THE GERONTOLOGICAL SOCIETY OF AMERICA®

Journals of Gerontology: Medical Sciences
cite as: *J Gerontol A Biol Sci Med Sci*, 2017, Vol. 72, No. 3, 431–437
doi:10.1093/gerona/glw211
Advance Access publication November 1, 2016

OXFORD

Research Article

Cerebral Amyloid Deposition and Dual-Tasking in Cognitively Normal, Mobility Unimpaired Older Adults

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Received May 10, 2016; Accepted September 27, 2016

Decision Editor: Stephen Kritchevsky, PhD

Abstract

Background: We examined relationships between cerebral amyloid-beta (Aβ) and cognitive-gait dual-task performance in 27 cognitively normal, mobility unimpaired elders.
Methods: We assessed Aβ on Pittsburgh Compound B (PiB)-PET. We measured gait speed separately and while performing working-memory, response-inhibition, motor-sequencing, and phone-dialing tasks. We compared dual-task costs on gait and cognitive performance in high-Aβ (PiB(+)) and low-Aβ (PiB(−)) groups and examined the association between Aβ and dual-task performance decrements.
Results: PiB(+) (n = 16) were comparable with the PiB(−) (n = 11) individuals on demographics, general cognitive and physical performance, and key brain MRI characteristics. PiB(+) group demonstrated greater dual-task costs on gait speed on all cognitive tasks ($p < .05$) except on response inhibition. Dual-task costs on cognition were similar between groups. Overall, Aβ was associated with dual-task decrement on gait speed but not on dual-task decrement on cognitive performance.
Conclusions: Preliminary evidence indicates that cerebral Aβ is associated with gait slowing on dual-tasking in healthy older adults.

Keywords: Cognition—Gait—Alzheimer's disease

Cognition and mobility, traditionally considered as independent functions, are in fact centrally integrated, functionally interrelated, and commonly affected by Alzheimer's disease (AD) pathology (1–3). Amyloid-beta (Aβ), involved in AD pathology, is present in up to 50% of cognitively healthy octogenarians (4) and is emerging as a risk factor for falls (5). In dementia-free populations, slower gait speed is associated with greater Aβ deposition in the striatum, anterior cingulate, and precuneus (6) regions important to working-memory processes (7). The combination of cognitive complaints with measures of slow gait speed improves the prediction of mobility disability than either one alone in older individuals without dementia or mobility disability (8) and is also associated with twofold increase in cognitive impairment in older adults who perform within normal range on general cognitive measures (9). Therefore, gait and cognitive tasks performed concurrently may be related to burden of AD pathology in clinically normal older adults than either one performed separately.

In healthy older adults, executive function is an essential cognitive resource for walking (10–12); poor performance in this domain and related subdomains such as working-memory and attention is associated with reduced gait speed in healthy older adults and in individuals with preclinical AD (12). Dual-tasking, or executing a cognitively challenging task while walking, places additional attentional demands on gait leading to a decrement in gait and/or cognitive performance. Patients with AD demonstrate greater dual-task gait decrement than cognitively normal (CN) older adults on working-memory compared with spatial-attention paradigms (13). In CN individuals, Aβ deposition influences attention and working-memory

performance (14–17), and mental-tracking and working-memory tasks cause greater reductions in gait speed than other executive function processes under dual-task conditions (18); however, it is not known whether Aβ is associated with dual-task decrements on gait and cognitive performance by exerting its influence on cognitive processes involved in walking in CN individuals.

We compared dual-task performances in two groups of CN mobility impaired older adults divided on the basis of their cerebral Aβ deposition burden, and examined the association between cerebral Aβ and dual-task decrements in the whole sample. We hypothesized that the high-Aβ group would perform worse than the low-Aβ group on dual-task gait and cognitive measures relative to their single-task performance, and greater cortical Aβ will be associated with greater decrements on gait speed and cognitive performance while dual-tasking in the whole sample.

