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Association of cognitive domains with postural instability/gait disturbance in Parkinson's disease

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Abstract

Introduction—Research suggests an association between global cognition and postural instability/gait disturbance (PIGD) in Parkinson's disease (PD), but the relationship between specific cognitive domains and PIGD symptoms is not clear. This study examined the association of cognition (global and specific cognitive domains) with PIGD symptoms in a large, well-characterized sample of individuals with PD.

Methods—Cognitive function was measured with a detailed neuropsychological assessment, including global cognition, executive function, memory, visuospatial function, and language. PIGD symptoms were measured using the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III, Motor Examination subscale. Multiple linear regression analyses were performed to assess the relationship between cognition and PIGD symptoms with models adjusting for age, sex, education, enrollment site, disease duration, and motor symptom severity.

Results—The analysis included 783 participants, with mean (standard deviation) age of 67.3 (9.7) years and median (interquartile range) MDS-UPDRS Motor Subscale score of 26 (17, 35). Deficits in global cognition, executive function, memory, and phonemic fluency were associated with more severe PIGD symptoms. Deficits in executive function were associated with impairments in gait, freezing, and postural stability, while visuospatial impairments were associated only with more severe freezing, and poorer memory function was associated only with greater postural instability.

Discussion—While impairments in global cognition and aspects of executive functioning were associated with more severe PIGD symptoms, specific cognitive domains were differentially related to distinct PIGD components, suggesting the presence of multiple neural pathways contributing to associations between cognition and PIGD symptoms in persons with PD.

Keywords

cognition; executive function; balance; gait; freezing of gait

1. Introduction

Cognitive dysfunction is a common non-motor feature of Parkinson disease (PD), with estimated point prevalence rates of up to 60% for mild cognitive impairment (PD-MCI) [1] and 30% for dementia (PD-D) [2]. Cognitive impairments in PD-MCI and PD-D are among the most consequential features of the disease, contributing to reduced quality of life [3] and increased risk for disability and mortality [4, 5].

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Previous research suggests a relationship between global cognitive dysfunction and motor symptoms of postural instability/gait disturbance (PIGD). Compared to those with tremor-dominant phenotype, people with PIGD-dominant phenotype have greater impairment on measures of global cognition [6], a higher frequency of PD-MCI [7], and an increased risk for developing dementia [8]. However, the relationship between specific cognitive domains and PIGD symptoms is not well characterized, with varying reports of distinct associations between PIGD symptoms and visuospatial function [9] or language [7]. Importantly, associations between specific cognitive domains and PIGD symptoms could implicate distinct neural pathways underlying cognitive dysfunction and PIGD symptoms in PD.

The aim of this study was to examine the association between global cognition as well as specific cognitive domains and PIGD symptoms in a large, well-characterized cohort of individuals with PD. An improved understanding of this relationship is important to elucidate common mechanisms underlying cognitive and PIGD symptoms and to tailor interventions specific to the cognitive and motor status of each individual with PD.

2. Methods

2.1. Participants

Participants were recruited and enrolled through the Pacific Northwest Udall Center (PANUC) of Excellence in Parkinson's Disease Research, a collaboration among the University of Washington and the Veterans Administration (VA) Puget Sound Health Care System in Seattle, Washington, and Oregon Health and Science University and the Portland VA Medical Center in Portland, Oregon; the University of Cincinnati in Cincinnati, Ohio; and the Emory University Movement Disorders Program in Atlanta, Georgia. Eligibility criteria included: (1) fulfillment of the United Kingdom Parkinson's Disease Society Brain Bank (UKBB) criteria for idiopathic PD; and (2) no history of other neurologic disorders known to impact cognition. Participants were recruited without consideration of cognitive diagnostic status in order to examine associations between cognition and PIGD symptoms across a range of cognitive functions. Approval for studies involving human subjects was received from the institutional review boards of all participating sites. All participants (or their legally authorized representative, as appropriate) provided written informed consent in accordance with approved procedures.

2.2. Study design and data collection

Cross-sectional data reported here were collected continuously across the four sites from February 2010 through April 2014 as part of an ongoing longitudinal study. Data collection procedures were aligned across all sites. Each participant was assessed while on their regular medication regimen, with motor and cognitive testing sessions completed within a 30-day time frame.

