

Cognitive correlates of dual tasking costs on the timed up and go test in Parkinson disease

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ABSTRACT

Introduction: Dual tasking impairments are an increasingly recognized contributor to falls in Parkinson disease (PD) and may be a promising therapeutic target for PD fall prevention trials. Depending on the context, ambulatory dual tasking difficulties may be caused by different types of neurocognitive impairments.

Methods: We performed a cross-sectional analysis of 21 participants with PD. All participants underwent detailed neuropsychological testing that was quantified using normative z-scores. All participants completed the 3-meter timed up and go test (TUG), with and without a dual tasking assignment. Biomechanistic properties of the TUG were quantified using APDM wearable OPAL sensors. We explored correlations between dual tasking cost (DTC) in 1) total TUG duration, 2) Sit-to-stand duration, 3) Stand-to-sit duration, and 4) turn velocity.

Results: Impaired total DTC in the TUG correlated inversely with global cognitive performance measured using the Montreal Cognitive Assessment (MoCA) ($r = -0.4649$, $p = 0.0337$). Sit-to-stand DTC impairments correlated inversely with processing speed on the WAIS-IV Coding ($r = -0.5762$, $p = 0.0063$), semantic fluency ($r = -0.5100$, $p = 0.0182$) and learning and memory on the Hopkins Verbal Learning Test-Revised total recall ($r = -0.5502$, $p = 0.0098$). Impaired stand-to-sit DTC function correlated inversely with visuospatial cognitive function on the Benton Judgement of Line Orientation (JOLO) test ($r = -0.5181$, $p = 0.0161$).

Conclusions: The link between dual tasking and fall risk in PD may be caused by cognitive features other than executive dysfunction and may vary based on the ambulatory task in question. These findings shed light on the cognitive contributions to falls in PD.

1. Introduction

Falls in individuals with Parkinson Disease (PD) cause serious injury, hospitalization, and activity restriction due to fear of falling and/or physical disability, all leading to decreased quality of life [1,2]. Given their prevalence, understanding factors contributing to falls in PD has strong public health relevance (Fig. 1).

Although various motor features of PD each contribute to PD fall risk [3,4], mild cognitive impairment (MCI) is increasingly acknowledged as an independent risk factor for PD falls [5]. Difficulties seen during cognitive dual tasking ambulatory tests in particular can be a mediator of fall risk in PD [6] given the dual tasking elements inherent to maintaining postural stability when turning or walking in complex or unpredictable environments.

The 3-meter Timed Up & Go (TUG) test is a standard examination

test used in clinical practice to detect gait and ambulatory function in aging and PD. Adding a cognitive dual tasking component to the TUG test has been shown to further improve the detection of fall risk in this population [7]. The objective of the present study was to investigate the relationship between sensor-based quantitative assessments of dual tasking cost seen on different components of TUG test with various elements of cognitive performance on neuropsychological testing in people with PD. We hypothesized that worse dual tasking TUG performance would correlate primarily with impairments in executive function directly reflecting dual tasking capacity.

2. Methods

We conducted a cross-sectional study of 21 participants (17 men, 4 women) with PD. Individuals in this study were recruited for a separate

