HHS Public Access

Author manuscript

J Alzheimers Dis. Author manuscript; available in PMC 2018 January 01.

Published in final edited form as:

J Alzheimers Dis. 2017 ; 55(2): 559–567. doi:10.3233/JAD-160697.

Comparison of Gait Parameters for Predicting Cognitive Decline: The Mayo Clinic Study of Aging

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Abstract

Objective—To investigate and compare the association with, and prediction of, specific gait parameters for cognition in a population-based sample.

Background—Previous studies reported that slower gait speed might predict cognitive impairment and dementing illnesses, supporting the role of gait speed as a possible subclinical marker of cognitive impairment. However, the predictive value of other gait parameters for cognitive decline is unclear.

Methods—The analysis included 3,426 cognitively normal participants enrolled in the Mayo Clinic Study of Aging. At baseline and every 15 months (mean follow-up = 1.93 years), participants had a study coordinator evaluation, neurological examination, and a neuropsychological assessment using nine tests that covered four domains. Gait parameters were

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DISCLOSURES FOR AUTHORS

Dr. Savica, Dr. Wennberg, Mr. Hagen, and Ms. Edwards report no disclosures.

Dr. Roberts receives research support from the NIH.

Dr. Knopman serves on a Data Safety Monitoring Board for Lundbeck Pharmaceuticals and for the DIAN study; is an investigator in clinical trials sponsored by TauRX Pharmaceuticals, Lilly Pharmaceuticals and the Alzheimer's Disease Cooperative Study; and receives research support from the NIH.

Dr. Boeve reported that he has served as an investigator for clinical trials sponsored by Myriad Pharmaceuticals and Cephalon, Inc.; has served as a one-time consultant to GE Healthcare; receives royalties from the publication of a book entitled Behavioral Neurology Of Dementia (Cambridge Medicine, 2009); and receives research support from the NIH and from the Alzheimer's Association.

Dr. Machulda receives research support from the NIH.

Dr. Petersen reported that he serves on Safety Monitoring Committees for Elan Pharmaceuticals, Wyeth Pharmaceuticals, and as a consultant for Elan Pharmaceuticals and GE Healthcare; receives royalties from the publication of a book entitled Mild Cognitive Impairment (Oxford University Press, 2003); and receives research support from the NIH.

Dr. Mielke receives research support from the NIH/NIA and the Michael J. Fox Foundation and has consulted for Lysosomal Therapeutics, Inc.

assessed with the GAITRite® instrument. General linear mixed effects models were used to compute the annualized rate of change in cognitive domain z-scores, controlling for age, sex, education, depression, comorbidities, body mass index, APOE ε4 allele, and visit number, and excluding individuals with a history of stroke, alcoholism, Parkinson's disease, subdural hematoma, and normal pressure hydrocephalus.

Results—Spatial (stride length), temporal (ambulatory time, gait speed, step count, cadence, double support time), and spatiotemporal (cadence) gait parameters, and greater intraindividual variability in stride length, swing time, and stance time were associated with a significant decline in global cognition and in specific domains including memory, executive function, visuospatial, and language.

Conclusions—Spatial, temporal, and spatiotemporal measures of gait and greater variability of gait parameters were associated with and predictive of both global- and domain-specific cognitive decline.

Keywords

cognition; epidemiology; gait variability; GAITRite® instrument

INTRODUCTION

Walking is a physiological milestone of normal human neurodevelopment and a crucial part of daily life; however gait is a complex task that requires the integration of multiple signals. Several individual characteristics are important components of a normal gait (e.g., speed, arm swinging, pace, support time) and abnormalities of one or several may be indicators of disease [1]. The presence of gait disturbances increases with advancing age [2] and impacts the independence of daily living, especially in the elderly.