2.3. Clinical examination

Participants completed a focused interview to determine demographic characteristics, symptom history, medications, and past medical history. The Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III, Motor Examination

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subscale was used to assess the severity of motor symptoms (performed in the “on” state, if receiving medication), with higher scores indicating more severe impairments [10]. The total PIGD score was calculated as the sum of scores on the gait (3.10), freezing of gait (3.11), and postural stability (3.12) items, based on recommended MDS-UPDRS Part III items for determining the PIGD phenotype [11]. Each item is rated on a 5-point ordinal scale, with a score of 0 indicating no impairment and a score of 4 indicating severe impairment.

2.4. Neuropsychological assessment

Participants completed a comprehensive cognitive assessment based on published consensus guidelines [12]. We selected tests common to all study sites to assess global cognition as well as specific cognitive domains. Global cognitive function was assessed using the total scores for the Montreal Cognitive Assessment (MoCA) and the Mattis Dementia Rating Scale-2 (DRS-2). Executive function, including attention, processing speed, and working memory, was assessed using the total scores for Letter-Number Sequencing, Trail Making, and Digit Symbol tests. Memory was assessed with the Hopkins Verbal Learning Test-Revised (HVLT-R), delayed recall score. Visuospatial function was assessed using the total score for the Judgment of Line Orientation (JoLO). Language was assessed using semantic verbal fluency (‘animals’ category) and phonemic verbal fluency (sum of F-A-S); however, it is recognized that phonemic fluency is a more frontally mediated task that depends heavily on and is often considered a measure of executive function [13]. For a subset of participants, additional assessments of memory and language were available and included Logical Memory (delayed recall score) from the Wechsler Memory Scale-Revised and the Boston Naming Test, respectively.

2.5. Statistical analysis

Multiple linear regression analysis was used to examine the relationship between cognitive domains and PIGD symptoms after adjusting for age, sex, years of education, enrollment site, time since symptom onset (disease duration), and motor symptom severity. Motor symptom severity was calculated by the MDS-UPDRS Part III total score minus the total PIGD score (as described above, the sum of items 3.10, 3.11, 3.12). Analyses of Trail Making Test Part B times were also adjusted for Part A times to control for motor slowing or tremor. The primary analysis examined associations between neuropsychological tests (global cognition and specific domains of executive function, memory, visuospatial function, and language) and total PIGD scores. Secondary analyses utilized separate models to examine: (1) associations between neuropsychological tests and item scores for gait, freezing of gait, and postural stability; and (2) associations between Logical Memory and Boston Naming and PIGD symptoms (both total and item scores) in the smaller subset of participants completing these neuropsychological tests. All available participant data were used for each analysis, regardless of whether a participant completed all tests in the neuropsychological assessment. Statistical analyses were performed using Stata 12.0 (Stata Corp., College Station, Texas), with significance set at $\alpha \leq 0.05$ for all tests. As these were exploratory analyses, no adjustments for multiple comparisons were made in order to identify all potential associations for follow-up study in additional cohorts.

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3. Results

3.1. Participant characteristics

Table 1 shows demographic characteristics and cognitive status of eligible participants. A total of 850 people were enrolled at the participating sites. Individuals were excluded due to missing data for disease duration (n=22), incomplete MDS-UPDRS (n=19), not fully meeting UKBB criteria (n=16), absent neuropsychological assessment (n=2), having an additional diagnosis impacting cognition (n=1), or completing motor and cognitive testing more than 30 days apart (n=7). The final sample included 783 individuals. Participants had a mean (standard deviation) age of 67.3 (9.7) years and 67.8% were male. Mean disease duration was 9.4 (6.5) years, and motor symptom severity was moderate as reflected by a median MDS-UPDRS Part III score of 26 (interquartile range: 17, 35). Cognitive diagnostic status was established at clinical consensus conferences [1] at three of the four sites (91.2% of the sample), with 18.9% of the sample classified as having no cognitive impairment, 53.1% having mild cognitive impairment, and 19.2% having dementia. Also shown are the numbers of participants in each analysis, as some participants did not complete all neuropsychological tests.

