Cognition-Mobility Interface and AD Pathology in Healthy Older Adults

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Cognition-Mobility Interface

- Cognition and mobility are centrally integrated
- Dual-task walking: assesses the interface between cognition & mobility
- Individuals with AD perform poorly on dual-tasks {Camicioli 1997; Sheridan 2003; Nadkarni 2012}
- In cognitively normal older adults, is Aβ deposition associated with:
  - Gait speed measured on usual self-paced walking (single-task condition)?
  - Gait speed change while performing a cognitive task (dual-task condition)?

Research
JAMA Neurol. 2017;74(1):82-90.

JAMA Neurology | Original Investigation

Association of Brain Amyloid-β With Slow Gait in Elderly Individuals Without Dementia
Influence of Cognition and Apolipoprotein E ε4 Genotype

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Associations Between Global PiB SUVR and Gait Speed in Cognitively Normal (n=144)

Variable	Unadjusted β (95% CI)	*P* Value	Adjusted β (95% CI)[a]	*P* Value
Global PiB SUVR	−0.072 (−0.140 to −0.003)	.04	−0.074 (−0.145 to −0.003)	.04
Global PiB SUVR and MMSE	−0.059 (−0.126 to 0.008)	.08	−0.055 (−0.124 to 0.013)	.11

[a]Covariates: Age, sex, education, HTN, CHD, stroke, Hipp vol, WMH

Is Aβ associated with dual-task performance ?

- Does the cognitive process underlying the dual-task matter?

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OXFORD

Research Article

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

Neelesh K. Nadkarni,[1,2] Oscar L. Lopez,[2,3,4] Subashan Perera,[1,5] Stephanie A. Studenski,[6] Beth E. Snitz,[2,3] Kirk I. Erickson,[7] Chester A. Mathis,[8] Robert D. Nebes,[4] Mark Redfern,[9] and William E. Klunk[2,3,4]

