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Association between dual-task function and neuropsychological testing in older adults with cognitive impairment☆

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ABSTRACT

Introduction: Despite the current high prevalence of dementia, more than half of older adult patients never receive an evaluation. Current evaluation methods are lengthy, cumbersome, and not viable for busy clinics. This indicates that, despite recent improvements, a quick and objective routine test for screening cognitive decline in older adults is still needed. Poor dual-task gait performance has been previously associated with decreased executive and neuropsychological function. However, gait tests are not always viable for clinics or older patients.
Methods: The aim of this study was to assess the relationship between a novel upper-extremity function (UEF) dual-task performance and neuropsychological test results in older adults. For UEF dual-tasks, participants performed a consistent elbow flexion and extension, while counting backwards in increments of threes or ones. Wearable motion sensors were attached to the forearm and upper-arm to measure accuracy and speed of elbow flexion kinematics to calculate a UEF cognitive score.
Results: We recruited older adults at three stages: cognitively normal (CN) ($n = 35$), mild cognitively impaired (MCI) of the Alzheimer's type ($n = 34$), and Alzheimer's disease (AD) ($n = 22$). The results demonstrate significant correlations between UEF cognitive score and mini-mental state examination (MMSE), Mini-Cog, Category fluency, Benson complex figure copy, Trail making test, and Montreal cognitive assessment (MOCA) (r values between -0.2355 and -0.6037 and $p < 0.0288$).
Discussion: UEF dual-task was associated with executive function, orientation, repetition, abstraction, verbal recall, attention and calculation, language and visual construction. Of the associated brain domains, UEF dual-task was most significantly associated with executive function, visual construction, and delayed recall. The results from this study convey potential for UEF dual-task as a safe and convenient cognitive impairment screening method.

1. Introduction

Cognitive impairment is an increasingly relevant health concern, as estimates demonstrate that by 2060 there will be over 152 million older adults with dementia globally, approximately a 200 % increase compared to 2019 (Nichols et al., 2022). Among dementia types, Alzheimer's disease (AD) is the most common and affects up to 11.3 % of older adults (Rajan et al., 2021). Despite this high prevalence, one-half to two-thirds of early-stage AD cases may go undiagnosed (Lang et al., 2017). The most common current screening tools for cognitive impairment, written neuropsychological tests, are often subjective and affected by education and language biases (e.g., clock-drawing test) (Shenkin et al., 2014; Ehsani et al., 2020; Toosizadeh et al., 2019; Toosizadeh et al., 2016a; Ehsani et al., 2019). Additionally, it is more difficult to track changes in cognitive function using these tests as retesting can introduce learning biases.

Simultaneous declines in motor and cognitive performance occur with aging (Volkow et al., 1998; Verhaeghen et al., 2003; Blazer et al.,

Abbreviations: UEF, upper extremity function; CN, cognitively normal; AD, Alzheimer's disease; MMSE, mini-mental state examination; MOCA, Montreal cognitive assessment; MCI, mild cognitive impairment; ANOVA, analysis of variance; fMRI, functional resonance magnetic imaging.

☆ We certify that this work is novel. This study is the first of its kind to identify the relationship between dual-task function and neuropsychological test results in older adults using an upper-extremity function dual-task.

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2015). Furthermore, assessing deficits in dual-tasking can provide a powerful tool for screening cognitive impairments. Gait is commonly the motor component in dual-task assessments. Poor dual-task gait performance is significantly correlated with decreased executive and neuropsychological function and associated with mild cognitive impairment (MCI) and AD (Sheridan et al., 2003; Camicioli et al., 1997; Montero-Odasso et al., 2012). However, many older adults have mobility impairments and many clinics lack adequate space to perform gait measures.

We have previously developed and validated an upper-extremity function (UEF) test to assess frailty among older adults (Toosizadeh et al., 2016b; Toosizadeh et al., 2017a). The UEF test integrates low-cost sensors and a data acquisition system (as low as $200), the physical assessment (including preparation/calibration) is easily performed in <5 min, and the post-processing is performed in <2 min. Strong correlations between UEF, gait speed, and six-minute walk distance were also previously determined (Toosizadeh et al., 2017b). Further, we have compared the UEF dual-task performance and demonstrated UEF proved more sensitive than did gait as the motor task components within the dual-task challenges (Ehsani et al., 2019). Additionally, the UEF test may be more ideal than a gait test for assessing cognitive impairment as it is less physically demanding and less influenced by confounders such as poor balance. Further, the UEF test may require some degree of skill learning which can increase the demand on attentional resources and working memory.