3.2. Association between cognition and total PIGD scores

Table 2 summarizes associations between neuropsychological test performance and total PIGD scores. In fully adjusted models, poorer performance on measures of global cognitive function (MoCA, DRS-2), working memory (LNS), processing speed (Digit Symbol), memory (HVLT-R, delayed recall), and phonemic fluency was associated with more severe PIGD symptoms (higher total PIGD scores). Visuospatial function (JoLO) and language (semantic fluency) were not associated with total PIGD scores. A substantially smaller subset of participants had Logical Memory, delayed recall (n=356) and Boston Naming (n=342) scores available for secondary analysis (Tables 2). In fully adjusted models, neither test was significantly associated with total PIGD scores.

3.3. Association between cognition and component PIGD items

A secondary analysis examined associations between neuropsychological test performance and component PIGD items (Table 3). In fully adjusted models, poorer performance on tests of global cognition (MoCA, DRS-2), working memory (LNS), processing speed (Digit Symbol), and phonemic fluency was associated with more severe gait impairments. Poorer performance on tests of global cognition (MoCA, DRS-2), processing speed (Digit Symbol), and visuospatial function (JoLO) was associated with more severe freezing of gait. Poorer performance on tests of global cognition (MoCA, DRS-2), processing speed (Digit Symbol), and memory (HVLT-R, delayed recall) was associated with more severe postural instability. In the secondary analysis of a smaller subset of participants, neither memory (Logical Memory, delayed recall) nor language (Boston Naming) was associated with component PIGD items (Table 3).

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4. Discussion

This study examined the association of global cognition and specific cognitive domains with PIGD symptoms in a broad sample of individuals with PD, adjusting for potential confounders of age, sex, education, enrollment site, disease duration, and motor symptom severity. Deficits in global cognitive function, executive function (working memory and processing speed), memory, and phonemic fluency were associated with more severe deficits in posture and gait. In addition, we observed specific associations between cognitive domains and component PIGD items, suggesting that relationships between cognition and PIGD symptoms are multi-faceted. Deficits in executive function (processing speed) were associated with more severe impairment in all component PIGD items – gait, freezing of gait, and postural stability. In contrast, visuospatial impairments were associated only with more severe freezing of gait, and poorer memory function was associated only with greater postural instability.

These findings are consistent with previous research demonstrating an association between global cognitive dysfunction and PIGD-dominant phenotype. In longitudinal studies, individuals with PIGD-dominant or mixed PIGD-tremor phenotypes were more likely than those with tremor-dominant phenotype to develop global cognitive decline and dementia [8, 14]. In cross-sectional studies, the PIGD-dominant phenotype was more common in those demonstrating poorer performance on measures of global cognitive function (Scales for Outcomes in Parkinson's Disease-Cognition) [6] and in those with PD-D [15]. The present study extends these findings in several important ways. While many previous studies examined those who were newly diagnosed and drug-naïve or those who were non-demented, the current study supports a relationship between PIGD symptoms and global cognitive function across a range of cognitive functioning, from normal to dementia. In addition, we assessed PIGD symptoms as a continuum of motor function, instead of categorizing individuals into groups based on motor symptom predominance. Previous research has noted that the overall severity of PIGD symptoms, rather than just the relative dominance of PIGD symptoms, may better inform an understanding of the relationship between cognition and motor symptoms [9]. Consistent with this idea, PIGD symptoms are greater in those with PD-MCI compared to those with PD who are cognitively intact [16]. Finally, due to the use of a large, well-characterized cohort, the current study adjusted for a number of relevant covariates that could confound the examination of relationships between cognition and PIGD symptoms.

Because cognitive profiles in PD are variable, the examination of associations between specific cognitive domains and PIGD symptoms was an important aspect of this study. In the current study, specific cognitive domains of executive function (working memory and processing speed), memory, and phonemic fluency were associated with higher total PIGD scores. Because phonemic fluency is heavily dependent on and can be considered a measure of executive function [13], this association may have been driven by executive function, rather than language per se. These findings contrast with previous studies, which have shown mixed evidence for relationships between PIGD symptoms and specific aspects of cognition. In studies of persons with newly diagnosed, drug-naïve PD, PIGD symptoms were related to measures of language (Boston Naming Test, short form) [7] or visuospatial

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function (Brief Visuospatial Memory Test-Revised, JoLO) [9]. In contrast, studies of non-demented persons with PD demonstrated no consistent relationships between specific cognitive domains and PIGD-dominant phenotype [17] or PIGD symptom severity [18].