Single-task performance

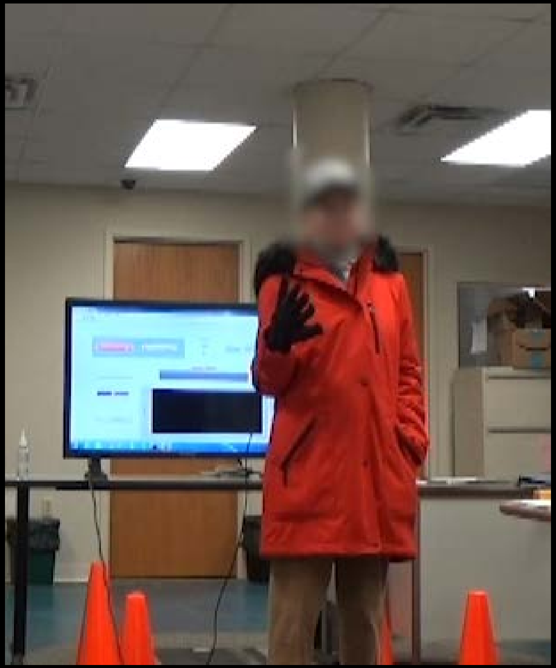
Response inhibition

Go-No go
60 sec

Working memory

N-back
60 sec

Motor sequencing



Luria sequencing
30 sec

Usual walk

Walking only
60 sec

Dual-task performance

Response inhibition

Go-No go + walk
60 sec

Working memory

N-back + walk
60 sec

Motor sequencing

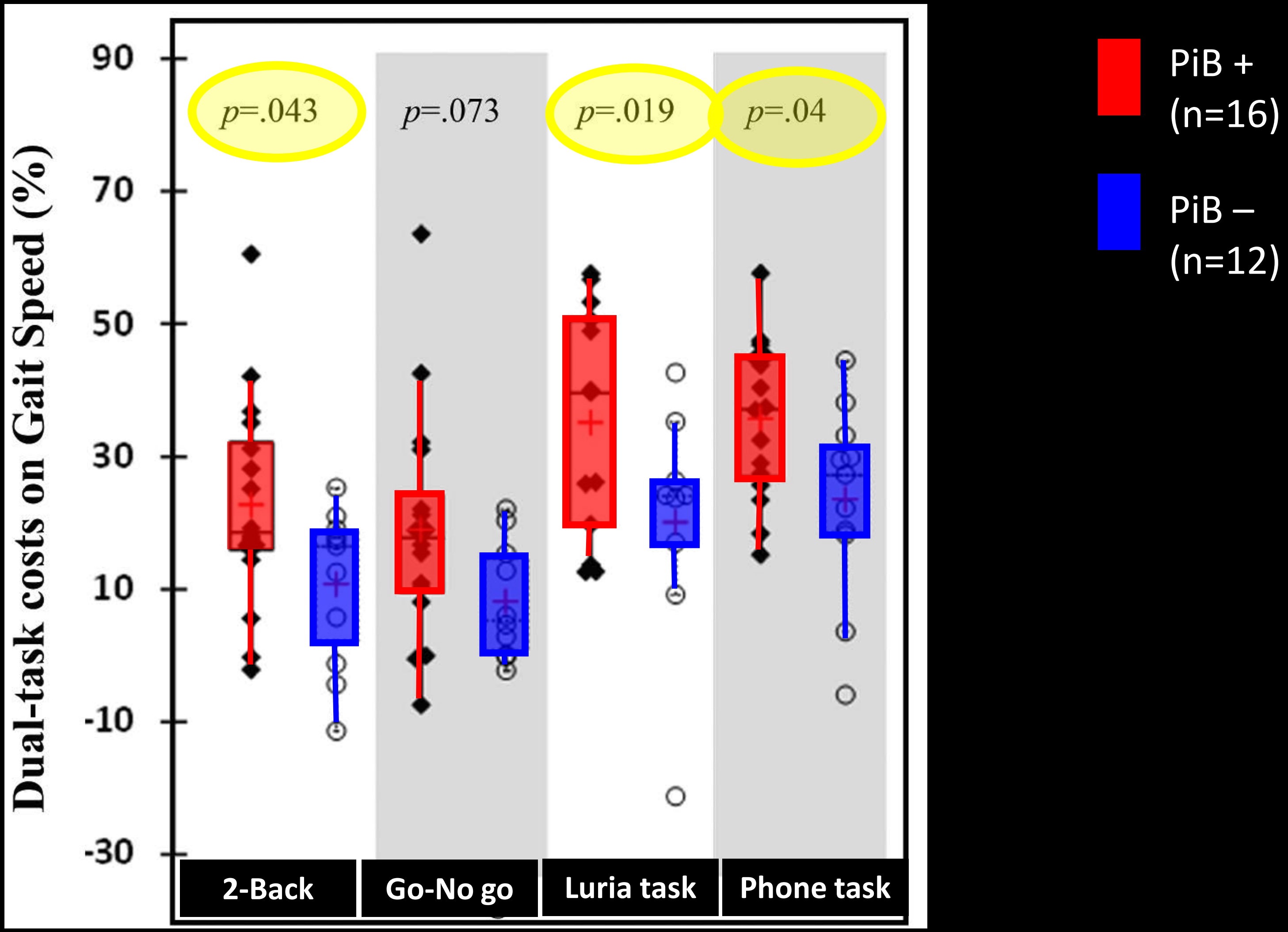
Luria task+ walk
30 sec

Phone task

10-digit entry + walk
One traverse

Amyloid Positivity and Dual-tasking

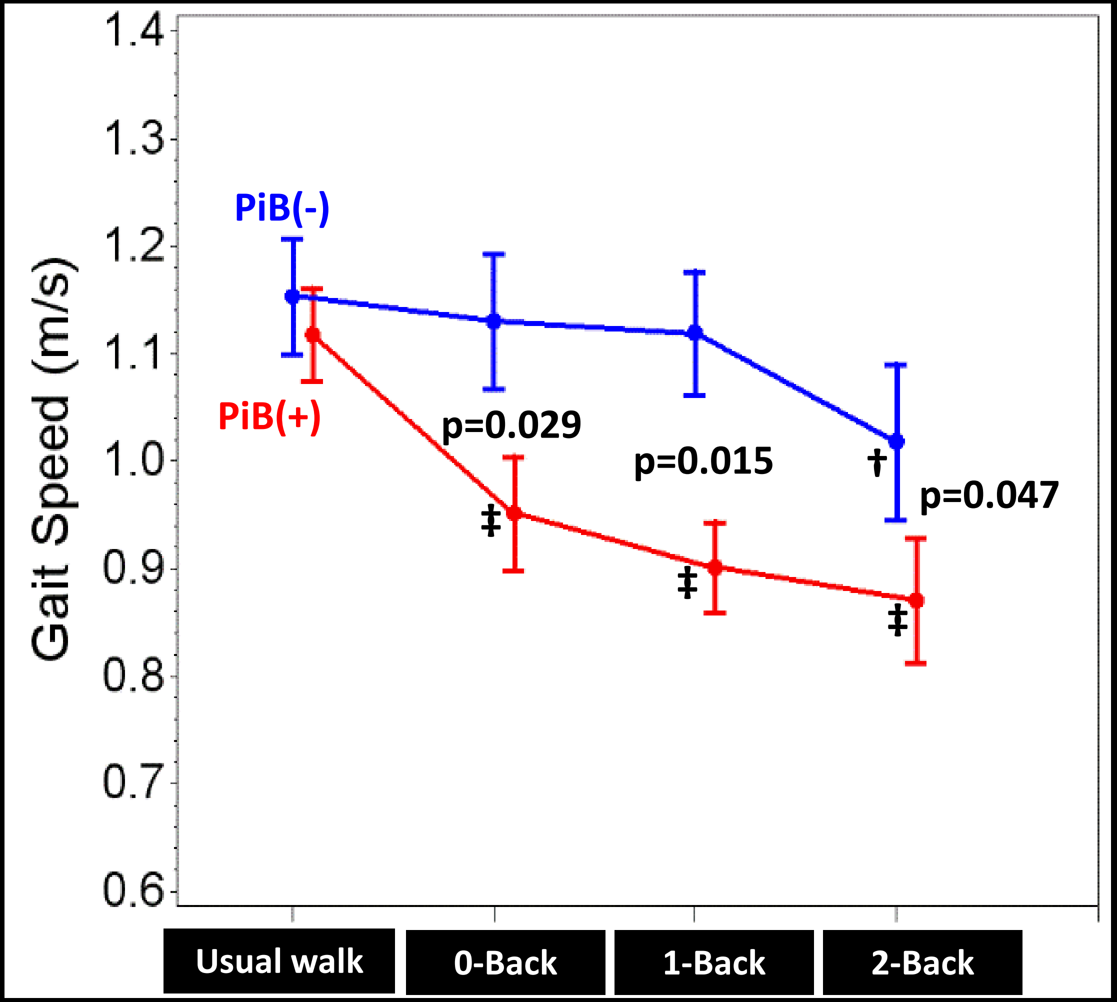
Dual-task cost on Gait speed = (Single task – Dual task / Single task) x 100