Cross-sectional studies have reported that changes in gait may be associated with cognitive impairment [3, 4]. Additional studies also reported that slow gait speed predicted cognitive impairment and dementia, supporting the role of gait as a possible subclinical marker of cognitive impairment [5–9]. However, other studies suggested that cognitive impairment preceded the gait changes [10–12]. Notably, few studies have moved beyond gait speed to explore the role of specific spatial and temporal gait parameters as predictors of cognitive decline, especially in a population-based sample [7, 12, 13]. Indeed, it is not understood what gait parameters are most associated with and predictive of specific cognitive domains. In the present study, we investigated and compared a number of spatial and temporal gait parameters, and intraindividual gait variability, analyzed with an electronic gait analyzer (GAITRite®). Our objective was to determine which gait parameters were most strongly associated with cross-sectional cognitive performance and longitudinal cognitive decline in a population-based study of cognitively normal individuals aged 50 and older.

MATERIALS AND METHODS

The study design and methodology have been published in detail elsewhere [14]. Briefly, we identified all Olmsted County, Minnesota, United States, residents aged 70–89 years on October 1, 2004, using the medical records-linkage system of the Rochester Epidemiology

Project [15, 16]. From this enumeration, subjects were randomly recruited using a 10-year age- and sex-stratified random sampling strategy such that men and women were equally represented in each 5-year age category. Since 2004, the population has been re-enumerated several times and has been extended to cover the ages of 50–90+ following the same sampling strategy. Participants are longitudinally evaluated every 15 months, blinded to previous diagnoses and data, using the same study protocol including a gait measurement and cognitive evaluation. The study group comprised 3,527 cognitively normal Mayo Clinic Study of Aging participants who had a complete GAITRite® assessment and neuropsychological assessment at the same visit. Persons with mild cognitive impairment or dementia were excluded. An informant (spouse, caretakers, etc.) confirmed the diagnosis of MCI and dementia [14]. We excluded 101 participants with a history of stroke, alcoholism, Parkinson's disease, subdural hematoma, and normal pressure hydrocephalus, leaving 3,426 participants for the present analysis.

Standard protocol approvals, registrations, and patient consent

The study was approved by the institutional review boards of Mayo Clinic and of Olmsted Medical Center. Written informed consent was obtained for all participants who were examined as part of the study.

Gait measurements

GAITRite® instrumentation (CIR systems Inc., Havertown, PA) consists of an electronic walkway of 5.6 m in length and 0.9 m in width. Each subject was instructed to walk at their normal pace without gait aids on the walkway, initiating and terminating their walk 1 m before and after the walkway. Each individual walked the GAITRite pad in one single pass. The study coordinator observed the gait without interfering with the gait of each individual. In the present analysis, we focused on individual spatial (stride length), temporal (ambulatory time, gait speed, step count, cadence, stance time), and spatiotemporal (cadence) parameters. Gait speed (m/s) was also measured by a nurse using a stopwatch over a marked distance of 7.62 m at a self-selected pace. Using the mean and standard deviation for each of these measures, we created z-scores for each of the continuous gait parameters so they were more easily comparable. Additionally, as variability may be an early indicator of gait disturbances, we examined the intraindividual variability in stride length, swing time, and stance time. We also created a dichotomous gait speed measure utilizing the International Working Group on Sarcopenia (IWGS) gait speed cut-off of <1.0 m/s for diagnosing sarcopenia [17]. All analyses of the gait were performed using the GAITRite software.

Because GAITRite® was not introduced into the study until part way through the first visit in 2004, some participants did not complete their first GAITRite® assessment until a later follow-up visit. Of the 3,426 participants, 2,646 (77%) of participants completed the GAITRite® assessment at their first visit. Compared to participants who completed GAITRite® at their first visit, those who completed GAITRite® at a subsequent visit were ($p < 0.05$) older, had fewer years of education, had more medical comorbidities, including higher Charlson comorbidity index score, hypertension, and lower cognitive test scores at baseline.

Measurements of cognitive function

At all visits, participants had a study coordinator interview, neurologic evaluation, and neuropsychological testing [14, 18]. The study coordinator interview included questions about memory administered to the participant; the Clinical Dementia Rating scale [19] and the Functional Activities Questionnaire [20]. The neurologic evaluation, performed by a physician, included the Short Test of Mental Status [21], a medical history review, the Unified Parkinson's Disease Rating scale [22], and a complete neurologic examination. An informant (spouse, caretakes, etc.) confirmed the diagnosis of cognitive complaints.