Materials and Methods

Participants

Participants were CN individuals between ages 65 and 80 years who underwent periodic detailed cognitive assessments, serial MRI, and PET since 2005 in an ongoing longitudinal study of Aβ pathology and cognition in normal older adults (19). Eligible participants had an Aβ-PET scan within the prior year, were able to walk 400 m (approximately one block) independently in 15 minutes without discomfort, used no assistive devices, had no gait complaints or falls in the previous year, and had no known diagnosis of concussion, neurodegenerative, or neurological condition or any health condition severe enough to limit mobility. Exclusion criteria at time of experimental procedures were gait speed less than 0.6 m/s, significant visual and hearing impairment, and cognitive task accuracy less than 50% on computerized cognitive paradigms used in this study.

Standard Protocol Approvals, Registrations, and Patient Consents

The study was approved by the institutional review board of the University of Pittsburgh, and all participants provided informed consent prior to undertaking the study.

Demographic, Physical Performance, Cognitive, and Behavioral Measures

Demographic and general measures of cognition and physical performance were collected at the time of gait and the dual-task assessments. We obtained self-reported information on falls, comorbidities (Charlson Comorbidity Index), and cardiac risk factors. Assessments included vital signs, weight, sensory and musculoskeletal exam, vision, audiometry (Welch Allyn, Skaneateles Falls, NY), global cognitive functioning (Montreal Cognitive Assessment [MOCA]), speed of information processing (Digit Symbol Substitution Test [DSST]), depressive symptoms (Geriatric Depression Scale), parkinsonism (Unified Parkinson's Disease Rating Scale [UPDRS]), Short Physical Performance Battery (SPPB), grip strength, and the Timed Up and Go (TUG).

Neuroimaging

[^{11}C] Pittsburgh Compound-B (PiB) was injected intravenously and PiB-PET data were acquired 50–70 minutes after injection. T1-weighted magnetization-prepared rapid gradient echo and fluid-attenuated inversion recovery (FLAIR) MR images were acquired on Siemens 3T MR scanner. Details of image registration, regions of interest delineation, and measures of PiB retention are described previously (19,20). Participant's native PET and MR image data were coregistered using Statistical Parametric Mapping (SPM8) software. Each coregistered MR image was spatially normalized to an MR template, and these transformation parameters were applied to the parametric PET images that were used for voxel-level group comparisons. A global PiB standardized uptake value ratio (SUVR), corrected for brain atrophy, was determined by averaging regional values from bilateral anterior cingulate, precuneus, temporal, parietal, and frontal cortices and striatum referenced to the cerebellar value (19,20). We divided participants into PiB(+) or PiB(−) groups using a biologically relevant atrophy-corrected PiB-SUVR cutoff of 1.4, which was previously established as a reliable cutoff to detect amyloid positivity and preclinical AD among CN older adults (21–23).

As gait parameters, both with and without concurrent cognitive tasking, are influenced by small-vessel disease burden in older adults (1,2,13), we quantified the volume of white matter hyperintensities (WMH) on FLAIR normalized to total brain volume (nWMH) for each participant.

Gait Speed Measures

Gait speed was measured on an 8-m long GaitMat II (EQ, Chalfont, PA). To capture single-task gait speed, participants were instructed to walk back and forth across the length of the walkway at their most comfortable pace as if on a stroll, without talking or multitasking. Dual-task gait speed was measured while walking back and forth on the GaitMat II while performing the cognitive tasks mentioned in the following sections. Changes in gait at initiation, at termination, and while turning at either ends of the walkway were not included in the gait speed estimation.

Cognitive tasks

Prior to data collection, all participants were trained on the cognitive tasks. Cognitive demands of maintaining an upright posture while standing overlap with those required for maintaining dynamic postural stability while walking (12,24). Hence, single-task cognitive task performance was measured while standing. Scripted instructions were read out prior to each task and data collection was performed uniformly. Details of the tasks administered are explained in the following subsections.