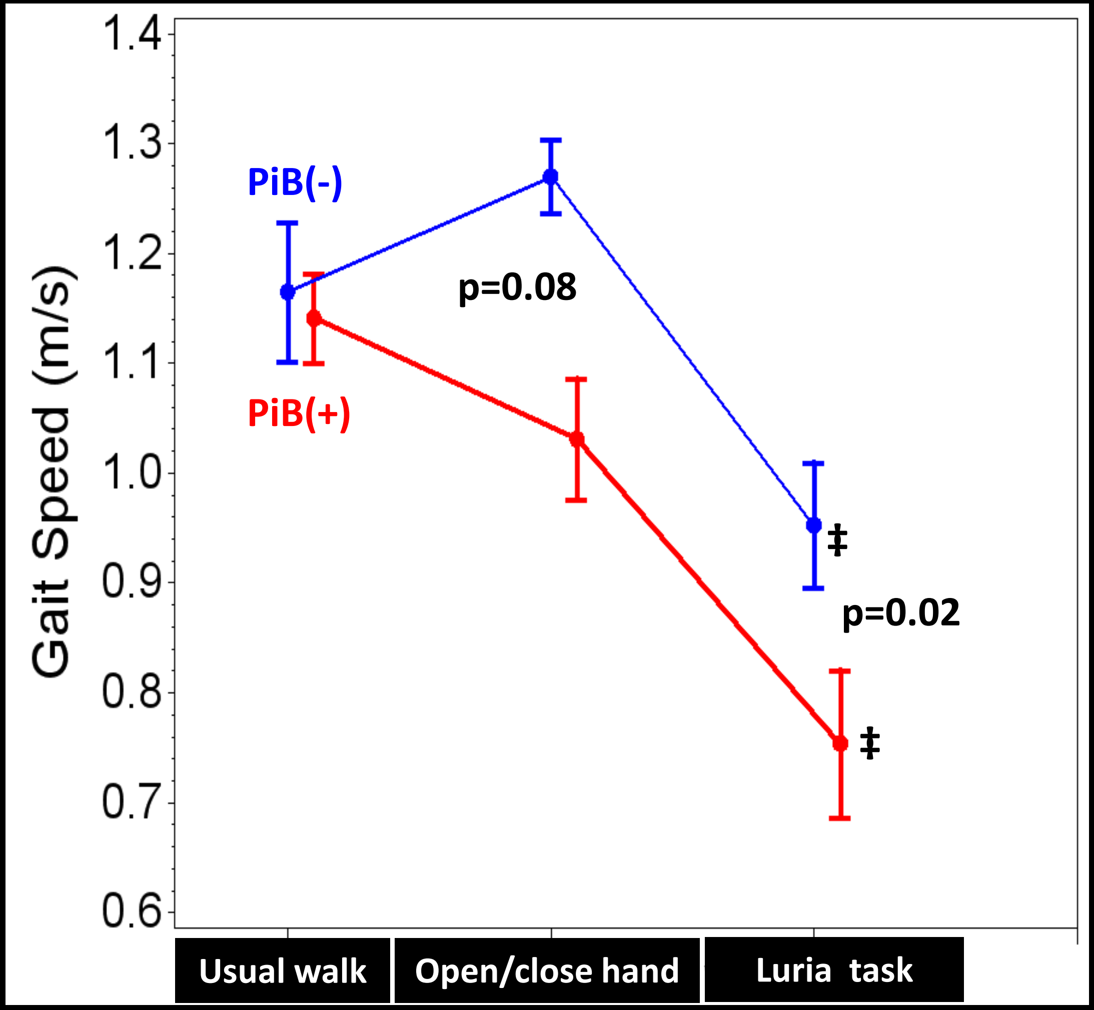
Nadkarni et al. 2017

Amyloid positivity and Dual-task Complexity

Working-memory + Walk



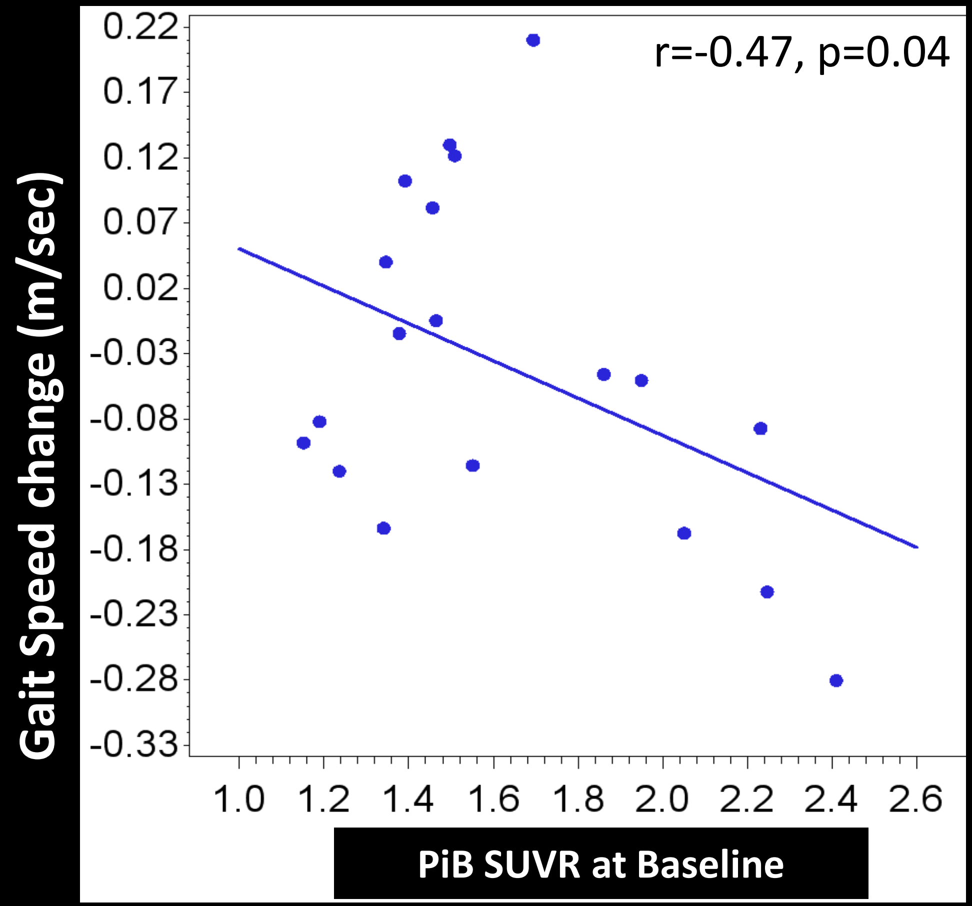