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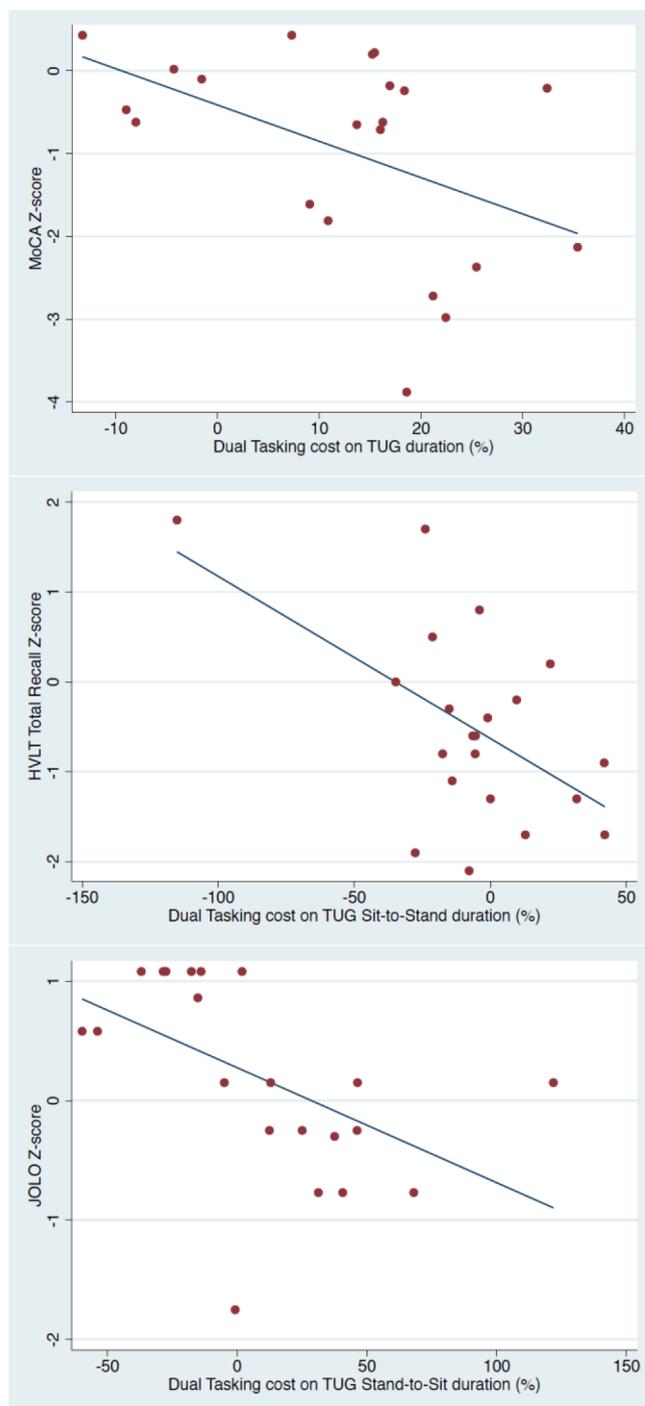


Fig. 1. Scatter plots depicting the inverse correlations between A) *top*: Montreal Cognitive Assessment (MoCA) Z-score (reflecting global cognition) and Dual Tasking cost on total TUG duration B) *middle*: The Hopkins Verbal Learning Test-Revised total recall (HVL-Recall) (reflecting learning and memory) with Dual Tasking cost on Sit-to-Stand duration and C) *bottom*: the Benton Judgment of Line Orientation (JOLO; reflecting visuospatial cognitive function) with Dual Tasking cost on Stand-to-Sit duration.

clinical trial [8] but underwent detailed neuropsychological and motor testing at the time of their screening visit. All participants were 65 years or older, met the clinical diagnostic criteria for PD established by the United Kingdom Parkinson's Disease Society Brain Bank Research Center [9], and had modified Hoehn and Yahr stages 2.0–3.0 [10]. Exclusion criteria included individuals with active depression, substantial cognitive impairment that might prevent a participant from

providing written informed consent, and/or a history of large-artery stroke or brain mass lesion. Participants were recruited from the University of Michigan Movement Disorders clinics. No specific cut-off value on a general cognitive screening exam was used to include/exclude potential subjects. This cross-sectional dataset includes data obtained on the day of a participant's baseline/screening visit. These visits began with participants providing written informed consent before participating in study activities. Participants were allowed to take their regular dopaminergic medications prior to cognitive testing. This cohort of 21 participants includes all participants who had complete baseline/screening visit gait sensor-based testing and finalized neuropsychological testing protocol. Fourteen additional potential participants were scheduled for baseline testing but were not included in this analysis for the following reasons: 7 were deemed to have exclusionary criteria when assessed at the time of baseline visit, 4 were missing gait sensor data, and 3 were missing complete neuropsychological testing data. This study was approved by the University of Michigan IRBMED.