Working-memory task (2-back verbal paradigm)

A stream of black capitalized alphabets (consonants only and excluding the consonant "X") on a white background were displayed over a 65-second duration on a 42″ screen (stimulus display interval [SDI] = 1,000 ms, interstimulus interval [ISI] = 1,500 ms). Participants were instructed to respond on the hand-held button whenever the stimulus letter displayed was the same as the letter that appeared two stimuli prior to it.

Response inhibition (Go/No-go paradigm)

Visual stimuli consisted of a series of black filled circles appearing rapidly on white background interspersed with black filled squares (SDI = 500 ms, ISI = 1,500 m, approximately 5:1) displayed centrally on a 42″ screen over a 65-second duration. Participants were instructed to respond by pressing a hand-held button after every circle (Go response) but not square (No-go response). Cognitive performance was monitored on reaction time and errors of omission on the Go responses and errors of commission on the No-go responses.

Motor sequencing (Luria task)

Participants were instructed to perform repeatedly a set of three hand positions in a predefined sequence as quickly as possible over a 30-second period using their dominant hand (25): a closed fist, open hand with palm facing downward in full prone position and open hand with palm facing inward in midprone position. Accuracy of motor sequencing was captured by a glove (DG5 VHand 2.0, DGTech, Bazzano, Italy) embedded with gyroscopes and accelerometers. The number of sequences performed accurately accounted for task accuracy.

Phone dialing while walking task

Dialing a phone while walking is an ecologically valid cognitive-gait dual-task. Two dissimilar sets of 10-digit numbers, one set for each condition (standing and walking), were read out at rate of one digit per second and after all the 10 digits were presented participants were instructed to enter the numbers on a large-button, hand-held phone device as quickly and accurately as possible. The digits entered (accuracy; range: 1 to 10) as displayed on the phone and the time to complete the 10-digit entry (response time) were recorded. Participants were instructed to enter zeros for any digit that they were unable to recall thus ensuring a total of 10 digits entered. On the walking condition, participants were instructed to walk while keying in the numbers on the hand-held phone device.

Dual-Task Performance Assessment

Reaction time (RT) and accuracy (where applicable) and gait speed were recorded separately (single-task conditions) and with each task performed while walking (dual-task conditions). On the dual-task conditions, participants were instructed to begin walking after 5 seconds of commencing the working-memory, response-inhibition, and motor-sequencing paradigms and to continue walking to and fro across the walkway while performing these tasks. Monitors that displayed stimuli for the working-memory and response-inhibition paradigms were placed on either sides of GaitMat II to enable their uninterrupted performance while dual-tasking. The working-memory and response-inhibition dual tasks were performed for 60 seconds each, the motor-sequencing dual-task was performed for 30 seconds, and the phone dialing while walking task was performed across a single traverse across the walkway. No explicit task prioritization was offered—participants were instructed to walk as in the single-task walking condition while achieving the fastest and fully accurate responses on the cognitive tasks as in the standing-only condition. Dual-task performance was quantified by the magnitude of change (Single-task value – Dual-task value) and dual-task costs or percent change ([100 × Magnitude of change] / Single-task value) in gait speed and cognitive performance (RT and accuracy, where applicable).

Both single-task and dual-task conditions were randomized within each condition for each participant. All single-task conditions preceded dual-task conditions to maintain consistency. All participants performed the same number of tasks within each condition with single-task preceding the dual-task conditions. The experimental procedures were conducted at fixed time of the day, in a research space dedicated for gait analysis and were performed under abundant lighting, without any other sensory distractions with one participant at a time.