Motor-sequencing + Walk



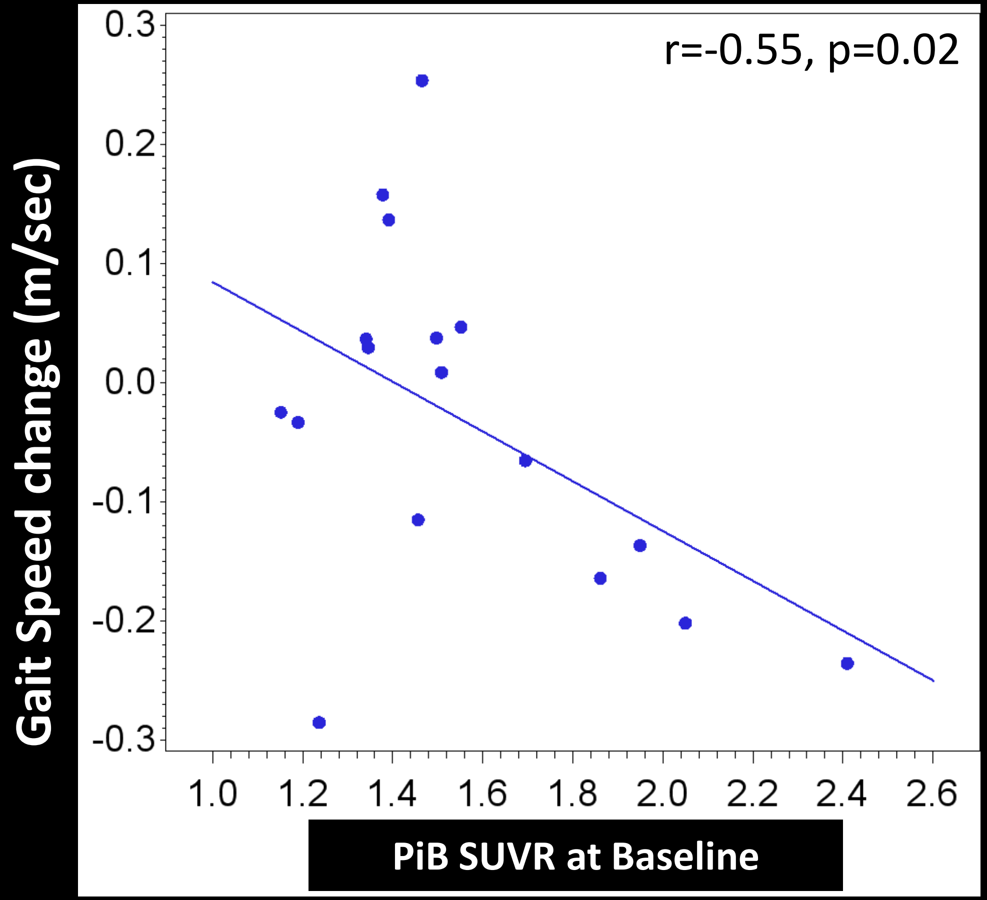
‡ = $p<0.001$, † = $p<0.01$: dual-task gait speed decline within groups