Likewise, relative to written neuropsychological tests, the proposed approach is objective and the cognitive score is available immediately and automatically after testing. The UEF test may be readministered to effectively track changes in cognitive function. UEF test results are presented in a numeric scale, allowing for more subtle changes in function to be tracked versus stratifying patients into groups of cognitive function (CN, AD, and MCI).

In continuation of previous work, the current study investigated the relationship between UEF dual-task performance and neuropsychological test results in older adults. Ultimately, the goal is to assess physical and cognitive function with a single testing platform using UEF. The purpose of the current study is to validate the cognitive component for the testing platform. The hypotheses were: (1) UEF scores would be significantly associated with various cognitive tests including mini-mental state examination (MMSE), Mini-Cog, Category fluency, Benson complex figure copy, Trail making test, and MoCA; (2) UEF scores would be significantly associated with various cognitive domains including executive function, orientation, repetition, abstraction, verbal recall, attention and calculation, language and visual construction; and (3) UEF task counting interval does not affect correlations with the respective neuropsychological tests.

2. Methods

2.1. Participants

Older adult participants were recruited from the Banner Sun Health Research Institute from September 2017 to May 2018 and categorized into cognitive groups based on the National Institute of Aging – Alzheimer's Association (NIA-AA) criteria (Sperling et al., 2011; McKhann et al., 1984). Inclusion criteria were: (1) age 65 years or above; (2) ability to understand study instructions; (3) English language proficiency; and (4) normal cognitive status, AD, or MCI diagnosis of the Alzheimer's type within 6-month of the study. Exclusion criteria were: (1) diagnosed diseases associated with severe motor performance deficits including stroke or Parkinson's disease; (2) severe speech disorders; and (3) severe upper-extremity disorders. Eligible participants provided written informed consent in accordance with the Declaration of Helsinki (Association, G. A. o. t. W. M, 2014) before participation. The University of Arizona Institutional Review Board approved the study.

2.2. Clinical measures

Participants performed neuropsychological tests within 6 months prior or during data collection. The neuropsychological tests were MoCA, MMSE, Stroop color-word interference, Craft story 21 recall (immediate and delayed), Benson complex figure copy (immediate and delayed), Wechsler digit span task, Category fluency, Verbal fluency: phonemic test, Trail making test, and multilingual naming test (MINT). These standardized tests assessed several cognitive domains including executive function, orientation, repetition, abstraction, verbal recall, attention and calculation, language, working memory, and visual construction.

The following questionnaires were also included: 1) frailty (the Fried Index) (Fried et al., 2001); 2) comorbidity (CMS Hierarchical Condition Category (CMS-HCC)) (Charlson et al., 1987); and 3) depression (Center for Epidemiological Studies Depression (CES—D)) (Kroenke and Spitzer, 2002). Physical frailty was assessed to check differences in motor function between groups. Comorbidity was measured as it is associated with an increased risk of cognitive impairment (Vassilaki et al., 2015). Depression was assessed as it is associated with cognitive deficits in executive function, memory, and attention (Rock et al., 2014).

2.3. UEF measures

Participants performed the UEF elbow flexion test with their dominant arm or non-dominant in case of severe injury of the dominant side. We previously determined similar results using either arm (Toosizadeh et al., 2017a). Tri-axial wearable gyroscopes (sample frequency = 100 Hz, BioSensics LLC, Boston, MA, USA), were attached near the biceps and the wrist.

Participants were instructed to perform elbow flexion as consistently as possible for 60 s with a self-selected pace in combination with a cognitive condition. Cognitive conditions included counting backward by ones (dual-task 1) and counting backward by threes (dual-task 2) starting from a random two-digit number. Participants completed each dual-task once. Similar instruction was used for all participants as follows: “Please completely open and close your arm as consistently as possible for 60 s with a normal speed you desire. “We will let you know when to stop”. We considered speed and consistency to represent delay and accuracy aspects of dual-tasking, as they are related to cognitive aging (Verhaeghen et al., 2003). Trial order was randomized to minimize confounding fatigue and learning effects. Counting was selected as the cognitive task because it involves working memory and relates to executive functioning (Lee and Kang, 2002).