Statistical Analysis

We used both standard analytic techniques to summarize data at the group level and graphical techniques to portray findings at the individual level. We used PiB retention both as a dichotomous [PiB(+), PiB(−)] and continuous variable [PiB SUVR]. We compared single- and dual-task gait speed and cognitive performance measures, dual-task decrements, and dual-task costs on gait speed and cognitive performance between PiB(+) and PiB(−) using independent samples *t* tests. Our overall strategy was to examine the association of global PiB SUVR with (a) single-task performance, (b) raw magnitude of change, and (c) dual-task cost or percent change. We anticipated little or no associations in (a) but significant associations in (b) and (c) to support our hypothesis. Correlations were explored using Pearson's coefficient. We also fitted a series of linear mixed models with gait speed as the dependent variable; participant group (PiB(+), PiB(−)), task condition (single-task and dual-task 2-back, Go/No-go, Luria, and phone tasks), and their interaction as fixed effects; and a participant random effect to account for multiple measurements from the same participant and the resulting nonindependence of observations. For dual-task cost outcomes, we used a similar model, with PiB group, dual-task condition (2-back, Go/No-go, Luria, and phone tasks), and their interaction as fixed effects. We used appropriately constructed contrasts to compare tasks and groups. To examine associations controlling for participant characteristics, we fitted another set of models with gait speed as the dependent variable; global PiB as a continuous variable, dual task and each covariate (one-at-a-time due to limited sample size) as fixed effects, and a participant random effect. A similar overarching modeling strategy is difficult for RT and accuracy measures, where the scale of measurement and variability is substantially larger for some tasks such as phone dialing. Therefore, we compared RT and accuracy measures separately for tasks using independent samples *t* tests. SAS version 9 (SAS Institute, Cary, NC) was used for all statistical analyses, with SAS MIXED procedure for the main analyses.

Results

Sample Characteristics

Table 1 depicts the demographic characteristics and general cognitive and motor performance measures including structural brain MRI measures for the whole sample and for the PiB(+) and PiB(−) groups. There were no significant differences between groups on age, gender, education, body mass index, number of comorbidities, grip strength, performance on the MOCA and DSST, UPDRS motor score, and key brain characteristics (total WMH, and total gray and white matter volumes). SPPB score showed a trend toward better performance in the PiB(−) group; however, both groups were comparable on the TUG task.

Group Differences on Gait Speed and Cognitive Performance on Single- and Dual-Task Conditions

There were no significant differences between PiB(+) and PiB(−) groups on single-task gait speed (performed without concurrent cognitive task, Table 2). Within each group, participants walked slower on every dual-task condition; the magnitude of decline in gait speed while dual-tasking attained statistical significance on all dual tasks but narrowly missed it on the response-inhibition dual-task condition in the PiB(−) group. Between groups, gait speed on the motor-sequencing dual-task condition was slower in the PiB(+) group than in the PiB(−) group ($p = .048$). The PiB(+) group showed a greater magnitude of decline in gait speed on the working-memory ($p = .05$), motor-sequencing ($p = .039$), and phone-dialing dual tasks ($p = .07$). The dual-task costs on gait speed were also significantly greater in the PiB(+) group than in the PiB(−) group on all but the response-inhibition task (Figure 1).

Table 1. Sample Characteristics of the Whole Sample of Cognitively Normal, Mobility Unimpaired Older Adults and Comparisons Between Groups Divided by PiB Status

	Whole Group	PiB(+)	PiB(−)	*P* Value for PiB Group Differences
	N = 27	*n* = 16	*n* = 11	
Age (y)	75.5 ± 5.6	75.97 ± 5.02	74.81 ± 6.65	.61
Women, *n* (%)	14 (50%)	8 (57%)	6 (43%)	.81
Education (y)	15.2 ± 2.7	15 ± 2.8	15.4 ± 2.6	.74
MOCA	26.2 ± 2.5	26.5 ± 2.5	25.9 ± 2.6	.59
DSST	54 ± 13	51.7 ± 12.3	59 ± 14	.24
SPPB	10.6 ± 1.6	10.2 ± 1.7	11.4 ± 1.1	.08
TUG (s)	10.1 ± 2.2	10.2 ± 1.8	9.9 ± 3.4	.8
Grip strength (kg)	35.7 ± 17.2	34.6 ± 18.4	37.4 ± 15.6	.69
UPDRS	3.7 ± 2.5	3.9 ± 2.8	3.4 ± 2.1	.7
Charlson Comorbidity Index (*n*)	3 ± 1.4	3.2 ± 1.4	2.7 ± 1.4	.4
BMI (kg/m^2)	26. 4 ± 4.2	27.1 ± 3.9	25.0 ± 5	.29
nWMH (% of brain volume × 1,000)	5.93 ± 6.2	5.32 ± 4.8	6.7 ± 7.8	.6
Total gray matter volume (cc × 10^3)	55.25 ± 64.33	59.29 ± 15.84	73.03 ± 22.02	.8
Total white matter volume (cc × 10^3)	44.46 ± 49.77	54.5 ± 14.56	43.88 ± 13.23	.4
PiB SUVR	1.63 ± 0.4	1.8 ± 0.4	1.3 ± 0.1	<.0001