PiB SUVR and 2-yr Change in Dual-task Gait Speed

Phone task + Walk



Motor sequencing + Walk



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TBP: AAIC 2018

Conclusions and Future Directions

Conclusions:

- Amyloid deposition may influence dual-task performance
- Dual-task type matters: working memory and motor sequencing dual-tasks
- Dual-task complexity matters: the key is to strike a right balance

Future directions:

- Dual-tasks determining progression to AD in relation to AD biomarkers
- Dual-tasks determining progression to mobility disability
- Examine the cognition-mobility interface in disorders with parkinsonism

Mentors and Collaborators

- **Oscar Lopez, MD**
- **William Klunk, MD, PhD**
- Robert Sweet, MD
- **Subashan Perera, PhD**
- **Beth Snitz, PhD**
- Chester Mathis, PhD
- Jennifer Lingler, PhD
- **Annie Cohen, PhD**
- Caterina Rosano, MD, MPH
- Anne Newman, MD, MPH
- Robert Boudreau, PhD
- **Jim Becker, PhD**
- **Howard Aizenstein, MD, PhD**
- Stephanie Studenski, MD, MPH
- Kirk Erickson, PhD
- Mark Redfern, PhD
- **Research participants and staff**

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Slides for Q & A……….

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Associations Between Global PiB SUVR and Gait Speed in Dementia-free sample (n=183)

Variable	Unadjusted β (95% CI)	*P* Value	Adjusted β (95% CI)[a]	*P* Value
Global PiB SUVR	−0.086 (−0.146 to −0.027)	.005	−0.068 (−0.127 to −0.008)	.03
Global PiB SUVR and MMSE	−0.073 (−0.132 to −0.013)	.02	−0.057 (−0.115 to −0.002)	.06

[a]Covariates: Age, sex, education, HTN, CHD, stroke, Hipp vol, WMH

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Unadjusted and Adjusted Associations Between Global PiB SUVR and Gait Speed in Cognitively Normal (n=144)

Variable	Unadjusted β (95% CI)	*P* Value	Adjusted β (95% CI)[a]	*P* Value
Global PiB SUVR	−0.072 (−0.140 to −0.003)	.04	−0.074 (−0.145 to −0.003)	.04
Global PiB SUVR and MMSE	−0.059 (−0.126 to 0.008)	.08	−0.055 (−0.124 to 0.013)	.11
Global PiB SUVR and TMT-A	−0.063 (0.131 to 0.005)	.07	−0.068 (−0.14 to 0.004)	.06
Global PiB SUVR and TMT-B	−0.068 (−0.137 to 0.002)	.06	−0.077 (−0.148 to −0.005)	.04
Global PiB SUVR and *APOE* ε4 status	−0.06 (−0.134 to 0.013)	.10	−0.058 (−0.134 to 0.018)	.13

[a] Covariates included in the adjusted model were age, sex, race, educational level, weight, hypertension, coronary heart disease, stroke, and volume of hippocampal and white matter hyperintensities on magnetic resonance imaging normalized to intracranial volume.

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Figure. Association Between Global and Regional Amyloid-β and Gait Speed in the Whole Sample and the Cognitively Normal Subsample