Participants underwent gait and balance testing as measured by the Timed Up & Go (TUG) test while wearing Ambulatory Parkinson's Disease Monitoring (APDM) OPAL sensors [11]. Participants completed two trials of the TUG test: a single tasking trial and a dual tasking trial. In the single tasking trial, participants were instructed to stand up from a chair, walk forward at their regular pace to a marker 3 m away, turn around, walk back to the chair, and sit down. In the dual tasking trial, participants were asked to complete the same procedure while simultaneously counting backward from 100 by threes. 1) Total time, 2) turn velocity in degrees/second, 3) stand-to-sit time, and 4) sit-to-stand time were recorded for each trial using the APDM wearable sensors. We calculated the intra-individual dual tasking cost (DTC) of each of these 4 TUG domains using standard methods [12] by subtracting the single tasking result per each subject from the dual tasking results and dividing this value by a subject's single tasking results, thereby providing a percentage value of change in time or velocity when moving from a single to dual task context in each of these TUG domains.

Cognitive functioning of all participants was evaluated using a neuropsychological battery comprised of tests with strong psychometric properties. Adjusted z-scores were calculated for individual tests based on normative data. Global cognition was assessed using age-adjusted performance on the Montreal Cognitive Assessment (MoCA) [13]. Intellectual estimate was evaluated using age-adjusted performance on the Wechsler Test of Adult Reading (WTAR) [14]. Attention/working memory was assessed using the Wechsler Adult Intelligence Scale 4th Edition (WAIS-IV) Digit Span Sequencing [15]. Digit Span Sequencing was evaluated using age-adjusted performance. Processing speed, attention, and working memory were evaluated by the Trails Making Test A (TMT-A) [16]—adjusted for the age, years of education, sex, and race—and WAIS-IV Coding—adjusted for age [15]. Visuospatial abilities were assessed by the Benton Judgment of Line Orientation Test (JoLO) [17]—adjusted for age and sex—and the Clock Drawing Test [18]. Clock Drawing z-scores were calculated based on previously published normative data [19].

Processing speed, language, and executive function were evaluated using phonemic and semantic fluency assessments including the Controlled Oral Word Association Test (COWAT) [20], adjusted for the age and years of education and through an assessment of Semantic fluency (asking participants to name as many animals as they could in 60 s [21])—adjusted for age, years of education, sex, and race. Learning and memory was assessed by the Hopkins Verbal Learning Test-Revised (HVL-R) Form 1 [22], adjusted for age. Domains including executive functioning, processing speed, attention and working memory along were also assessed using Trails Making Test B (TMT-B) [16], with TMT-B z-scores adjusted for the age, years of education, sex, and race.

We evaluated the bivariate Pearson's r statistic between normalized z-scores on elements of neuropsychological testing with DTC on the 4 elements of the TUG test mentioned above (total duration, sit-to-stand time, turn velocity, and standing-to-sit time). In this exploratory

Table 1

Cognitive Z-scores [mean and (standard deviation) provided in italics] and Pearson r and p-values between neuropsychological tests and dual tasking cost by task in participants with Parkinson disease (n = 21). Cells that are bolded and underlined denote significant correlations with $p < 0.05$.