Note: BMI = body mass index; DSST = Digit Symbol Substitution Test (range: 0 to 76, higher indicates better performance); MOCA = Montreal Cognitive Assessment (range: 0 to 30, higher indicates better performance); nWMH = white matter hyperintensities normalized to total brain volume; PiB SUVr = Pittsburgh B compound standardized uptake values ratio; SPPB = Short Physical Performance Battery (range 0–12, higher indicates better performance); TUG = Timed Up and Go test (seconds, higher indicates worse performance); UPDRS = Unified Parkinson's Disease Rating Scale (range: 0 to 108, higher score indicated worse parkinsonism).

Table 2. Group and Task Differences ± *SE*s on Gait Speed Estimated Using a Linear Mixed Model and *p* Values

		PiB(+)	PiB(−)	PiB(+) vs PiB(−) Difference ± *SE*
		(*p* Value)	(*p* Value)	(*p* Value)
Single-task gait speed (m/s)		1.14 ± 0.04	1.16 ± 0.06	−0.02 ± 0.08 (.7)
Working-memory (2-back)	Dual-task gait speed (m/s)	0.88 ± 0.06 (.099)	1.04 ± 0.07 (.099)	−0.16 ± 0.08 (.064)
	Magnitude of decline	0.26 ± 0.04 (<.0001)	0.13 ± 0.05 (.016)	0.13 ± 0.07 (.053)
	Dual-task costs	22.7 ± 3.7 (<.0001)	10.7 ± 4.5 (.02)	12.0 ± 5.8 (.043)
Response-inhibition (Go/No-go)	Dual-task gait speed (m/s)	0.93 ± 0.06 (.11)	1.08 ± 0.06 (.11)	−0.14 ± 0.08 (.106)
	Magnitude of decline	0.21 ± 0.04 (<.0001)	0.09 ± 0.05 (.079)	0.11 ± 0.07 (.101)
	Dual-task costs	18.9 ± 3.7 (<.0001)	8.1 ± 4.6 (.084)	10.8 ± 5.9 (.073)
Motor-sequencing (Luria task)	Dual-task gait speed (m/s)	0.75 ± 0.07 (.05)	0.94 ± 0.06 (.05)	−0.17 ± 0.09 (.049)
	Magnitude of decline	0.39 ± 0.05 (<.0001)	0.24 ± 0.05 (<.0001)	0.15 ± 0.07 (.04)
	Dual-task costs	34.4 ± 4.0 (<.0001)	19.4 ± 4.8 (.0001)	15.0 ± 6.2 (0.019)
Phone task	Dual-task gait speed (m/s)	0.74 ± 0.05 (.066)	0.89 ± 0.06 (.066)	−0.15 ± 0.08 (.081)
	Magnitude of decline	0.40 ± 0.04 (<.0001)	0.28 ± 0.05 (<.0001)	0.12 ± 0.07 (.071)
	Dual-task costs	35.6 ± 3.7 (<.0001)	23.5 ± 4.5 (<.0001)	12.2 ± 5.8 (.04)

