoCA (used as a reference tool in this study) [37]. However, the critical importance of early-stage screening tools in the prevention of dementia [38] amplifies the need for research that would compare the validity and usefulness of existing tools in different settings and populations, and that would generate evidence towards the usefulness of novel tools based on new paradigms such as the dual task paradigm. Our study contributes further evidence that tests based on dual tasks have high validity and can be applied as a regularly used screening tool for MCI not only in individuals in clinical settings, but also in settings where groups of individuals can be screened at once, such as elderly homes and elderly sports centers – such an approach may be a way of "mass" screening for early signs of MCI in an informal way (e. g., not as part of a visit to a physician and without the stress of a clinical examination).

Limitations of the study

We recognize that there are several limitations to our study. First, we have used a relatively small sample size to address our research questions. While this may not pose a bias as such, higher sample sizes could increase the power and generalizability of our findings. On the other hand, similar studies used sample sizes of comparable size (e. g., 50 [29] or 87 [23]), suggesting that our study is in this respect fully comparable to the published research. Secondly, a limited sampling pool was available for the study, thus there may be some selection bias. However, we do not expect this to have a significant effect on the results and generalizability of our findings. Again, also with respect to sampling strategy, our design is similar to other published studies [23,29]. In general, we suggest that future research in this area should use an expanded sample size and more elaborate randomized sampling if possible – this would bring more power to the study and help answer the questions for which the available literature does not give equivocal answers.

Conclusions

The dual component TWT can be effectively used to screen older adults with pMCI with a very good ability to discriminate these people from healthy persons of younger and older ages. This may improve early detection of pMCI in clinical and non-clinical settings. While increasing complexity of the test increases its predicting performance, based on our findings, there seems to be a cutoff beyond which the added value of more complex tests diminishes.

Ethics approval and consent to participate

The study has been approved by the Ethical committee of the Faculty of Health Sciences and Social Work of Trnava University (Trnava, Slovakia) – approval ID: EK-5/3K/2021, date: 14. 4. 2021. All participants signed a written informed consent to participate in the study. All methods in the presented study were performed in accordance with the relevant guidelines and regulations.

Availability of data and materials

The dataset supporting the conclusions of this article is available from the authors upon reasonable request. Iva Hereitová should be contacted for such requests, email: ivlckova@kfe.zcu.cz.

Authors' contributions

IH and MM made substantial contributions to the conception and design of the work, data analysis and interpretation; AMH made substantial contributions to the conception of the work and acquisition, and interpretation of data; IH and MM have drafted the work; and AMH substantively revised it. All authors have approved the submitted version (and any substantially modified version that involves the author's contribution to the study) and have agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution is documented in the literature.

Conflict of interest

The authors declare they have no potential conflicts of interest concerning drugs, products, or services used in the study.

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