Cognitive domain	Cognitive Test Z-score	Cognitive Z-score univariate statistics	Total TUG Duration (seconds)– Dual Task Cost	Sit to Stand Duration (seconds)–Dual Task Cost	Stand to Sit Duration (seconds)–Dual Task Cost	Turn Velocity (seconds/degree)– Dual Task Cost
General Cognition	MoCA	<i>-0.95 (1.24)</i>	<u>$r = -0.4649$</u> <u>$p = 0.0337$</u>	$r = -0.3512$ $p = 0.1185$	$r = -0.2924$ $p = 0.1984$	$r = 0.3063$ $p = 0.1769$
	WTAR	<i>0.51 (0.89)</i>	$r = -0.3447$ $p = 0.1260$	$r = -0.1359$ $p = 0.5569$	$r = 0.0218$ $p = 0.9253$	$r = 0.1473$ $p = 0.5239$
Processing speed, attention, and working memory	WAIS-IV Total Digit Span Sequencing	<i>0.09 (1.06)</i>	$r = -0.4066$ $p = 0.0674$	$r = -0.3402$ $p = 0.1314$	$r = -0.4177$ $p = 0.0596$	$r = -0.0054$ $p = 0.9816$
	Trails Making Test -A	<i>-0.50 (0.99)</i>	$r = -0.3546$ $p = 0.1147$	$r = -0.2923$ $p = 0.1985$	$r = -0.1614$ $p = 0.4846$	$r = -0.1939$ $p = 0.3998$
	WAIS-IV Coding	<i>-0.33 (0.90)</i>	$r = -0.4316$ $p = 0.0508$	<u>$r = -0.5762$</u> <u>$p = 0.0063$</u>	$r = -0.3273$ $p = 0.1475$	$r = -0.1271$ $p = 0.5830$
Processing speed, attention, working memory and executive function	Trails Making Test -B	<i>-0.64 (1.30)</i>	$r = -0.4200$ $p = 0.0580$	$r = -0.3082$ $p = 0.1740$	$r = -0.3764$ $p = 0.0926$	$r = 0.0332$ $p = 0.8863$
Visuospatial Function	JOLO	<i>0.19 (0.80)</i>	$r = -0.2882$ $p = 0.2052$	$r = -0.3973$ $p = 0.0745$	<u>$r = -0.5181$</u> <u>$p = 0.0161$</u>	$r = 0.1691$ $p = 0.4637$
	Clock Drawing test unprompted	<i>0.15 (0.81)</i>	$r = -0.3366$ $p = 0.1357$	$r = -0.1769$ $p = 0.4431$	$r = -0.1517$ $p = 0.5116$	$r = 0.0996$ $p = 0.6675$
Processing speed, language, Executive Function	COWAT total C, F, L words	<i>0.53 (1.27)</i>	$r = -0.2665$ $p = 0.2429$	$r = -0.1895$ $p = 0.4106$	$r = 0.1202$ $p = 0.6037$	$r = -0.2223$ $p = 0.3329$
	Semantic Fluency Animals	<i>-1.17 (1.69)</i>	$r = -0.3348$ $p = 0.1379$	<u>$r = -0.5100$</u> <u>$p = 0.0182$</u>	$r = -0.3138$ $p = 0.1660$	$r = -0.0950$ $p = 0.6822$
Learning and Memory	HVLT-R Total recall	<i>-0.51 (1.07)</i>	$r = -0.2089$ $p = 0.3635$	<u>$r = -0.5502$</u> <u>$p = 0.0098$</u>	$r = -0.3003$ $p = 0.1860$	$r = 0.0574$ $p = 0.8049$

study, we defined a significant correlation as one showing a p-value of < 0.05. All analyses were performed using STATA 17 (College Station, TX). A limited research dataset may be made available upon qualified request.

3. Results

Enrolled participants (n = 21) showed a mean age of 72.0 years (SD: 4.3), mean years of education of 15.5 (SD: 2.9), and a mean unadjusted MoCA score of 23.8 (SD: 3.3). Previous MoCA cutoffs have been tested and identified as either screening ($\leq 26/30$) or diagnostic ($\leq 16/30$) thresholds for classifying PD-MCI [23,24]. One participant with a MoCA score of 16 met the diagnostic threshold for MCI and 17 participants scored less than 27, meeting the screening threshold. The mean Movement Disorders Society Unified Parkinson’s Disease Rating scale (MDS-UPDRS) motor exam score was 33.0 (SD: 10.4). The mean levodopa dose equivalents (LED) were 638.0 (SD: 365.5). 17 participants had a modified HY score of 2.0, 3 participants had an HY of 2.5 and 1 participant had an HY of 3.0. The relationship between higher MDS-UPDRS motor exam scores and greater DTC in total TUG duration reached statistical significance ($r = 0.439, p = 0.049$). Table 1 summarizes the bivariate correlations between neuropsychological testing performance seen on normative z-scores and DTC during the TUG. Greater DTC on the total duration of the TUG correlated inversely with global cognitive impairment measured via the MoCA. Greater DTC on the sit-to-stand component of the TUG correlated inversely with processing speed, attention, and working memory (WAIS-IV Coding), semantic fluency, and learning and memory on the HVLT. Turn velocity DTC showed no significant neuropsychological correlates. Greater DTC on the stand-to-sit component of the TUG correlated inversely with visuospatial cognitive function on the JoLO. Trails B impairments showed a non-significant trend towards association with both total TUG duration DTC and stand-to-sit DTC.