On the cognitive domain, the PiB(+) group had a slower RT than the PiB(−) group on both the single- and dual-task conditions of the response-inhibition and working-memory tasks while accuracy on each of these tasks was comparable between groups (Supplementary Table 1). There were no group differences on cognitive performance on both single- and dual-task conditions of the motor-sequencing and the phone-dialing tasks. On dual-tasking, the PiB(+) group demonstrated greater slowing in RT on the response-inhibition task than the PiB(−) group (p = .042) but the magnitude of change in RT on the working-memory and phone-dialing tasks were comparable between groups

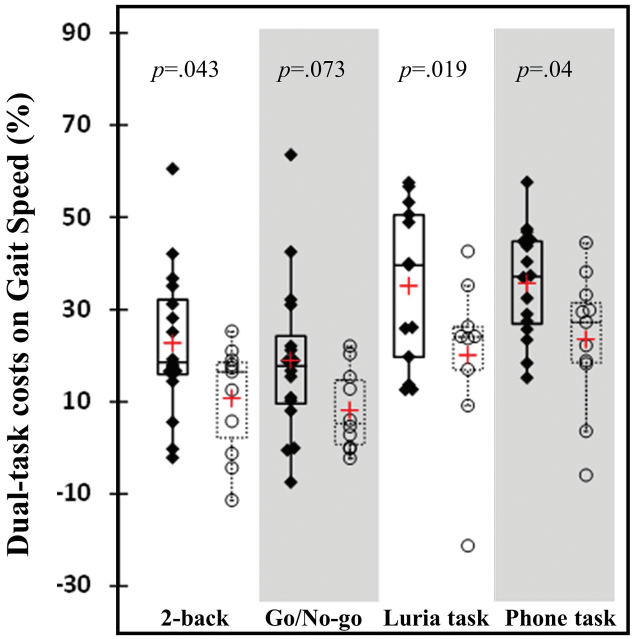

Figure 1. Dual-task cost on gait speed in the PiB(+) group (solid lines, diamonds) and PiB(–) group (dotted lines, open circles) on working memory (2-back task), response inhibition (Go/No-go task), motor sequencing (Luria task) , and dialing a phone (Phone task) while walking. Mean values of dual-task cost on gait speed are marked in red.

(Supplementary Table 1); however, there were no significant group differences on dual-task costs on cognitive performance on the response-inhibition task or on any other cognitive task while dual-tasking.

Association Between PiB Retention and Single-Task and Dual-Task Gait Speed

In the entire sample, global PiB SUVR correlated significantly with the magnitude of gait slowing on the working-memory ($r = .39$, $p = .044$), complex motor-sequencing ($r = .48$, $p = .024$), and phone-dialing tasks ($r = .4$, $p = .037$) and showed a trend on the response-inhibition task ($r = .35$, $p = .07$). PiB SUVR did not correlate significantly with single-task or any dual-task gait speed ($p = .2$) or with SPPB score ($p = .8$) or TUG time ($p = .6$). Table 3 shows that the relationship between every 0.1-unit increase in PiB SUVR and magnitude of gait slowing was statistically significant on the complex motor-sequencing task ($p = .0079$), working-memory task ($p = .032$), and the phone-dialing task ($p = .042$), whereas a trend toward significance was observed on the response-inhibition task ($p = .084$). Albeit both PiB groups were comparable on baseline characteristics, we adjusted for covariates, each one separately (age, gender, education, grip strength, body mass index, number of comorbidities, nWMH, and single-task gait speed), and the associations between global PiB SUVR and gait slowing on each of the tasks were not substantially altered (Table 3). Similarly, accounting for single-task RT on cognitive tasks did not alter the strength of association between PiB retention and magnitude of gait slowing on the respective dual-task conditions (data not shown).

Association Between PiB Retention and Cognitive Performance on the Standing and While Walking

In the whole group, the association between global PiB SUVR and cognitive measures (RT and/or accuracy where applicable) on both the single-task and dual-task conditions, or with magnitude of change in cognitive performance while dual-tasking, was not statistically significant (p value ranged from .2 to .9, data not shown).