A psychometrist administered a neuropsychological battery that used nine tests to assess function in four domains: (i) *memory* (delayed free recall percent retention scores for Wechsler Memory Scale-Revised Logical Memory and Visual Reproduction tasks [23], and the Auditory Verbal Learning test [24]); (ii) *language* (Boston Naming test [25] and category fluency [26]); (iii) *executive function/attention* (Trail Making test B [27] and Digit Symbol Substitution subtest from the Wechsler Adult Intelligence Scale-Revised [28]); and (iv) *visuospatial skills* (picture completion and block design [29]). Using the mean and standard deviation from the baseline visit for the Mayo Clinic Study of Aging study population ages 50 and older and excluding subjects with dementia, participants' test scores were converted to z-scores. Up-weighting was used for gender and ages under-represented in the Mayo Clinic Study of Aging sample as comparted to the local population. A global cognitive domain score was created using the z-transformation of the average of the four aforementioned domains.

Diagnostic determination

For each participant, performance in a cognitive domain was compared with the age-adjusted scores of cognitively normal individuals previously obtained using Mayo's Older American Normative Studies [30]. This approach relies on prior normative work and extensive experience with the measurement of cognitive abilities in an independent sample of subjects from the same population. Subjects with scores of ≥1.5 SD below the age-specific mean in the general population were considered for possible cognitive impairment. A final decision to diagnose mild cognitive impairment was based on a consensus agreement between the study coordinator, examining physician, and neuropsychologist, after taking into account education, prior occupation, visual or hearing deficits, and reviewing all other participant information [18]. Individuals who performed in the normal range and did not meet criteria for mild cognitive impairment or dementia were deemed cognitively normal.

Covariates

Participant demographics including age, sex, and education, and measures of body composition including height (cm), weight (kg), girth (cm), and hip circumference (cm), used to calculate body mass index and waist-to-hip ratio, respectively, were recorded at the in-clinic interview. At each exam, participants also completed the Beck Depression Inventory; a score ≥13 was considered indicative of depressive symptoms [31]. The Charlson comorbidity index score [32] was ascertained by medical record abstraction using the medical records-linkage system of the Rochester Epidemiology Project [14, 33].

Additional medical comorbidity diagnoses (e.g., hypertension, diabetes) were also abstracted from the medical records by trained nurses [14] ..

Statistical analyses

To determine whether each gait parameter predicted cognitive decline, we examined the association between the baseline gait parameter and change in each domain-specific and global z-score from baseline using mixed effects models, treating subject-specific intercepts and linear change with time as random effects. This approach permitted assessment of the baseline gait parameter, a key fixed effect, on average rate of change in the cognitive z-scores while accounting for the dependence of within-subject repeated measures over time. The models included the baseline gait parameter (indicating the relationship between the baseline gait parameter and baseline cognitive z-score), time (indicating annual change in the cognitive z-score over the follow-up), and the interaction between gait and time (indicating whether the baseline gait parameter predicted change in cognition). All models were adjusted for age, sex, education, depression, the Charlson comorbidity index, body mass index, presence of an APOE ε4 allele, and cycle number. By adjusting for cycle number, we were able to account for practice effects on cognitive test performance since not all individuals had available GAITRite® data at their first visit with a neuropsychological assessment. All analyses were completed using Stata version 12.0 (StataCorp, College Station, TX).

RESULTS

Participant characteristics at the first visit with both a GAITRite® and neuropsychological assessment (i.e., baseline) are presented in Table 1. Briefly, participants had a median age of 73 years, a median 14 years of education, and about half were men. Approximately 27% of participants had an APOE ε4 allele, 6% had depression, 65% had hypertension, and 17% had diabetes. In analyses that compared gait speed measured by GAITRite® instrumentation to that measured by a nurse using a stopwatch, we found that these two measurements were highly correlated both at baseline (Spearman's rho = 0.791, $p < 0.001$) and over time (Spearman's rho = 0.826, $p < 0.001$).