Using recorded angular velocity several outcome measures representing kinematics of the elbow flexion were derived. To extract these measures, the angular velocity signals from the sensors were filtered to remove drifting (first order high pass butter-worth filter with a cutoff frequency of 2.5 Hz). Then, using a peak detection algorithm to determine the maximum and minimums of the angular velocity signal, elbow flexion cycles were detected.

The UEF cognitive score (range: cognitive normal = 0; cognitive impairment = 1) was derived based on speed and accuracy of motor function performance (Toosizadeh et al., 2017a). Points are assigned based on parameter comparisons to previously determined ranges: 1) flexion number, 2) range of motion variability (coefficient of variation [COV] of the flexion angle range), and 3) flexion variability (COV of consecutive timing of angular velocity peaks).

2.4. Statistical analysis

Analysis of variance (ANOVA) models in JMP Statistical Software evaluated the differences in the continuous demographic and clinical parameters between the three groups ($\alpha = 0.05$). Chi-square χ^2 assessed gender and comorbidity categories differences, and the Fisher's exact test assessed frailty prevalence differences between groups. The

associations between UEF score and various neuropsychological tests were calculated using one-way ANOVA and Pearson correlation for normally distributed tests and Spearman's rank correlation for not normally distributed tests were presented. To adjust for multiple comparisons and limit the proportion of significant results that are false positive, we calculated the false discovery rate (FDR) with criteria $q \leq 0.05$.

3. Results

3.1. Participants

Ninety-one participants were recruited, including 35 CN (age = 83.8 ± 6.9), 34 MCI (age = 83.9 ± 6.6), and 22 AD (age = 84.1 ± 6.1) older adults. Age, gender, height, weight, body mass index and education were not significantly different between these groups ($p > 0.07$, Table 1). Frailty status, and comorbidity and depression scores were also not significantly different between cognitive groups ($p > 0.08$, Table 1).

Due to the recruitment nature of the study, some participants had not previously completed all investigated neuropsychological tests. For the CN group, 1.02 % (SD: 1.42) of neuropsychological test results are not recorded. For the MCI group, 16.39 % (SD: 14.07) of neuropsychological test results are not recorded. For the AD group, 21.1 % (SD 17.70) of neuropsychological test results are not recorded. The number of participants for each neuropsychological test is outlined in Table 1.

3.2. UEF dual-task performance and neuropsychological tests

ANOVA models showed significant results for the following neurophysiological tests: MMSE, Mini-Cog, MOCA, Benson complex figure copy-delayed, category fluency and trail making test for both dual-tasks 1 and 2 ($p < 0.0068$, Table 2, Fig. 1). Based on this, dual-task results were significantly associated with the following neuropsychological domains: executive function, orientation, repetition, abstraction, verbal recall, attention and calculation, and language and visual construction. Dominant domains were determined by investigating which domains are significantly associated with each neuropsychological test. Dominant domains were defined to be the domains associated with MMSE, Mini-Cog, MOCA, Benson complex figure copy-delayed, category fluency and trail making test as those neuropsychological tests demonstrated significant results. Among the two cognitive components of counting intervals, neither produced stronger correlation trends than the other (Table 3).

4. Discussion

As hypothesized, UEF scores, regardless of task counting interval, were significantly associated with various cognitive tests including MMSE, Mini-Cog, Category fluency, Benson complex figure copy, Trail making test, and MoCA. The UEF test has its most important advantage in that it does not rely on the patients' ability to walk and can be performed with limited space and among bedbound patients. Motor function can help predict cognitive decline and increase diagnostic sensitivity, thus providing increased opportunities for early intervention. Within a previous study, flexion number and sensor-based motion variability parameters, within the normal pace elbow flexion, showed significant between-group differences. Using these parameters, the cognitive status (both MCI and AD) was predicted (sensitivity = 0.82 and specificity = 0.72) (Toosizadeh et al., 2019). Interestingly, it was recently identified that UEF motor variability had 15 % higher accuracy in predicting cognitive impairment compared to gait measures (Montero-Odasso et al., 2012). In this study, as hypothesized, the results further demonstrated a significant correlation between UEF cognitive score and most neuropsychological tests (Table 2).