Discussion

This study provides first empirical evidence indicating that dual-task performance is associated with cerebral Aβ burden in CN, mobility unimpaired older adults. In our sample of well-screened, high-functioning older adults, individuals with high Aβ had a greater decrement in gait speed, and dual-task costs on gait speed, than those with low Aβ on the working-memory, motor-sequencing, and phone-dialing dual-task conditions. These dual-task cost differences are particularly interesting as both groups were similar on single-task gait speed and general cognitive and physical performance; albeit, the high-Aβ group had slower responses on the response-inhibition and working-memory tasks under both single- and dual-task conditions. Nevertheless, these CN high-Aβ individuals maintained cognitive performance while dual-tasking but at the cost of gait speed. In the entire sample, we found that greater cerebral Aβ was significantly associated with greater decrement in gait speed on the working-memory, motor-sequencing, and phone-dialing dual-task conditions, withstanding adjustments for covariates; however, cerebral Aβ was not associated with cognitive performance or its decline on dual-tasking.

AD pathology plays an important role in both cognitive and mobility declines in older adults (3). A recent report on older adult participants with predominantly subjective memory complaints, functional deficits, and slow gait reported that regional Aβ deposition was associated with slow gait speed (6). In contrast, our study sample recruited from an ongoing study of normal cognitive aging were deemed CN at entry and annually (19) and were further screened for mobility and balance impairments. We did not find any association between cortical Aβ burden and single-task measures of gait speed in our sample. However, we found that this sample who appear cognitively resilient to Aβ (19) may show subtle differences in the degree of gait slowing while performing certain cognitive tasks while walking.

Why cognitive performance is preserved at cost of gait speed when both these functions compete for limited neural resources in face of a high-Aβ burden? Older adults prioritize balance and posture over cognitive task performance by slowing down to maintain gait stability when perturbed by an attention-dividing task (26). The degree of gait slowing on dual-tasking also reflects overall attentional capacity, which could be constrained by Aβ in the brain (27). Consistent with other studies, we found that both the high- and low-Aβ groups reduced gait speed likely focusing on cognitive task performance while dual-tasking (27). However, those with high Aβ had greater dual-task costs on gait speed on the working-memory and motor-sequencing tasks suggesting that Aβ pathology associated with cognitive processes important to gait control may negatively affect gait speed on dual-tasking.

We found that Aβ deposition had a weaker association with gait slowing on certain cognitive tasks such as response inhibition than on others such as working memory. Some reasons that could explain these findings may be to do with the influence of Aβ on cognitive processes involved in gait and the underlying neuroanatomical substrates shared by cognitive processes and gait. In CN individual, Aβ deposition is associated with poor performance on attention, working-memory, and related executive function processes (14–17). These cognitive processes are largely attributed to large fronto-parietal and cingulate networks (7,28,29), which also serve as neural resources for gait control (10,12). Aβ deposited in these regions (30) disrupts

Table 3. Unadjusted and Adjusted Associations Between Cortical PiB Retention (as a continuous variable) and Change in Gait Speed From Single Task. Regression Coefficients Corresponding to 0.1 Unit in PiB From Linear mixed Models ± *SE* (*p* value)

