

**Supplemental Table 1.** Association of walking intercept and slope with year 10 variables.

Outcome (measured at year 10)	Walking Intercept		Walking Slope	
	Estimate (SE)	P value	Estimate (SE)	P value
<i>Hippocampus</i>				
Volume (cm <sup>3</sup> )	-0.001 (0.09)	.993	-0.007 (0.09)	.938
Mean diffusivity (10 <sup>-3</sup> mm <sup>2</sup> /s)	-0.02 (0.02)	.306	0.01 (0.02)	.534
<i>Global brain measures</i>				
GM volume (cm <sup>3</sup> )	-0.68 (3.52)	.846	-2.37 (3.53)	.502
GM mean diffusivity (10 <sup>-3</sup> mm <sup>2</sup> /s)	-.0002 (.005)	.954	0.001 (0.005)	.750
WM fractional anisotropy	-0.01 (0.01)	.215	0.004 (0.01)	.694
WM radial diffusivity (10 <sup>-3</sup> mm <sup>2</sup> /s)	0.002 (0.003)	.571	0.001 (0.003)	.734
WM axial diffusivity (10 <sup>-3</sup> mm <sup>2</sup> /s)	-0.002 (0.003)	.525	0.002 (0.003)	.506
WM hyperintensities <sup>1</sup>	0.06 (0.47)	.900	-0.47 (0.47)	.322
<i>Cognition</i>				
Modified Mini-Mental State Examination	0.01 (0.44)	.979	-0.09 (0.44)	.830

*Notes.* Adjusted for intracranial volume (volume and mean diffusivity measures only), age, gender, race, education, and APOE ε4 carrier status.

<sup>1</sup>Log-transformed.

GM = gray matter. WM = white matter.

**Supplemental Table 2.** Comparison of the study sample to the parent HABC sample and to participants with baseline MRI only.

	Study sample (n = 141)	Remaining HABC sample (n = 2934)	P value <sup>1</sup>
Baseline age, <i>M</i> (SD)	72.4 (2.4)	73.7 (2.9)	<.001
Sex, female, n (%)	84 (60%)	1422 (52%)	.08
Race, black, n (%)	59 (42%)	1080 (39%)	.60
Education, > high school, n (%)	72 (51%)	1184 (43%)	.06
Body mass index, <i>M</i> (SD)	27.5 (4.4)	27.4 (4.9)	.74
Cerebrovascular disease, n (%)	7 (5%)	203 (7%)	.36
Diabetes, n (%)	12 (9%)	415 (15%)	.04
Modified mini-mental examination, <i>M</i> (SD)	92.5 (6.4)	90.3 (7.5)	<.001
Gait speed, <i>M</i> (SD)	1.3 (0.2)	1.2 (0.2)	<.001
Current or former smoker, n (%)	69 (49%)	1559 (57%)	
Alcohol consumption, once or more per week, n (%)	54 (38%)	802 (29%)	.02
Walking intercept, <i>M</i> (SD)	3.3 (1.6)	2.8 (1.6)	<.001
Walking slope, <i>M</i> (SD)	-0.09 (0.11)	-0.12 (0.11)	.05
Alive at year 10	141 (100%)	2195 (75%)	n/a

  

	Study sample (n = 141)	Remaining MRI sample (n = 172)	P value <sup>1</sup>
Baseline age, <i>M</i> (SD)	72.4 (2.4)	73.4 (2.9)	.002
Sex, female, n (%)	84 (60%)	95 (56%)	.63
Race, black, n (%)	59 (42%)	65 (38%)	.62
Education, > high school, n (%)	72 (51%)	87 (52%)	.90
Body mass index, <i>M</i> (SD)	27.5 (4.4)	27.2 (4.7)	.51
Cerebrovascular disease, n (%)	7 (5%)	5 (3%)	.54
Diabetes, n (%)	12 (9%)	23 (14%)	.22
Modified mini-mental examination, <i>M</i> (SD)	92.5 (6.4)	91.9 (6.3)	.41
Gait speed, <i>M</i> (SD)	1.3 (0.2)	1.3 (0.3)	.58
Current or former smoker, n (%)	69 (49%)	79 (47%)	.15
Alcohol consumption, once or more per week, n (%)	54 (38%)	47 (28%)	.05
Walking intercept, <i>M</i> (SD)	3.3 (1.6)	3.3 (1.5)	.99
Walking slope, <i>M</i> (SD)	-0.09 (0.11)	-0.12 (0.11)	.15
Alive at year 13, n (%)	141 (100%)	134 (78%)	n/a

<sup>1</sup>Determined from Welch two sample t-test for continuous measures or chi squared tests for categorical measures.

