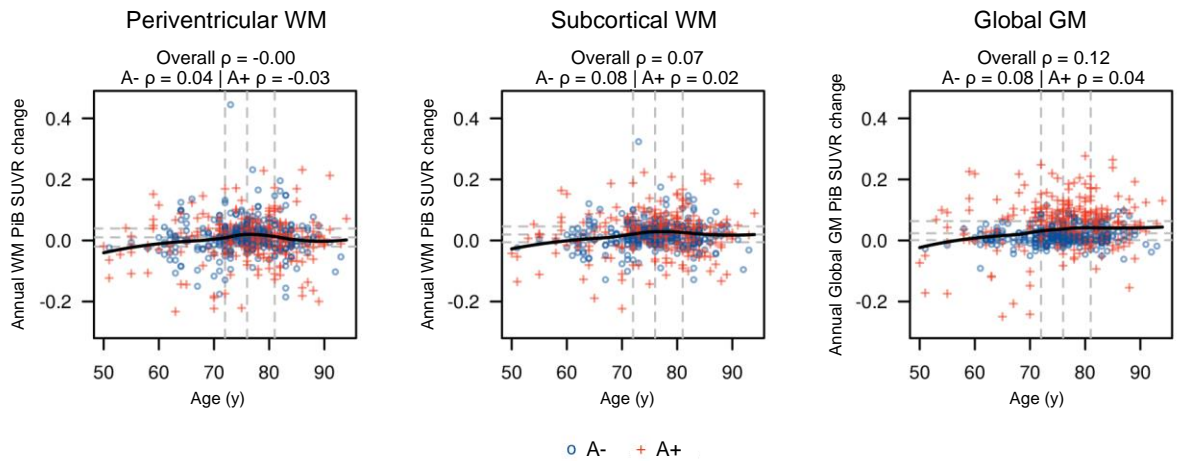


Supplemental Figure 1. Confirming cerebellum reference region atrophy effect.

Assessing cerebellum reference region atrophy effect by applying PVC3 on the cerebellum GM compared to PVC2. A WM age trend is present and the slope is similar between atrophy uncorrected (A, using PVC2) and corrected (B, using PVC3), lending support that the age effect is not due to age-related cerebellar GM atrophy effect.



Supplemental Figure 2. The relationship between within-subject annual change in SUVR and baseline age. The relationship between within-subject annual SUVR change and baseline age had no distanced effect, implying the annual increase rate itself shows minimum age related effect; PV WM ($\rho = -0.00$), SC WM ($\rho = 0.07$), and global GM ($\rho = 0.12$).

Supplemental Table 1. Annual WMPiB SUVR % change in longitudinal data. Mixed effects models on SUVR were fit within each region adjusting for time and baseline age with subject specific intercept and slope. Log transformation on SUVR allows the predictions to be interpreted as approximate annual percentage change. We summarize the model-based mean difference between A- and A+ SUVR (Positive values indicate A+ group increasing faster).

Region		SUVR increase		A- vs A+	
		percent per year (95% CI)	P-value	percent per year (95% CI)	P-value
Periventricular	All	0.6 (0.4, 0.8)	<0.001	-0.3 (-0.7, 0.1)	0.10
	Frontal	0.4 (0.2, 0.6)	<0.001	-0.4 (-0.8, 0.0)	0.06
	Occipital	1.1 (0.9, 1.3)	<0.001	-0.1 (-0.4, 0.3)	0.78
	Parietal	0.4 (0.2, 0.6)	<0.001	-0.5 (-0.9, -0.1)	0.01
	Temporal	0.7 (0.5, 0.9)	<0.001	-0.3 (-0.6, 0.1)	0.76
Subcortical	All	1.3 (1.1, 1.5)	<0.001	0.4 (0.1, 0.7)	0.02
	Frontal	1.2 (1.0, 1.4)	<0.001	0.3 (-0.0, 0.6)	0.09
	Occipital	1.3 (1.2, 1.5)	<0.001	0.5 (0.2, 0.8)	<0.001
	Parietal	1.3 (1.2, 1.5)	<0.001	0.5 (0.1, 0.8)	0.009
	Temporal	1.5 (1.3, 1.6)	<0.001	0.5 (0.2, 0.9)	0.002
Eroded SC		0.9 (0.7, 1.0)	<0.001	-0.2 (-0.5, 0.2)	0.39
Anterior CC		0.4 (0.2, 0.6)	<0.001	-0.5 (-0.9, -0.1)	0.02
Posterior CC		0.3 (0.1, 0.5)	0.007	-0.6 (-1.1, -0.2)	0.003
Brainstem		0.6 (0.5, 0.8)	<0.001	-0.5 (-0.8, -0.2)	0.003
Cerebellum WM		0.9 (0.7, 1.0)	<0.001	-0.3 (-0.7, -0.0)	0.03
Cerebellum GM+WM		0.2 (0.2, 0.3)	<0.001	0 (-0.1, 0.1)	0.82
Composite		0.6 (0.5, 0.8)	<0.001	-0.2 (-0.4, 0.1)	0.20
Global GM-PiB		1.9 (1.7, 2.1)	<0.001	1.8 (1.4, 2.1)	<0.001

Abbreviation: A-, A β negative; A+, A β positive; CC, corpus callosum; CI, confidence interval; GM, gray matter; PiB, ¹¹C-Pittsburgh Compound B; SC, subcortical; SUVR, Standardized uptake value ratio; WM, white matter

Supplemental Table 2. SUVR and SUV linear regression slopes for 10-years in CU cross-sectional data. Summary of slopes of linear regression model on SUVR and SUV adjusting for age and age by abnormal PiB interaction in cross-sectional data are shown with the slope for a 10-year increase in age among CU.

Region	SUVR		SUV	
	slope	rho	slope	rho
Periventricular	0.03	0.19**	0.04	0.17**
PV frontal	0.04	0.19**	0.04	0.17**
PV occipital	0.05	0.30**	0.05	0.23**
PV parietal	0.03	0.16**	0.04	0.15**
PV temporal	0.03	0.20**	0.04	0.17**
Subcortical	0.07	0.37**	0.07	0.28**
SC frontal	0.07	0.37**	0.07	0.29**
SC occipital	0.05	0.35**	0.06	0.26**
SC parietal	0.07	0.36**	0.07	0.28**
SC temporal	0.07	0.36**	0.07	0.28**
Eroded SC WM	0.05	0.27**	0.05	0.22**
Anterior CC	0.05	0.25**	0.05	0.21**
Posterior CC	0.03	0.17**	0.04	0.16**
Brainstem	0.04	0.26**	0.05	0.18**
Cerebellum WM	0.03	0.19**	0.03	0.14**
Cerebellum GM+WM	0.01	0.34**	0.02	0.12**
Cerebellum crus1+crus2 GM	NA	NA	0.01	0.06*
Composite	0.02	0.23**	0.03	0.16**
Global GM-PiB	0.14	0.38**	0.12	0.35**

Abbreviation: CC, corpus callosum; CU, cognitively unimpaired; GM, gray matter; PiB, ¹¹C-Pittsburgh Compound B; PV, periventricular; SC, subcortical; SUV, standardized uptake value; SUVR, standardized uptake value ratio; WM, white matter