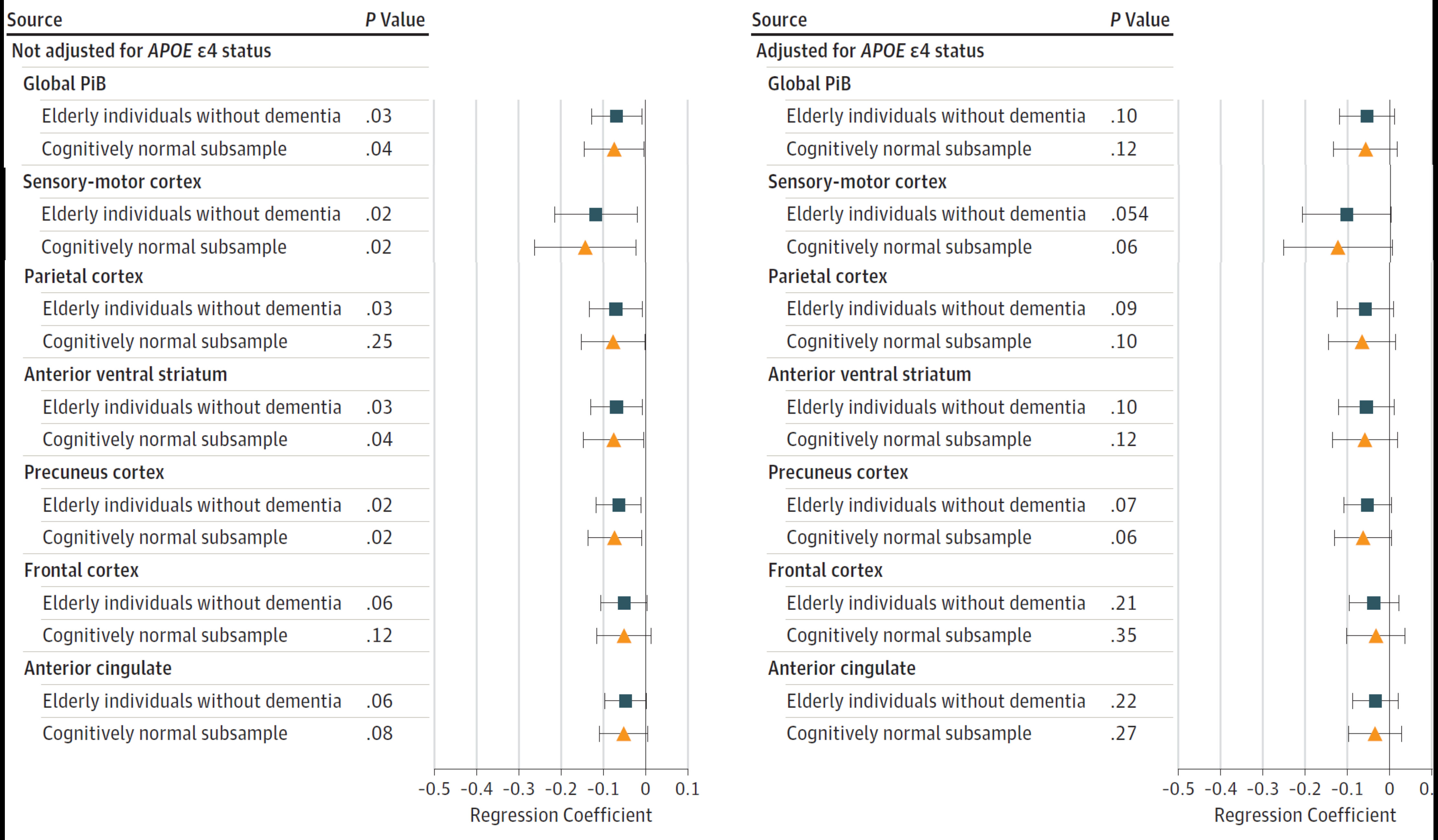

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Table 1. Sample Characteristics of the Whole Sample of Cognitively Normal, Mobility Unimpaired Older Adults and Comparisons Between Groups Divided by PiB Status

	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

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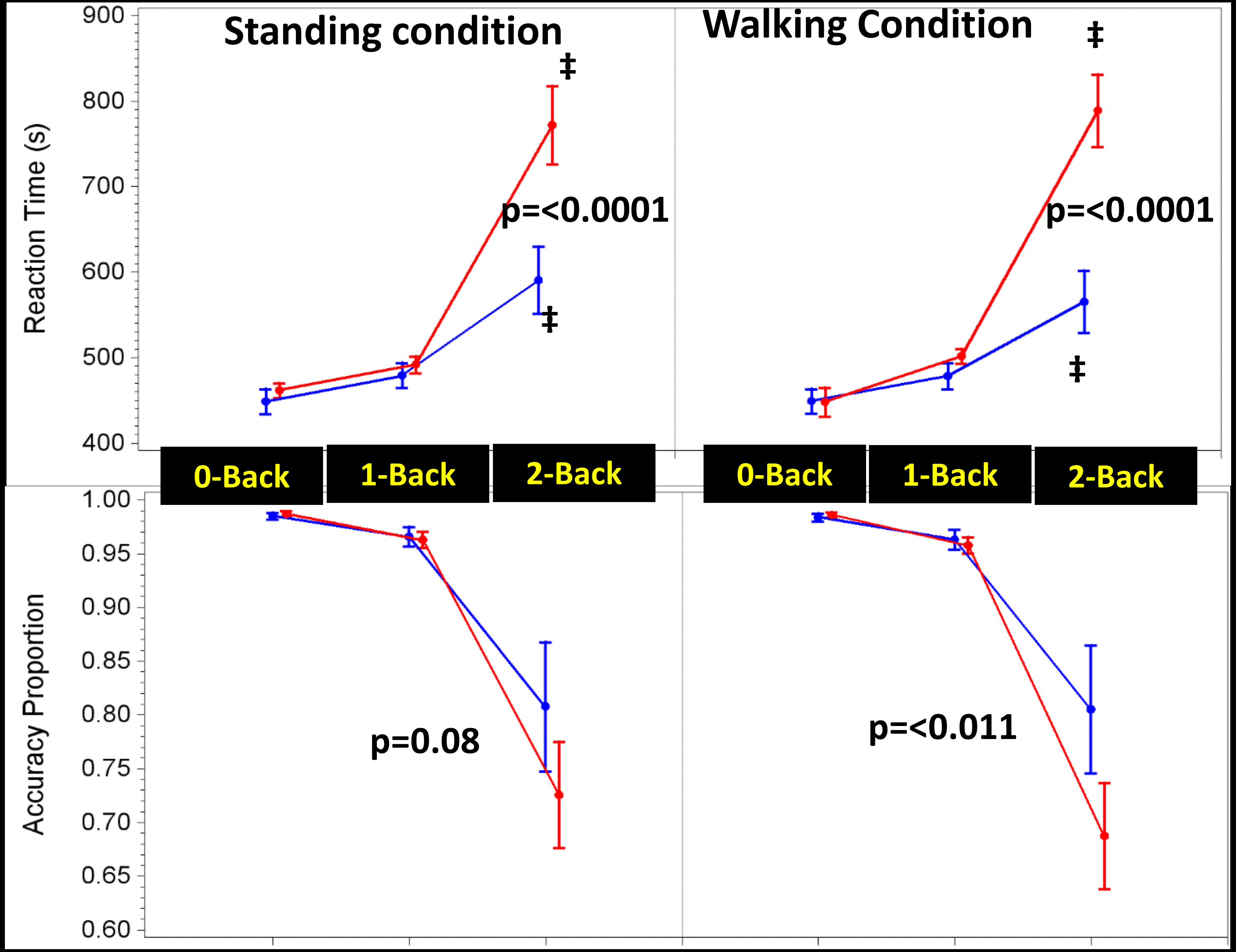
Table 3. Unadjusted and Adjusted Associations Between Cortical PiB Retention (as a continuous variable) and Change in Gait Speed From Single Task. Regression Coefficients Corresponding to 0.1 Unit in PiB From Linear mixed Models ± *SE* (*p* value)