**Supplemental Table 3.** Descriptive statistics for self-reported time spent walking at each time point.

Time point	Mean (SD)	Median (25 <sup>th</sup> , 75 <sup>th</sup> percentiles)	Median assessment date (and range)
Year 1	188.6 (447.0)	45 (0, 181.25)	December 11, 1997 (April 28, 1997 – June 22, 1998)
Year 2	161.3 (241.9)	90 (0, 210.0)	January 21, 1999 (February 24, 1998 – June 17, 1999)
Year 3	128.3 (208.4)	60 (0, 175)	January 19, 2000 (July 6, 1999 – September 25, 2000)
Year 4	135.9 (382.4)	60 (0, 142.5)	January 2, 2001 (July 5, 2000 – December 8, 2001)
Year 5	116.7 (179.0)	60 (0, 140.0)	December 14, 2001 (June 20, 2001 – June 20, 2002)
Year 6	78.7 (127.1)	30 (0, 120.0)	November 21, 2002 (June 5, 2002 – May 20, 2003)
Year 7	103.7 (281.2)	30 (0, 116.0)	November 12, 2003 (May 1, 2003 – June 4, 2004)
Year 8	97.0 (184.8)	30 (0, 140.0)	January 20, 2005 (July 30, 2004 – May 31, 2005)
Year 9	117.8 (207.4)	40 (0, 120.0)	December 13, 2005 (July 11, 2005 – May 2, 2006)
Year 10	86.1 (121.2)	45 (0, 105.0)	November 21, 2006 (June 7, 2006 – June 5, 2007)

**Supplement Table 4.** Correlation of Walking Intercept and Slope Scores with Sample Characteristics.

	Walking Intercept	Walking Slope
<b>Demographics</b>		
Age	.17*	-.11
Sex, female	.03	-.05
Race, black	-.12	-.04
Education	.13	-.07
Body mass index	-.07	.04
<b>Chronic disease conditions at first MRI</b>		
Cardiovascular disease	.01	-.10
Stroke	.05	-.13
Diabetes	-.05	-.03
APOE ε4 carrier	-.19**	.11
Gait speed at first MRI	.05	.21*
<b>Health behavior at first MRI</b>		
Current or former smoker	.01	.05
Current or former alcohol drinker	.03	.11
Systolic blood pressure at first MRI	-.12	-.005
Use of medications for hypertension	-.05	-.06

*Notes.* For continuous variables, Pearson correlations were calculated; for categorical variables, Kendall correlations were calculated. \* $p < .05$ ; \*\* $p < .01$

**Supplemental Table 5.** Summary of primary analyses with individuals with chronic stroke excluded

Outcome	Adjusted for demographic factors and genetic risk for cognitive decline <sup>1</sup>				Further adjusted for physical health at year 10 <sup>2</sup>			
	Walking Intercept		Walking Slope		Walking Intercept		Walking Slope	
	Estimate (SE)	P value	Estimate (SE)	P value	Estimate (SE)	P value	Estimate (SE)	P value
<i>Hippocampus</i>								
Volume (cm <sup>3</sup> )	0.09 (0.08)	.256	0.19 (0.08)	.016	0.03 (0.09)	.745	0.21 (0.09)	.017
Mean diffusivity (10 <sup>-3</sup> mm <sup>2</sup> /s)	.008 (.009)	.357	-.005 (.009)	.570	.007 (.009)	.414	-.005 (.009)	.524
<i>Global brain measures</i>								
GM volume (cm <sup>3</sup> )	0.18 (2.24)	.934	4.85 (2.19)	.027	0.57 (2.39)	.810	6.49 (2.32)	.005
GM mean diffusivity (10 <sup>-3</sup> mm <sup>2</sup> /s)	.001 (.003)	.632	-.008 (0.003)	.006	.002 (.003)	.425	-.005 (.003)	.090
WM fractional anisotropy	.006 (.006)	.385	.005 (.006)	.463	.003 (.006)	.655	.004 (.006)	.535
WM radial diffusivity (10 <sup>-3</sup> mm <sup>2</sup> /s)	.0002 (.002)	.869	-.004 (.002)	.009	.0004 (.002)	.833	-.004 (.002)	.038
WM axial diffusivity (10 <sup>-3</sup> mm <sup>2</sup> /s)	.003 (.002)	.224	-.007 (.002)	<.001	.003 (.002)	.265	-.006 (.002)	.006
WM hyperintensities <sup>3</sup>	0.37 (0.30)	.209	0.20 (0.29)	.504	0.28 (0.31)	.368	0.36 (0.30)	.237
<i>Cognition</i>								

Δ Modified Mini-Mental State Examination	0.30 (0.39)	.439	1.05 (0.37)	.004	0.35 (0.44)	.432	1.07 (0.41)	.009
--	-------------	------	-------------	------	-------------	------	-------------	------

---

<sup>1</sup>Adjusted for intracranial volume (volumetric and mean diffusivity measures only), age, gender, race, education, and APOE ε4 carrier status.

<sup>2</sup>Further adjusted for body mass index, gait speed, chronic disease conditions (diabetes, stroke, cardiovascular disease), health behaviours (smoking and drinking status), systolic blood pressure, and use of hypertensive medications.