Table 2 shows the associations between each gait parameter and cognitive test performance at baseline and over time. Faster gait speed, as measured by GAITRite®, was cross-sectionally associated with and longitudinally predictive of better performance across all cognitive domains and global cognition. In contrast, faster gait speed, as measured by a study coordinator, was only cross-sectionally associated with better performance on tests of attention. Longitudinally, faster gait speed measured by a nurse was predictive of cognitive decline among all cognitive domains but the strength of the association was less compared to the strengths of the associations when gait speed was measured by GAITRite®. Using the IWG cut-off of gait speed <1.0 m/s, as measured by GAITRite®, predicted decline across all cognitive domains, with the strongest associations with attention and global z-scores.

Most of the other spatial and temporal gait parameters measured by GAITRite® were also cross-sectionally and longitudinally associated with cognitive decline (Table 2). Cross-sectionally, a longer support time was most strongly associated with poorer cognitive

performance across all domains and in global cognition. Longitudinally, a shorter stride length and an increased step count were the spatial and temporal parameters most strongly associated with poorer cognitive performance in all domains and global cognition.

The cross-sectional and longitudinal associations between greater intraindividual variability in gait parameters and decline in cognitive test performance over time are shown in Table 3. Greater variability in stride length, swing time, and stance time at baseline were cross-sectionally associated with and longitudinal predictive of cognition across domains. The only exceptions were that we did not observe a longitudinal association between stride length and stance time variability or visuospatial ability. Of the intraindividual variability measures, variability in swing time was cross-sectionally and longitudinally most strongly associated with all cognitive domains.

Sensitivity analyses

We also conducted several additional analyses. First, we investigated whether the association between gait parameters and cognitive test performance differed for those who completed their first GAITRite® measure at the time of their first cognitive assessment compared to those who completed their GAITRite® at a later visit. We found no difference in the strength or the direction of the associations. Second, in multivariate models, we substituted waist to hip ratio for body mass index, and diabetes and hypertension for the Charlson comorbidity index. However, when we adjusted for these other variables, there were no changes in the relationships between gait and cognition. Lastly, we determined whether there were interactions between GAITRite® parameters, medical conditions (myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, chronic pulmonary disease, diabetes, hypertension), presence of APOE ε4 allele and sex in predicting cognitive decline, but did not find any (data not shown). In addition, we conducted additional sensitivity analyses to verify whether only individuals that would develop MCI or dementia drove the changes in gait parameters; thus, we excluded all individuals who developed MCI or dementia during the follow-up period (N=750). We found that excluding these participants did not affect the observed association between gait and both cross-sectionally and longitudinally.

DISCUSSION

Our study results confirm that specific gait parameters are strong predictors of both global and domain-specific cognitive decline among cognitively normal individuals, aged 50 and older, enrolled in a large population-based study. Our results support the role of computerized gait analysis (GAITRite®) because gait speed assessment by GAITRite® was a stronger predictor of cognitive decline compared to gait speed assessment by a nurse with a stopwatch. Our study also demonstrated that impairment in spatial and temporal motor parameters is also associated with domain-specific and global cognitive decline. Further, greater variability in gait parameters, and the presence of sarcopenia at baseline, predict significant cognitive decline.

Gait is a complex integrated cognitive process that requires the perfect functioning and participation of multiple cognitive domains such as attention, planning, visuospatial, and

motor processes [34]. Therefore, the possibility of a complex and complete analysis of spatial and temporal parameters of gait can help to elucidate the cognitive integration of complex processes. Minimal modifications of gait parameters, which may not be detected by a well-trained eye, but only through a computerized tool, may be indicative of cognitive decline before the impairment can be detected with a standard neuropsychological battery.