This study demonstrated specific associations between cognitive domains and component PIGD items, consistent with the idea that relationships between cognitive domains and distinct aspects of balance and gait are mediated by multiple neural pathways. Deficits in executive function (processing speed and working memory) were associated with more severe gait impairments. While degeneration of dopaminergic systems could contribute to both cognitive and PIGD impairments via parallel basal ganglia-thalamocortical pathways, degeneration within cholinergic systems has also been proposed to contribute to both cognitive and axial motor symptoms in PD [19]. Cholinergic hypofunction has been associated with both impaired executive function [20] and slowed gait speed [21] in persons with PD, and cholinergic augmentation can reduce fall rates in this population [22]. In the current study, deficits in executive (processing speed) and visuospatial functions were associated with more severe freezing of gait. This finding is consistent with research showing greater deficits in executive function [23] and visuospatial function [24] in people with PD who have freezing of gait compared to those without freezing, and suggests involvement of premotor and parietal areas could contribute to freezing [25]. Finally, deficits in executive function (processing speed) and memory were specifically associated with more significant postural instability, which contrasts with previous research demonstrating associations between postural instability in the off-medication state and phonemic fluency [18]. Neuropathological changes consistent with Alzheimer's disease are present in approximately 30% of individuals with PD-D [26] and could contribute uniquely to memory and balance dysfunction in PD, in agreement with research demonstrating postural control deficits in people with mild cognitive impairment and Alzheimer's disease [27]. Overall, differential associations between cognitive domains and specific aspects of balance and gait are consistent with previous research demonstrating different clinical and genetic risk factors for distinct subtypes of the PIGD phenotype [28]. Further research using comprehensive neuropsychological testing, quantitative analysis of balance and walking tasks, and biomarkers is needed to determine the specific mechanisms underlying unique associations between cognitive domains and distinct aspects of postural control, gait, and freezing of gait.

Several limitations of this study should be taken into consideration. First, the cross-sectional nature of this study design does not support inferences of causation. Second, the neuropsychological tests used to represent function within cognitive domains vary across studies, and the tests utilized here differ from some previous research. The measures chosen in this study and their assignment to specific cognitive domains were based on recently published consensus guidelines designed to harmonize neuropsychological assessment across the PANUC Clinical Consortium [12], but it should be recognized that a given test does not necessarily assess only the assigned cognitive domain. Third, medications were not included as a covariate in the adjusted models, though they may impact both cognition and PIGD symptoms. The use of medication as a covariate is complicated by variable effects of medication on global cognition and cognitive domains as well as the diminished response of PIGD symptoms to medications with disease progression. Finally, we used MDS-UPDRS

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PIGD items as a simple and clinically expedient means of assessing balance and gait. This is pragmatic for large samples, and PIGD item selection was based on recent recommendations for determining PIGD-phenotype [11]. However, these items assess relatively simple balance and gait tasks compared to the repertoire of tasks required for functional mobility in daily life. As a result, total PIGD scores are likely less sensitive and specific to changes in balance and gait than clinical tests or quantitative analysis of balance and gait. Future research should incorporate quantitative measures and more complex balance and gait tasks to better represent typical mobility challenges in home and community environments.

In summary, deficits in both global cognition and specific executive functions (processing speed) were consistently associated with more severe PIGD symptoms in a large, well-characterized sample of persons with PD. Notably, the current study also demonstrates a complex pattern of associations between distinct aspects of PIGD and specific cognitive domains. These findings suggest that multiple neural pathways mediate the relationship between cognition and the control of balance and gait. Because safe and effective functioning in daily life requires a complex interplay between cognition and mobility, understanding these mechanisms is critical to inform individualized medical and rehabilitative interventions tailored to the specific cognitive and motor profiles of each person with PD.

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Highlights

- We examined the association of cognitive domains with balance and gait symptoms.
- Global cognitive deficits were related to more severe balance and gait impairments.
- Executive function deficits were related to more severe gait impairment.
- Deficits in executive and visuospatial functions were associated with freezing.
- Memory deficits were associated with more severe postural instability.

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Table 1

Demographic and cognitive characteristics of participants for the total sample and each recruitment site. The Pacific Northwest Udall Center includes both the Seattle and Portland recruitment sites.