As hypothesized, UEF scores were significantly associated with various cognitive domains including executive function, orientation, repetition, abstraction, verbal recall, attention and calculation, language and visual construction. The dominant domains were identified to be executive function, visual construction, and delayed recall. Previous studies have validated the relationship between brain functions and dual-tasking; attention and executive function were found to be the strongest indicators of dual-task performance using delayed visual recognition tasks (Holtzer et al., 2005). Similarly, another study indicated dual-task performance of visual tasks to be a highly sensitive tool

Table 1
Number of participants for neuropsychological tests across cognitive groups.

Neuropsychological test	CN	MCI	AD
MMSE	n = 35	*n* = 28	*n* = 17
Stroop color-word interference	n = 34	*n* = 34	*n* = 19
Mini-Cog	*n* = 35	n = 34	*n* = 21
Benson complex figure copy - Immediate	*n* = 34	*n* = 24	*n* = 18
Benson complex figure copy - delayed	n = 34	*n* = 27	n = 19
Weschler digit span task - span forward total	*n* = 35	n = 24	*n* = 12
Weschler digit span task - span forward longest	n = 35	*n* = 32	n = 18
Weschler digit span task - span back total	*n* = 35	*n* = 21	*n* = 10
Weschler digit span task - span back longest	n = 35	n = 32	n = 18
Category fluency - category animal	n = 35	*n* = 27	n = 18
Category fluency - category vegetable	n = 35	*n* = 20	n = 10
Trail making test - trail part A	n = 34	*n* = 30	*n* = 21
Trail making test - trail part B	n = 34	*n* = 31	n = 21
MOCA	n = 35	n = 34	n = 21

Table 2
Differences in demographic and clinical measures among cognitive groups.

Demographic information	CN (*n* = 35)	MCI (*n* = 34)	AD (n = 22)	p-Value[a] (effect size[b])
Male, n (% of the group)	13 (37 %)	16 (47 %)	11 (50 %)	0.57 (0.11)
Age, year (SD)	83.83 (6.92)	83.88 (6.57)	84.05 (6.21)	0.99 (0.01)
Height, cm (SD)	167.83 (9.97)	170.32 (9.47)	166.93 (11.06)	0.41 (0.14)
Weight, kg (SD)	71.15 (15.67)	71.09 (17.45)	67.02 (12.47)	0.57 (0.11)
Body mass index, kg/m^2 (SD)	25.27 (5.26)	24.39 (5.35)	23.97 (3.54)	0.59 (0.11)
Education, year (SD)	16.00 (2.47)	14.70 (2.89)	14.48 (2.89)	0.07 (0.25)
Clinical measures	**CN (n = 35)**	**MCI (n = 34)**	**AD (n = 22)**	**p-Value[a] (effect size[b])**
Montreal cognitive assessment, 0–30 (MoCA) (SD)	26.82 (2.48)	21.94 (2.63)	17.29 (1.59)	<0.0001[c] (1.58)
Mini-Cog, 0–5 (SD)	4.44 (0.86)	3.24 (1.33)	1.57 (1.08)	<0.0001[c] (1.01)
Mini-mental state examination, 0–30 (MMSE) (SD)	28.5 (1.58)	26.54 (2.38)	21.33 (4.20)	<0.0001[c] (1.07)
Frailty category, n (%)				
Non-frail	12 (34.3 %)	12 (35.3 %)	3 (13.6 %)	0.24 (0.18)
Pre-frail	19 (54.4 %)	16 (47.1 %)	16 (72.7 %)	
Frail	3 (8.6 %)	6 (17.7 %)	2 (9.1 %)	
Charlson-Deyo Comorbidity Index = 1, n (%)	21 (60.0 %)	20 (58.8 %)	7 (31.8 %)	0.08 (0.24)
Patient Health Questionnaire (PHQ-9), 0–27 (SD)	1.74 (2.74)	2.61 (2.95)	2.15 (2.61)	0.45 (0.14)

CN: cognitive normal; MCI: mild cognitive impairment; AD: Alzheimer's disease. SD: standard deviation.
[a] One-way analysis of variance (ANOVA) *F*-test, except chi-square for gender and Charlson-Deyo, and Fisher's exact for frailty.
[b] Cohen's F for ANOVA, and Cramér's V for Chi-square and Fisher's tests.
[c] Significant difference.