The present results are consistent with previous cross-sectional and longitudinal studies that also reported that changes in gait speed were associated with cognitive decline and incident cognitive impairment and dementia [3, 5, 6, 11]. However, most of these studies examined change in a single test measuring global cognition (i.e., MMSE or 3MS) or executive function (i.e., Digit Symbol Substitution). Our results extend these previous findings by utilizing a computerized gait analysis that included spatial and temporal assessments and a comprehensive neuropsychological battery covering four domains (memory, attention, visuospatial skills, and language), as well as global cognition. Indeed, our study is one of the largest to date to utilize GAITRite® in a longitudinal cohort study. A cross-sectional study conducted in Australia explored gait parameters using GAITRite® instrument in 422 individuals [35]. The authors reported that poorer performance in all gait measures were associated with worse executive function, but not associated with memory. In addition, a recent 3-year longitudinal study (284 individuals) conducted in Tasmania, reported that a decline in gait speed, measured using GAITRite®, was also associated with a decline of executive function [36]. Our results, in a larger population, found that alterations in several gait parameters were associated with decline in all four cognitive domains (memory, executive functioning, visuospatial, and language) and in the global score. The discrepant results between the studies may be explained by our larger sample and the longitudinal design that possibly revealed associations that may be not seen in a smaller study. In particular, the association of the spatial and temporal gait parameters, as well as greater gait variability, with all the cognitive domains supports the hypothesis that gait requires an effective integration of multiple domains and functional areas of the brain [37, 38].

Our study has a number of strengths. First, it is a population-based prospective design of cognitively normal individuals, with a comprehensive cognitive assessment at baseline and during follow-up in a large cohort. Therefore, we were able to more accurately assess the relationship between gait and domain-specific and global cognitive changes over time. Second, because previous studies have suggested that gait changes could be caused by cognitive changes, the exclusion of individuals with mild cognitive impairment or dementia at baseline allowed a better assessment of the temporality between gait performance and subsequent cognitive decline. Third, measurement of gait was performed using an established, reproducible, and valid process with a computerized objective tool, GAITRite®. Lastly, the medical records-linkage system of the Rochester Epidemiology Project provided a unique resource with which to assess and validate covariates and comorbidities (stroke, parkinsonism, NPH, SDH, and alcoholism); thus, we did not have to rely on self-report [39].

Despite these strengths, our findings must be viewed within the limitations of the study. First, because GAITRite® was not initially included at the in-clinic exam, there were several participants who did not complete their first GAITRite® assessment at the time of their first neuropsychological assessment, which may have introduced bias. As in all longitudinal

studies that examine cognitive test performance at multiple time points, practice effects are a concern. We addressed this issue by controlling for visit number. Further, in sensitivity analyses, we excluded individuals who did not have a gait assessment at their baseline visit but the associations remained. Second, our findings may not be directly generalizable to other populations.

In conclusion, our findings suggest that declines in spatial and spatiotemporal gait parameters are both predictive of cognitive decline across domains (memory, executive function, language, visuospatial). Computerized gait analyses are a simple, non-invasive biomarker of cognitive decline and could potentially be used to identify high-risk populations to target for therapeutic interventions.

Acknowledgments

This work was supported by the National Institutes of Health (P50 AG016574, U01 AG006786). This study was also supported by the Robert H. and Clarice Smith and Abigail van Buren Alzheimer's Disease Research Program, and was made possible by the Rochester Epidemiology Project (R01 AG034676).

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Table 1

Baseline participant characteristics (N = 3,426)

Male, N (%)	1,712 (50)
Age, median (IQR)	72.93 (63.95, 78.70)
Education, median (IQR)	14 (12, 16)
Depression, N (%)	210 (6)
Charlson Index, median (IQR)	5 (3, 7)
Hypertension, N (%)	2,178 (65)
Diabetes, N (%)	567 (17)
APOE ε4, N (%)	871 (27)
BMI (kg/m^2), median (IQR)	27.83 (24.84, 31.49)
Cognitive z-scores	
Memory, median (IQR)	0.08 (−0.64, 0.78)
Language, median (IQR)	0.06 (−0.57, 0.67)
Attention, median (IQR)	0.08 (−0.55, 0.68)
Visual-spatial, median (IQR)	0.07 (−0.63, 0.76)
Global, median (IQR)	0.10 (−0.56, 0.72)

BMI, body mass index; IQR, interquartile range. Depression was determined by a score of ≥13 on the Beck Depression Inventory.