	Overall N=783	Seattle (UW & Puget Sound VA) n=495	Portland (OHSU & Portland VA) n=152	Emory University n=69	University of Cincinnati n=67
Demographic Characteristics					
Age (years)	67.3 (9.7)	67.8 (9.9)	68.5 (8.4)	65.1 (9.3)	63.4 (10.5)
Sex (% male)	67.8	64.2	86.8	56.5	62.7
Education (%)					
HS or less	13.5	13.8	13.6	17.4	11.9
Bachelor's or less	52.1	52.6	51.9	47.8	65.7
Grad. / prof. degree	34.4	33.6	34.4	34.8	22.4
Disease Status Characteristics					
Years since disease onset	9.4 (6.5)	9.4 (6.6)	9.6 (6.6)	10.8 (5.9)	7.5 (5.4)
MDS-UPDRS Part III*	26 (17, 35)	26 (18, 35)	30 (21, 40)	16 (11, 22)	22 (18, 30)
PIGD subscore*	1 (1, 4)	2 (1, 4)	2 (1, 4)	1 (0, 1)	0 (0, 1)
Gait*	1 (1, 2)	1 (1, 2)	1 (0.5, 1)	1 (0, 1)	0 (0, 1)
Freezing of gait*	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
Postural stability*	0 (0, 2)	0 (0, 3)	1 (0, 2)	0 (0, 0)	0 (0, 1)
Hoehn & Yahr*	2 (2, 2.5)	2 (2, 3)	2.5 (2, 3)	2 (2, 2)	2 (2, 2.5)
Global Cognition					
MoCA (n=753)	24.1 (3.8)	24.3 (3.7)	23.1 (3.9)	24.5 (3.4)	23.7 (4.0)
DRS-2 (n=678)	135.0 (9.3)	135.8 (8.2)	131.5 (11.7)	135.3 (9.4)	137.3 (7.1)
Executive function					
LNS (n=679)	8.9 (2.8)	8.8 (3.0)	8.6 (2.5)	8.8 (2.3)	9.9 (2.3)
Trails A (n=703)	39.9 (22.5)	41.1 (25.6)	41.7 (14.7)	35.4 (14.7)	31.5 (12.7)
Trails B (n=703)	116.1 (70.3)	124.3 (75.5)	109.3 (59.1)	94.2 (46.3)	90.9 (59.2)
Digit Symbol (n=756)	39.1 (13.4)	38.0 (13.3)	39.2 (13.4)	41.5 (13.8)	44.4 (13.1)

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	Overall N=783	Seattle (UW & Puget Sound VA) n=495	Portland (OHSU & Portland VA) n=152	Emory University n=69	University of Cincinnati n=67
Memory					
HVLT-R, delayed (n=707)	6.9 (3.7)	7.1 (3.6)	5.6 (3.6)	8.1 (3.8)	6.6 (3.8)
Logical Memory, delayed (n=356)	10.3 (4.4)	9.5 (4.4)	11.3 (4.2)	10.4 (4.5)	11.3 (4.4)
Visuospatial					
JoLO (n=754)	11.7 (2.6)	11.8 (2.5)	11.6 (2.6)	11.6 (2.4)	11.1 (2.9)
Language					
Semantic Fluency (n=752)	18.5 (6.0)	18.4 (6.4)	18.5 (5.3)	18.9 (5.7)	19.1 (5.5)
Phonemic Fluency (n=740)	38.8 (13.0)	38.5 (13.0)	37.9 (12.4)	40.2 (13.5)	41.4 (13.6)
Boston Naming (n=342)	28.1 (2.1)	28.3 (2.2)	28.4 (1.3)	27.8 (2.5)	27.9 (2.0)

* Median (interquartile range), else Mean (standard deviation).

Abbreviations: DRS-2 = Mattis Dementia Rating Scale-2; HS = high school; HVLT-R = Hopkins Verbal Learning Test-Revised; JoLO = Judgment of Line Orientation; LNS = Letter Number Sequencing; MDS-UPDRS = Movement Disorder Society Unified Parkinson's Disease Rating Scale Part III, Motor Examination; MoCA = Montreal Cognitive Assessment; OHSU = Oregon Health and Science University; UW = University of Washington.

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Table 2

Associations between tests of both global cognition and specific cognitive domains and total PIGD scores in models adjusted for age, sex, education, enrollment site, disease duration, and motor symptom severity. Table shows the standardized regression coefficients (β weights), 95% confidence intervals (CI), and *p*-values for fully-adjusted models.