GM = gray matter. WM = white matter.

<sup>3</sup>Log-transformed

**Supplemental Table 6.** Association of year 10 walking score (log-transformed) with structural MRI variables

<b>Outcome</b>	<b>Estimate (SE)</b>	<b>P value</b>
<i>Hippocampus</i>		
Δ Volume (cm <sup>3</sup> )	0.11 (0.07)	.142
Δ Mean diffusivity (10 <sup>-3</sup> mm <sup>2</sup> /s)	.003 (.008)	.694
<i>Global brain measures</i>		
Δ GM volume (cm <sup>3</sup> )	0.39 (2.08)	.850
Δ GM mean diffusivity (10 <sup>-3</sup> mm <sup>2</sup> /s)	-.004 (.003)	.132
Δ WM fractional anisotropy	.013 (.006)	.018
Δ WM radial diffusivity (10 <sup>-3</sup> mm <sup>2</sup> /s)	-0.003 (.002)	.071
Δ WM axial diffusivity (10 <sup>-3</sup> mm <sup>2</sup> /s)	-0.001 (0.002)	.765
Δ WM hyperintensities	0.56 (0.30)	.065
<i>Cognition</i>		
Δ Modified Mini-Mental State Examination	0.34 (0.34)	.318

*Notes.* Adjusted for intracranial volume (volumetric and mean diffusivity measures only), age, gender, race, education, and APOE ε4 carrier status.

GM = gray matter. WM = white matter.

**Supplemental Table 7.** Association of walking slope from year 6 to year 10 with changes in outcome variables between year 10 and year 13.

Outcome (measured at year 10)	Walking Slope	
	Estimate (SE)	P value
<i>Hippocampus</i>		
Δ Volume (cm <sup>3</sup> )	0.07 (0.10)	.518
Δ Mean diffusivity (10 <sup>-3</sup> mm <sup>2</sup> /s)	0.004 (0.01)	.750
<i>Global brain measures</i>		
Δ GM volume (cm <sup>3</sup> )	3.03 (2.94)	.303
Δ GM mean diffusivity (10 <sup>-3</sup> mm <sup>2</sup> /s)	-0.008 (0.004)	.031
Δ WM fractional anisotropy	0.02 (0.01)	.028
Δ WM radial diffusivity (10 <sup>-3</sup> mm <sup>2</sup> /s)	-0.003 (0.002)	.146
Δ WM axial diffusivity (10 <sup>-3</sup> mm <sup>2</sup> /s)	-0.003 (0.003)	.327
Δ WM hyperintensities <sup>1</sup>	-0.43 (0.44)	.328
<i>Cognition</i>		
Δ Modified Mini-Mental State Examination	0.17 (0.50)	.729

*Notes.* Adjusted for intracranial volume (volume and mean diffusivity measures only), age, gender, race, education, APOE ε4 carrier status, and walking intercept.

<sup>1</sup>Log-transformed.

GM = gray matter. WM = white matter.



**Supplemental Table 8.** Association of 400-meter walk performance with changes in outcome variables between year 10 and year 13.

Outcome	Predictor			
	400 Meter Intercept		400 Meter Slope	
	Estimate (SE)	P value	Estimate (SE)	P value
<i>Hippocampus</i>				
Δ Volume (cm <sup>3</sup> )	-0.06 (0.09)	.472	-0.10 (0.08)	.230
Δ Mean diffusivity (10 <sup>-3</sup> mm <sup>2</sup> /s)	-0.02 (0.01)	.084	-0.01 (0.01)	.110
<i>Global brain measures</i>				
Δ GM volume (cm <sup>3</sup> )	-2.23 (2.39)	.350	-2.21 (2.31)	.339
Δ GM mean diffusivity	-0.002 (0.003)	.546	0.001 (0.003)	.691
Δ WM fractional anisotropy	0.005 (0.006)	.429	-0.010 (0.006)	.102
Δ WM radial diffusivity (10 <sup>-3</sup> mm <sup>2</sup> /s)	-0.002 (0.002)	.301	0.002 (0.002)	.240
Δ WM axial diffusivity (10 <sup>-3</sup> mm <sup>2</sup> /s)	-0.002 (0.002)	.273	0.003 (0.002)	.224
Δ WM hyperintensities	-0.28 (0.35)	.428	-0.17 (0.34)	.613
<i>Cognition</i>				
Δ Modified Mini-Mental State Examination	0.01 (0.41)	.978	-0.03 (0.37)	.937

*Notes:* Time to walk 400 meters was assessed at years 1, 2, 4, 6, 8, and 10. Higher scores indicate poorer physical performance. Thus, a positive slope would indicate a worsening in performance over 10 years. The correlation between the time spent walking slope and the 400-meter walk slope was modest ( $r = -.13$ ).

Estimates are adjusted for intracranial volume (volumetric and mean diffusivity measures only), age, gender, race, education, and APOE ε4 carrier status.

GM = gray matter. WM = white matter.