Table 2

Associations between baseline gait parameters, baseline cognition, and cognitive decline

Gait measure	Memory z-score		Language z-score		Attention z-score		Visual-spatial z-score		Global z-score	
	B (95% CI)	***p***	**B (95% CI)**	***p***	**B (95% CI)**	***p***	**B (95% CI)**	***p***	**B (95% CI)**	***p***
GAITRite® Gait speed (m/s)										
Baseline	0.081 (0.046, 0.116)	**<0.001**	0.107 (0.072, 0.141)	**<0.001**	0.174 (0.142, 0.206)	**<0.001**	0.113 (0.079, 0.148)	**<0.001**	0.154 (0.123, 0.186)	**<0.001**
Time	−0.046 (−0.063, −0.029)	**<0.001**	−0.052 (−0.068, −0.036)	**<0.001**	−0.075 (−0.090, −0.059)	**<0.001**	−0.047 (−0.062, −0.031)	**<0.001**	−0.079 (−0.091, −0.061)	**<0.001**
Baseline*Time	0.016 (0.009, 0.024)	**<0.001**	0.022 (0.015, 0.028)	**<0.001**	0.031 (0.023, 0.038)	**<0.001**	0.012 (0.006, 0.018)	**<0.001**	0.030 (0.024, 0.036)	**<0.001**
Nurse-timed Gait speed (m/s)										
Baseline	0.006 (−0.014, 0.025)	0.559	0.004 (−0.014, 0.023)	0.654	0.028 (0.010, 0.047)	**0.003**	0.003 (−0.016, 0.023)	0.728	−0.003 (−0.017, 0.011)	0.693
Time	−0.039 (−0.055, −0.022)	**<0.001**	−0.045 (−0.061, −0.028)	**<0.001**	−0.063 (−0.079, −0.047)	**<0.001**	−0.039 (−0.055, −0.023)	**<0.001**	−0.066 (−0.080, −0.051)	**<0.001**
Baseline*Time	0.015 (0.009, 0.021)	**<0.001**	0.016 (0.010, 0.021)	**<0.001**	0.021 (0.015, 0.027)	**<0.001**	0.015 (0.009, 0.020)	**<0.001**	0.022 (0.018, 0.027)	**<0.001**
Cadence (steps/min)										
Baseline	0.011 (−0.020, 0.041)	0.497	0.015 (−0.016, 0.046)	0.346	0.067 (0.038, 0.096)	**<0.001**	0.014 (−0.017, −0.045)	0.365	0.035 (0.007, 0.063)	**0.015**
Time	−0.045 (−0.062, −0.028)	**<0.001**	−0.052 (−0.068, −0.036)	**<0.001**	−0.074 (−0.090, −0.058)	**<0.001**	−0.045 (−0.061, −0.029)	**<0.001**	−0.075 (−0.090, −0.060)	**<0.001**
Baseline*Time	0.003 (−0.004, 0.010)	0.401	0.007 (0.0008, 0.013)	**0.025**	0.005 (−0.002, 0.011)	0.177	0.00008 (−0.006, 0.006)	0.978	0.006 (0.0004, 0.011)	**0.035**
Stride Length (cm)										
Baseline	0.118 (0.069, 0.168)	**<0.001**	0.200 (0.151, 0.250)	**<0.001**	0.222 (0.176, 0.268)	**<0.001**	0.176 (0.127, 0.226)	**<0.001**	0.232 (0.187, 0.277)	**<0.001**
Time	−0.035 (−0.054, −0.015)	**<0.001**	−0.044 (−0.062, −0.026)	**<0.001**	−0.064 (−0.082, −0.046)	**<0.001**	−0.042 (−0.059, −0.024)	**<0.001**	−0.063 (−0.079, −0.046)	**<0.001**
Baseline*Time	0.023 (0.012, 0.035)	**<0.001**	0.028 (0.018, 0.038)	**<0.001**	0.042 (0.031, 0.052)	**<0.001**	0.019 (0.010, 0.029)	**<0.001**	0.043 (0.034, 0.052)	**<0.001**
Step count										
Baseline	−0.094 (−0.127, −0.062)	**<0.001**	−0.114 (−0.0146, −0.081)	**<0.001**	−0.128 (−0.159, −0.097)	**<0.001**	−0.107 (−0.140, −0.074)	**<0.001**	−0.142 (−0.172, −0.112)	**<0.001**
Time	−0.047 (−0.064, −0.030)	**<0.001**	−0.054 (−0.070, −0.038)	**<0.001**	−0.076 (−0.092, −0.060)	**<0.001**	−0.048 (−0.063, −0.032)	**<0.001**	−0.078 (−0.092, −0.063)	**<0.001**
Baseline*Time	−0.013 (−0.021, −0.006)	**<0.001**	−0.016 (−0.023, −0.010)	**<0.001**	−0.026 (−0.033, −0.019)	**<0.001**	−0.012 (−0.018, −0.006)	**<0.001**	−0.025 (−0.031, −0.019)	**<0.001**
Ambulation (sec)										
Baseline	0.002 (−0.018, 0.022)	0.823	−0.016 (−0.035, 0.003)	0.104	−0.036 (−0.055, −0.016)	**<0.001**	−0.020 (−0.040, −0.00007)	**0.049**	0.002 (−0.013, 0.017)	0.771
Time	−0.038 (−0.055, −0.020)	**<0.001**	−0.044 (−0.060, −0.027)	**<0.001**	−0.059 (−0.075, −0.043)	**<0.001**	−0.038 (−0.054, −0.022)	**<0.001**	−0.065 (−0.080, −0.050)	**<0.001**
Baseline*Time	−0.013 (−0.019, −0.008)	**<0.001**	−0.012 (−0.017, −0.007)	**<0.001**	−0.021 (−0.026, −0.016)	**<0.001**	−0.011 (−0.016, −0.006)	**<0.001**	−0.021 (−0.025, −0.017)	**<0.001**
Support time (sec)										
Baseline	−0.156 (−0.267, −0.045)	**0.006**	−0.211 (−0.323, −0.100)	**<0.001**	−0.444 (−0.550, −0.338)	**<0.001**	−0.195 (−0.307, −0.083)	**0.001**	−0.347 (−0.451, −0.243)	**<0.001**
Time	−0.047 (−0.063, −0.030)	**<0.001**	−0.054 (−0.071, −0.038)	**<0.001**	−0.077 (−0.093, −0.061)	**<0.001**	−0.047 (−0.063, −0.031)	**<0.001**	−0.078 (−0.093, −0.063)	**<0.001**