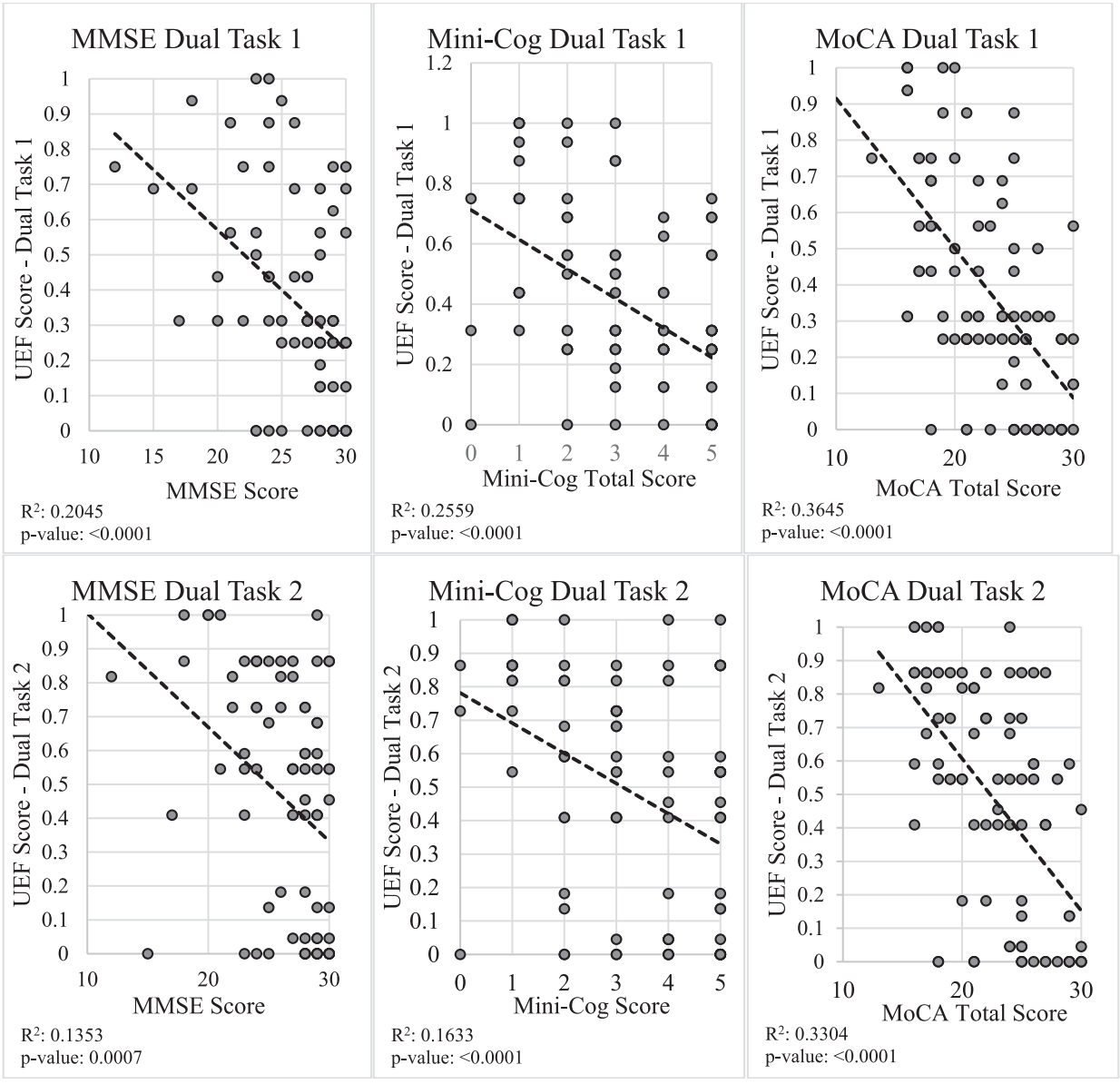

Fig. 1. Neuropsychological test scores and UEF scores across both dual-tasks for all participants. Individual data points represent a single participant's UEF Score and their corresponding neuropsychological test score. All groups are collapsed and included to better demonstrate the relationship between dual-task score and test results for varying levels of cognitive status. Some participants did not have complete records for all neuropsychological tests investigated in this paper. Additionally, due to fatigue, some participants were unable to complete both dual-tasks. In this case, depending on the randomized order of tasks, participants only completed dual-task 1 or dual-task 2. Furthermore, sample size varies for each plot.

in identifying deficits in working memory and executive function (McDowell et al., 1997).