		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.

Cognitive performance and n-back task complexity



‡ = p<0.0001, † = p<0.001: cognitive performance decline within groups c/t 0-back preformance

Impact of Subcortical Hyperintensities on Dual-tasking in Alzheimer Disease and Aging

Neelesh K. Nadkarni, MD, PhD, FRCPC,†‡ Brian Levine, PhD,‡§‖¶# William E. McIlroy, PhD,‡§‖¶** and Sandra E. Black, MD, FRCPC†‡§‖††*

TABLE 1. Baseline Characteristics of Patients With Mild Alzheimer Disease and Normal Controls

	AD (n = 24)	NC (n = 20)	*P*
Age (y)	75 ± 9	72 ± 8	0.16
Sex (female %)	60	47	0.25
Blood pressure (mm Hg)	130 ± 17/70 ± 9	127 ± 16/74 ± 10	0.5/0.2
MMSE score	25 ± 3	29 ± 1	< 0.001
Dementia rating scale (DRS)	122 ± 10	141 ± 2	< 0.001
Body mass index (BMI)	25 ± 5	25 ± 5	0.7
Waist circumference (cm)	94 ± 10	88 ± 18	0.17
Leg length (cm)	92 ± 5	91 ± 7	0.43
UPDRS motor subscore	6 ± 7	3 ± 4	0.056
Tinetti gait score	12 ± 0.6	12 ± 0.4	0.15
Timed-up-go (s)	12 ± 3	9 ± 1	< 0.01
SH score	8 ± 7	6 ± 4	< 0.01
Over-ground gait speed (m/s)	1.02 ± 1.9	1.24 ± 1.6	< 0.001

MMSE indicates Mini-Mental Status Examination; SH score, total score on the ARWMC (Age-related White Matter Change) scale; UPDRS, Unified Parkinson's Disease Rating Scale.