Gait measure	Memory z-score		Language z-score		Attention z-score		Visual-spatial z-score		Global z-score	
	B (95% CI)	*p*	B (95% CI)	*p*	B (95% CI)	*p*	B (95% CI)	*p*	B (95% CI)	*p*
Baseline*Time	−0.009 (−0.034, 0.016)	0.478	−0.028 (−0.049, −0.006)	**<0.001**	−0.037 (−0.061, −0.013)	**0.003**	−0.014 (−0.035, 0.006)	0.168	−0.037 (−0.056, −0.017)	**<0.001**
IWG cut-off										
Baseline	−0.077 (−0.151, −0.002)	**0.044**	−0.128 (−0.202, −0.055)	**0.001**	−0.227 (−0.296, −0.158)	**<0.001**	−0.132 (−0.204, −0.060)	**<0.001**	−0.202 (−0.269, −0.135)	**<0.001**
Time	−0.028 (−0.048, −0.009)	**0.005**	−0.033 (−0.052, −0.015)	**<0.001**	−0.051 (−0.069, −0.032)	**<0.001**	−0.030 (−0.048, −0.012)	**0.001**	−0.057 (−0.073, −0.040)	**<0.001**
Baseline*Time	−0.029 (−0.043, −0.015)	**<0.001**	−0.039 (−0.051, −0.026)	**<0.001**	−0.057 (−0.071, −0.044)	**<0.001**	−0.039 (−0.052, −0.027)	**<0.001**	−0.046 (−0.056, −0.036)	**<0.001**

Stride length SD: memory, n=3,292; language, n=3,254; attention, n=3,255; visual-spatial, n=3,248; global, n=3,216. Swing time SD: memory, n=3,276; language, n=3,238; attention, n=3,239; visual-spatial, n=3,232; global, n=3,200. Stance time SD: memory, n=3,282; language, n=3,244; attention, n=3,245; visual-spatial, n=3,238; global, n=3,206. Mean 1.90 (SD=2.00, range 0–8.09) years of follow-up; mean 1.44 (SD=1.93, range 0–7) follow-up visits.