In confirmation of current findings, our previous UEF dual-tasking within the function magnetic resonance imaging (fMRI) setting demonstrated that differences in brain function complexity are most easily identified across frontal and temporal brain regions (Peña et al., 2022). These findings agree with the current research, as the identified brain regions are associated with executive function, attention, and working memory (Stretton and Thompson, 2012; Chayer and Freedman, 2001). Further research, however, is required to establish the efficacy of UEF dual-tasking in comparison to visual dual-tasking as it is often used in cognitive assessment. It is expected that UEF dual-tasking could provide a more accurate assessment of motor function as previous work demonstrated differences in imagery and actual task (Allali et al., 2014; Beauchet et al., 2014).

5. Conclusions

UEF scores from dual-task trials were significantly associated with neuropsychological tests including MMSE, Mini-Cog, Category fluency, Benson complex figure copy, Trail making test, and MoCA. The association between UEF dual-task performance and neuropsychological tests was not dependent on task counting interval. UEF scores were significantly associated with cognitive domains including executive function, orientation, repetition, abstraction, verbal recall, attention and calculation, language and visual construction. The identified dominant domains were executive function, visual construction, and delayed recall.

6. Limitations and future directions

Several confounding parameters, including age, depression, comorbidity, and physical frailty were considered for adjustment within the

Table 3
Results from ANOVA for administered neuropsychological tests across both dual-tasks for all groups.

Neuropsychological test	Pearson or Spearman's rank correlation		*p*-Value[a]		FDR	
	UEF cognitive score (Dual-task 1)	UEF cognitive score (dual-task 2)	UEF cognitive score (dual-task 1)	UEF cognitive score (dual-task 2)	UEF cognitive score (dual-task 1)	UEF cognitive score (dual-task 2)
MMSE	−0.4522	−0.3678	<0.0001[b]	0.0007[b]	0.0026[b]	0.0017[b]
Stroop color-word interference	−0.1558[a]	−0.3188[a]	0.1761	0.0047[b]	0.2180	0.0087[b]
Mini Cog – total	−0.5058	−0.407	<0.0001[b]	<0.0001[b]	0.0013[b]	0.0026[b]
Mini Cog - word recall	−0.489	0.3061	<0.0001[b]	0.0033[b]	0.0009[b]	0.0072[b]
Mini Cog - clock	−0.3478	−0.4041	0.0008[b]	<0.0001[b]	0.0016[b]	0.0013[b]
Benson complex figure copy - Immediate	−0.2543	−0.2877	0.0288[b]	0.0129[b]	0.0394[b]	0.0186[b]
Benson complex figure copy - delayed	−0.4654	−0.5504	<0.0001[b]	<0.0001[b]	0.0007[b]	0.0009[b]
Weschler digit span task - span forward total	−0.0072	0.0649	0.9529	0.5983	0.9529	0.6482
Weschler digit span task - span forward longest	−0.2973	−0.1415	0.00578[b]	0.1963	0.0094[b]	0.2219
Weschler digit span task - span back total	−0.1422	−0.2431	0.2661	0.0549	0.3145	0.0751
Weschler digit span task - span back longest	−0.2931	−0.2102	0.0072[b]	0.0564	0.0110[b]	0.0733
Category fluency - category animal	−0.4071	−0.4308	<0.0001[b]	<0.0001[b]	0.0005[b]	0.0007[b]
Category fluency - category vegetable	−0.3943	−0.4375	0.0012[b]	0.0003[b]	0.0022[b]	0.0009[b]
Trail making test - trail part A	0.4283	0.2879	<0.0001[b]	0.0068[b]	0.0004[b]	0.0118[b]
Trail making test - trail part B	0.5459	0.4774	<0.0001[b]	<0.0001[b]	0.0004[b]	0.0005[b]
MOCA Total	−0.6037	−0.3688	<0.0001[b]	0.0003[b]	0.0003[b]	0.0008[b]
MOCA - visuospatial/ executive	−0.3964	−0.0337	0.0001[b]	0.7523	0.0003[b]	0.7523
MOCA- naming	−0.1104	0.0409	0.3005	0.7018	0.3255	0.7299
MOCA - attention read list of digits	−0.1541	−0.1439	0.1469	0.176	0.1910	0.2179
MOCA - attention read list of letters	−0.1179	−0.267	0.2684	0.0109[b]	0.3034	0.0167[b]
MOCA - attention serial 7 subtraction	−0.2355	−0.2742	0.0255[b]	0.0089[b]	0.0368[b]	0.0145[b]
MOCA - language repeat	−0.3114	−0.3021	0.0028[b]	0.0038[b]	0.0049[b]	0.0076[b]
MOCA - language fluency	−0.3998	−0.1383	<0.0001[b]	0.1937	0.0003[b]	0.2289
MOCA - abstraction	−0.0956	−0.4989	0.3701	<0.0001[b]	0.3849	0.0004[b]
MOCA - delayed recall	−0.4426	−0.4634	<0.0001[b]	<0.0001[b]	0.0002[b]	0.0004[b]
MOCA - orientation	−0.4756	−0.5748	<0.0001[b]	<0.0001[b]	0.0002[b]	0.0003[b]