Alzheimer Dis Assoc Disord 2012;26:28–35

ORIGINAL ARTICLE

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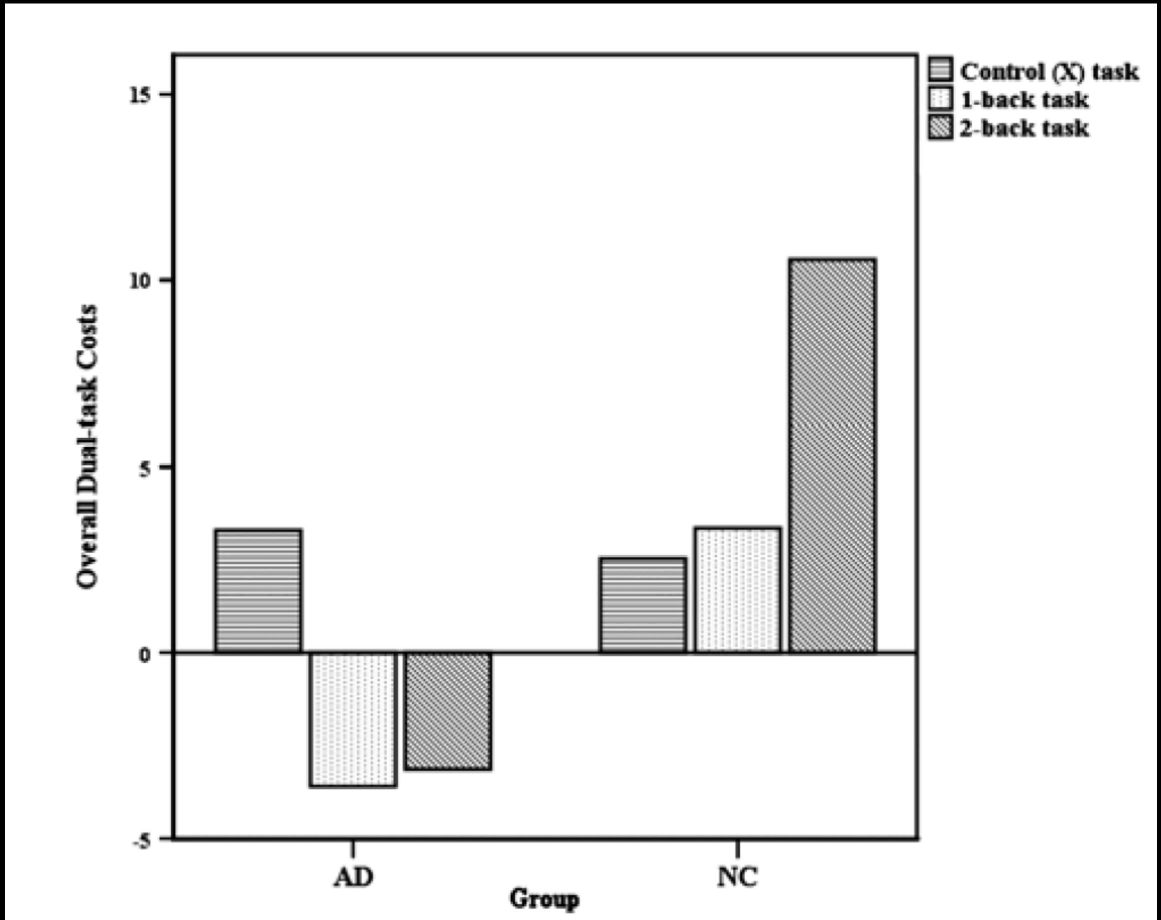

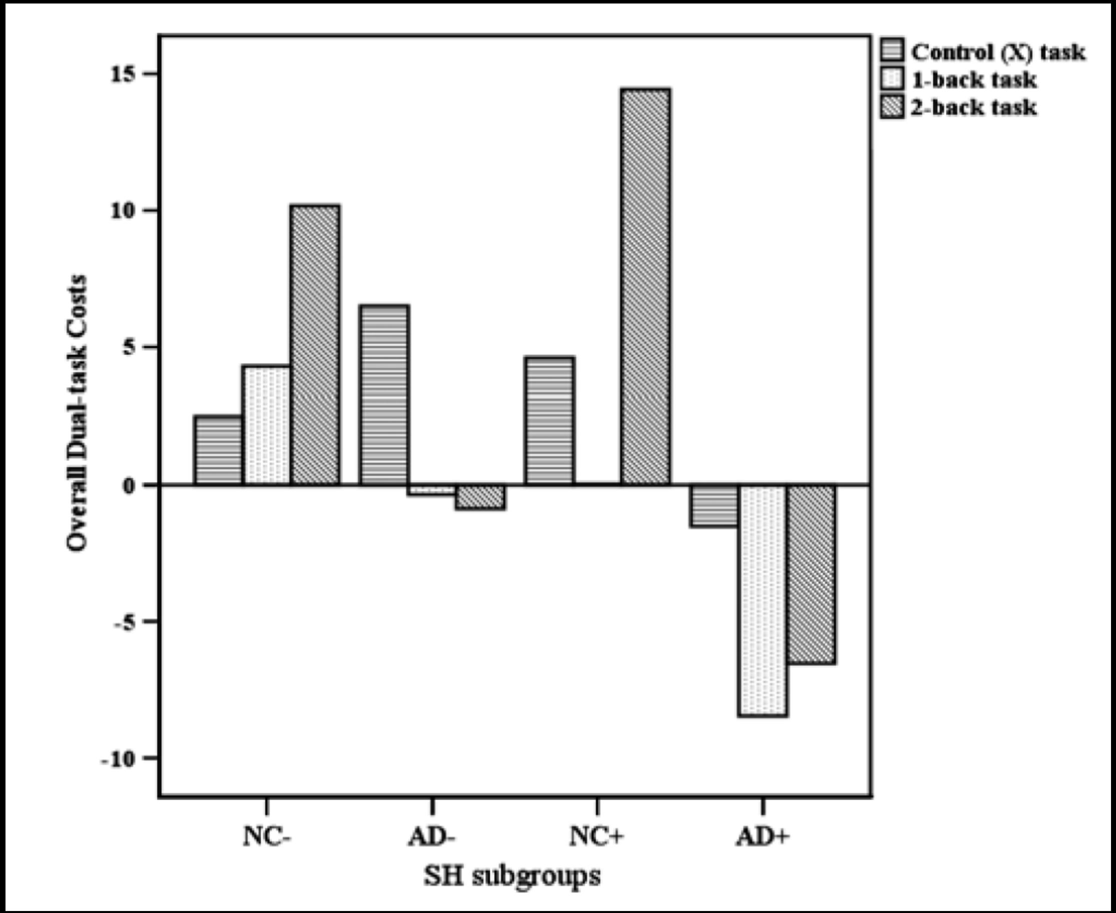

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