		Adjusted for:							
	Unadjusted	Age	Gender	Education	Grip strength	BMI	Comorbidities	nWMH	Single-task gait speed
Working-memory	0.018 ± 0.008 (.032)	0.018 ± 0.008 (.033)	0.019 ± 0.008 (.024)	0.018 ± 0.008 (.032)	0.018 ± 0.009 (.035)	0.015 ± 0.009 (.095)	0.018 ± 0.008 (.035)	0.019 ± 0.009 (.031)	0.017 ± 0.008 (.049)
Response-inhibition	0.014 ± 0.008 (.085)	0.014 ± 0.008 (.088)	0.015 ± 0.008 (.067)	0.014 ± 0.008 (.087)	0.016 ± 0.009 (.074)	0.015 ± 0.009 (.096)	0.014 ± 0.008 (.089)	0.016 ± 0.009 (.061)	0.014 ± 0.008 (.1)
Motor-sequencing	0.026 ± 0.01 (.008)	0.026 ± 0.01 (.009)	0.028 ± 0.01 (.006)	0.026 ± 0.01 (.008)	0.028 ± 0.01 (.006)	0.028 ± 0.01 (.007)	0.026 ± 0.01 (.009)	0.028 ± 0.01 (.008)	0.025 ± 0.01 (.012)
Phone task	0.017 ± 0.008 (.042)	0.017 ± 0.008 (.043)	0.018 ± 0.008 (.032)	0.017 ± 0.008 (.042)	0.018 ± 0.009 (.04)	0.019 ± 0.009 (.028)	0.017 ± 0.008 (.045)	0.019 ± 0.009 (.028)	0.016 ± 0.008 (.063)

nWMH = white matter hyperintensities normalized to total brain volume.

cortical signaling (31) with subtle effects on memory and executive function domains, particularly in the working-memory subdomains (14–17,19,20); dual-task conditions that involve specific executive functions such as working memory alter gait in older adults with and without AD (13,32,33).

Subtle group differences on RT on the working-memory and response-inhibition paradigms were observed in our sample—the PiB(+) group had a slower RT on single- and dual-task conditions compared with the PiB(−) group in keeping with prior studies (14–16,20). Slower RT of PiB(+) individuals on the working-memory and response-inhibition paradigms reflects poor attention and executive function previously reported in individuals with a PiB SUVR of 1.4 or greater (22), a cutoff that we used identify PiB(+) in our sample of CN individuals. However, it is noteworthy that the costs of dual-tasking on RT were similar between groups. We also found no significant associations between Aβ burden and cognitive performance on any of the cognitive tasks on either single- or dual-task condition or on cognitive decline while dual-tasking.

This study has several limitations. Due to the exploratory nature of the analysis and small sample size, our statistical adjustments were limited to key covariates. Factors such as sleep and mood that could potentially influence cognition and mobility were not included in the analyses. Lastly, we included adjustments for key measures of brain aging such as small-vessel disease and brain atrophy but did not include others such as glucose metabolism and changes in normal appearing white matter. Nevertheless, this study calls for larger studies on independent samples tracking changes in the dual-tasking concurrent with multimodal neuroimaging to further assess the predictive ability of cognitive-motor stress tests in identifying amyloid positivity in high-functioning healthy older adults.

In conclusion, this study provides preliminary evidence indicating that Aβ deposition is associated with changes in gait speed on dual-tasking in well-screened CN, mobility unimpaired older adults. This study proposes a new hypothesis-generating framework for further research on the relationship between cognitive-motor dual tasks and AD biomarkers in older adults.

Supplementary Material

Supplementary material can be found at: http://biomedgerontology.oxfordjournals.org/

Funding

This research was supported by the National Institute on Aging (RF1AG025516 and K23AG049945), the Pittsburgh Pepper OAIC (P30AG024827), and the Pittsburgh Alzheimer's Disease Research Center (P50AG005133).

Acknowledgments

We acknowledge the assistance of George Grove, Edye Halligan, and Courtney Igne with recruitment, and with data collection, Drs. Yihuang Kang and Tao Jiang with data and statistical analyses, Jarad Prinkey with programming and hardware, Rhaven Coleman and Erica Tamburo with image processing, and Drs. Howard Aizenstein and Julie Price with PET and MRI image acquisition, processing, and reconstruction.

Conflict of Interest

GE Healthcare holds a license agreement with the University of Pittsburgh. W.E.K. and C.A.M. are coinventors of the Pittsburgh B compound (PiB), and, as such, have a financial interest in this license agreement. GE Healthcare

provided no grant support for this study and had no role in the design or interpretation of results or preparation of this manuscript. All other authors have no conflicts of interest with this work.

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