MOCA: Montreal Cognitive Assessment; MMSE: Mini-Mental State Examination; Mini-Cog: Mental Status Assessment of Older Adults; FDR: False Discovery Rate.
[a] One-way analysis of variance (ANOVA) *F*-test.
[b] Significant difference.

current study. Potential limiting factors inherently may exist for performing UEF as a cognitive screening tool in clinical applications, such as the level of education and severe elbow arthritis. Within the current approach, an index was developed that only relies on motor function performance, and not the influence of education level in cognitive screening. Further, previous research and our previous UEF motor function assessment showed most older adults with arthritis can perform the UEF test as it involves elbow flexion (rather than other joints prone to injury such as shoulder) (Toosizadeh et al., 2017a).

Due to the selection criteria, the generalizability of the current findings is limited to MCI of the Alzheimer's type and early AD (these groups were selected to minimize between-subject variability within our small sample size). However, as AD is the most common type of dementia, current findings could provide a promising screening tool for assessing cognitive impairment in most older adults. Potential future research could investigate its use with other dementias.

As a result of the nature of participant recruitment of this study, not all selected participants had previously completed every neuropsychological test investigated in this study. As shown in Fig. 1, there was a larger sample size for some neuropsychological tests than others. Additionally, due to mental or physical exhaustion, some participants only completed one of the dual-tasks. Of note, it has been previously determined that counting backwards by threes during the dual-task is more sensitive to detecting cognitive impairment than counting by ones (Ehsani et al., 2019). Furthermore, completing both dual-tasks would not be necessary for screening. In future directions, increasing the sample size of the study would be useful in further solidifying results.

Due to small group sample sizes, between group differences were not identified. Furthermore, by increasing the sample size, it would also be possible to identify between group differences using ANOVA testing. By collapsing groups to identify correlation results, this study serves as a starting point for confirming the relationship between for the administered neuropsychological tests and both dual-tasks. Additionally, it demonstrates the generalizability of the correlation results.

More research is necessary to understand how often neuropsychological test scores should be administered for best accuracy without inducing learning effects. The neuropsychological tests were administered within a 6-month window of data collection, and therefore may not perfectly accurately represent the cognitive status of the individual at the time of data collection. However, we expect minimum changes in cognitive status during a 6-month period.

To increase usability and convenience of the proposed methods, in future research we plan to integrate them into the smart watch platform. The watch application would be capable of collecting the motion data within the UEF test procedure and providing the patient with results in minutes. After the development of this application, it would also be possible to compare the accuracy of the proposed screening method in relation to neuropsychological test results in a larger sample of

participants. As mentioned before, the goal is to assess physical and cognitive function with a single testing platform using UEF.

CRediT authorship contribution statement

KP: manuscript preparation, acquisition of participants, data and statistical analysis, discussion, data interpretation. BJ: manuscript preparation, acquisition of participants, data and statistical analysis, discussion, data interpretation. NT: concept, study management, study design, drafting the manuscript, discussion, and data interpretation.

Declaration of competing interest

The authors have no conflict of interest to disclose.

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