Table 3

Associations between gait variability, baseline cognition, and cognitive decline

Gait measure	Memory z-score		Language z-score		Attention z-score		Visual-spatial z-score		Global z-score	
	B (95% CI)	*p*	B (95% CI)	*p*	B (95% CI)	*p*	B (95% CI)	*p*	B (95% CI)	*p*
Stride Length SD										
Baseline	−0.077 (−0.134, −0.021)	**0.007**	−0.091 (−0.147, −0.034)	**0.002**	−0.152 (−0.205, −0.099)	**<0.001**	−0.157 (−0.213, −0.100)	**<0.001**	−0.152 (−0.203, −0.100)	**<0.001**
Time	−0.023 (−0.049, 0.003)	0.079	−0.024 (−0.047, −0.001)	**0.041**	−0.047 (−0.071, −0.022)	**<0.001**	−0.039 (−0.062, −0.017)	**<0.001**	−0.043 (−0.065, −0.022)	**<0.001**
Baseline*Time	−0.016 (−0.029, −0.002)	**0.025**	−0.020 (−0.031, −0.008)	**0.001**	−0.019 (−0.032, −0.006)	**0.003**	−0.004 (−0.015, 0.006)	0.428	−0.022 (−0.033, −0.012)	**<0.001**
Swing time SD										
Baseline	−0.151 (−0.229, −0.074)	**<0.001**	−0.237 (−0.315, −0.159)	**<0.001**	−0.214 (−0.288, −0.140)	**<0.001**	−0.158 (−0.238, −0.078)	**<0.001**	−0.245 (−0.317, −0.172)	**<0.001**
Time	−0.150 (−0.230, −0.071)	**<0.001**	−0.207 (−0.274, −0.139)	**<0.001**	−0.252 (−0.329, −0.174)	**<0.001**	−0.171 (−0.237, −0.106)	**<0.001**	−0.284 (−0.347, −0.221)	**<0.001**
Baseline*Time	−0.027 (−0.046, −0.007)	**0.007**	−0.038 (−0.055, −0.022)	**<0.001**	−0.043 (−0.062, −0.024)	**<0.001**	−0.031 (−0.047, −0.015)	**<0.001**	−0.051 (−0.066, −0.036)	**<0.001**
Stance time SD										
Baseline	−0.078 (−0.132, −0.024)	**0.005**	−0.119 (−0.173, −0.064)	**<0.001**	−0.172 (−0.223, −0.121)	**<0.001**	−0.134 (−0.188, −0.080)	**<0.001**	−0.157 (−0.206, −0.107)	**<0.001**
Time	−0.122 (−0.171, −0.073)	**<0.001**	−0.124 (−0.165, −0.082)	**<0.001**	−0.126 (−0.173, −0.079)	**<0.001**	−0.079 (−0.120, −0.039)	**<0.001**	−0.167 (−0.206, −0.128)	**<0.001**
Baseline*Time	−0.022 (−0.035, −0.009)	**0.001**	−0.020 (−0.031, −0.009)	**<0.001**	−0.014 (−0.027, −0.002)	**0.025**	−0.010 (−0.020, −0.001)	0.075	−0.206 (−0.036, −0.016)	**<0.001**

Stride length SD: memory, n=3,292; language, n=3,254; attention, n=3,255; visual-spatial, n=3,248; global, n=3,216. Swing time SD: memory, n=3,276; language, n=3,238; attention, n=3,239; visual-spatial, n=3,232; global, n=3,200. Stance time SD: memory, n=3,282; language, n=3,244; attention, n=3,245; visual-spatial, n=3,238; global, n=3,206. Mean 1.90 (SD=2.00, range 0–8.09) years of follow-up; mean 1.44 (SD=1.93, range 0–7) follow-up visits.

SD, Standard Deviation