4. Discussion

We found distinct cognitive correlates relate to different types of dual tasking costs seen on the TUG in PD. Overall dual tasking cost for the complete TUG correlated with global cognitive impairment but not with

any of the discrete cognitive subdomain tests. Dual tasking impairments when moving from a standing to seated position correlate specifically with impaired visuospatial cognition, whereas impairments when moving from a seated to standing position reflect multiple cognitive domains including Memory, processing speed, attention and working memory, and even semantic fluency. Interestingly, Trails B testing showed a non-significant trend towards an inverse correlation with total TUG dual tasking cost but was not a significant correlate of any TUG element. Given the role of the TUG [25], and more specifically dual tasking impairments on the TUG [7], as predictors of falls in PD, these findings carry implications for future non-pharmacological interventional trials, potentially combining both physiotherapy and/or computerized cognitive therapy [26], aiming to alter elements contributing to PD fall risk.

There are at least two cognitive models that conceptualize the mechanisms underlying dual tasking impairments: 1) capacity theory, which suggests that each individual has a finite quantity of cognitive capacity that can be overtaxed in dual tasking settings and 2) bottleneck theory which suggests that dual tasking problems arise when one cognitive task needs to be completed before the other is undertaken, thereby leading to a delay in the execution of the second task [12]. Previous PD literature has suggested impaired executive functioning [27] and/or global cognition [28] correlate with gait speed and stride parameters in usual, predominantly straight-line, walking. Our findings, showing a borderline non-significant ($r = -0.420, p = 0.058$) inverse association between Trails B testing and total DTC on the TUG, do not contradict this established dysexecutive-DTC association, which may be particularly evident when total DTC is focused on as the outcome variable of interest. Instead, our study’s results add important clinical nuance to these previous dysexecutive-focused literature by highlighting the cognitive correlates of individual elements of non-straight-line walking. This is relevant given that falls in people with PD and cognitive impairment are typically predicted by turning problems [29]. Our findings that visuospatial cognitive impairment correlates with DTC when moving from a standing to seated position are novel and make intuitive sense given that sitting down safely from a standing position requires continually calibrating the spatial properties of one’s body and the seat one is aiming for. This finding may impact how clinicians advise current PD patients with visuospatial cognitive impairment at risk for

injurious falls. Impaired performance on semantic fluency testing correlated with greater DTC when moving from a seated to standing position. This finding may in part be driven by the influence of processing speed components on semantic fluency performance and would fit with a model whereby moving from a seated to standing position during dual tasking reflects individual-specific characteristics of the “bottleneck” model mentioned earlier.

Our study has several relevant limitations that should be considered as well. First, although we thoroughly characterized a relatively small cohort of participants, we cannot rule out the possibility of a cohort effect and encourage replication and extension of our findings. Our sample size was too small to have adequate power for conducting multivariable regression analysis to study the influence of disease-specific confounders. Nevertheless, the observed effect sizes are encouraging and can be used to power future studies. We also attempted to control for the influence of demographic confounders including age, sex, race, and education level by using normative z-score values for cognitive tests where available. Second, we acknowledge that different research groups have used different specific dual tasking tests—including cognitive and motor tests to assess DTC in previous PD studies [12]. Future research would benefit from a uniform definition and measurement of DTC as it relates to PD. Future observational studies on DTC in PD may benefit from assessing DTC in the same session using several different motor and cognitive challenges that may highlight mechanistic similarities and differences between types of dual tasking. Finally, Table 1 shows a number of Pearson r values that, while not meeting the alpha threshold of < 0.05 , may merit investigation in other dual tasking studies moving forward.

Future PD clinical trials of goal-directed physiotherapy and current clinical care practices aimed at reducing PD fall risk may both benefit from individualizing a therapeutic intervention to fit the type of underlying cognitive impairments seen in a given person with PD.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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