	Total PIGD Scores		
	β	**95% CI**	**P**
Global Cognition			
MoCA Total (n=753)	−0.31	−0.46, −0.16	<0.0001*
DRS-2 Total (n=678)	−0.87	−1.31, −0.43	0.0001*
Executive Function			
LNS (n=679)	−0.13	−0.25, −0.01	0.030*
Trails B (n=703)	1.56	−0.94, 4.06	0.22
Digit Symbol (n=756)	−0.89	−1.35, −0.44	0.0001*
Memory			
HVLT-R, delayed (n=707)	−0.18	−0.32, −0.03	0.016*
Logical Memory, delayed (n=356)	−0.05	−0.34, 0.23	0.71
Visuospatial			
JoLO (n=754)	−0.12	−0.24, 0.00	0.051
Language			
Semantic Fluency (n=752)	−0.16	−0.40,0.08	0.19
Phonemic Fluency (n=740)	−0.73	−1.21, −0.26	0.003*
Boston Naming (n=342)	−0.14	−0.31, 0.03	0.10

Abbreviations: DRS-2 = Mattis Dementia Rating Scale-2; HVLT-R = Hopkins Verbal Learning Test-Revised; JoLO = Judgment of Line Orientation; LNS = Letter Number Sequencing; MoCA = Montreal Cognitive Assessment.

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Table 3

Associations between gait, freezing of gait, and postural stability scores and cognition based on models adjusted for age, sex, education, enrollment site, disease duration, and motor symptoms severity. Table shows the standardized regression coefficients (β weights), 95% confidence intervals, and *p*-values for fully-adjusted models.

	Gait (3.10)		Freezing of Gait (3.11)		Postural Stability (3.12)	
	β (95% CI)	***p***	**β (95% CI)**	***p***	**β (95% CI)**	***p***
Global Cognition						
MoCA Total (n=753)	−0.45 (−0.80, −0.09)	0.015*	−1.00 (−1.61, −0.38)	0.002*	−0.41 (−0.63, −0.19)	0.0003*
DRS-2 Total (n=678)	−1.55 (−2.60, −0.50)	0.004*	−2.27 (−4.13, −0.40)	0.017*	−1.15 (−1.76, −0.55)	0.0002*
Executive Function						
LNS (n=679)	−0.35 (−0.63, −0.08)	0.011*	−0.35 (−0.79, 0.09)	0.12	−0.12 (−0.31, 0.08)	0.24
Trails B (n=703)	4.98 (−0.71, 10.68)	0.086	1.72 (−7.40, 10.83)	0.71	1.43 (−2.32, 5.19)	0.45
Digit Symbol (n=756)	−2.07 (−3.16, −0.98)	0.0002*	−3.13 (−4.80, −1.45)	0.0003*	−0.79 (−1.52, −0.06)	0.034*
Memory						
HVLT-R, delayed (n=707)	−0.17 (−0.54, 0.20)	0.36	0.00 (−0.47, 0.47)	0.99	−0.38 (−0.61, −0.14)	0.002*
Logical Memory, delayed (n=356)	−0.43 (−1.08, 0.23)	0.20	−0.13 (−1.30, 1.03)	0.82	0.10 (−0.34, 0.54)	0.67
Visuospatial						
JoLO (n=754)	−0.26 (−0.52, 0.00)	0.052	−0.74 (−1.26, −0.21)	0.006*	−0.05 (−0.21, 0.11)	0.55
Language						
Semantic Fluency (n=752)	−0.44 (−0.98, 0.10)	0.11	0.15 (−0.67, 0.98)	0.71	−0.24 (−0.62, 0.13)	0.21
Phonemic Fluency (n=740)	−2.04 (−3.19, −0.89)	0.0005*	−0.67 (−2.35, 1.01)	0.43	−0.87 (−1.64, −0.11)	0.026*
Boston Naming (n=342)	0.04 (−0.32, 0.40)	0.84	−0.53 (−1.11, 0.06)	0.076	−0.25 (−0.50, 0.01)	0.060

Abbreviations: DRS-2 = Mattis Dementia Rating Scale-2; HVLT-R = Hopkins Verbal Learning Test-Revised; JoLO = Judgment of Line Orientation; LNS = Letter Number Sequencing; MoCA = Montreal Cognitive Assessment.