Supplementary Materials: The ARIC-PET Study.

Supplementary Methods. Florbetapir PET Image acquisition and processing methods

The scanners utilized in these sites were the Philips TruFlight (Washington County, MD), GE Discovery 690 (Jackson, MS), and GE Discovery ST (Forsyth County, NC). Weekly phantom scans involving ~1mCi of F-18 were conducted, for the course of the study duration, to ascertain spatial uniformity and quantitative accuracy over time. These phantom studies were additionally used to measure the effective resolution of each scanner (via analysis of the edge of phantoms), a more realistic measure than the commonly reported, idealized point-source measurements in air.[1-3]

Given the above-mentioned spatial resolution measurements, all PET images from Washington County, MD and Forsyth County, NC were additionally spatially smoothed to arrive at an effectively equivalent spatial resolution of 8.30 mm for the three sites.

All images were analyzed with PET and MRI at Johns Hopkins University , Section of High Resolution Brain PET imaging , Department of Radiology. Mean images of the 20-min acquisitions were generated from the aligned 4-frame dynamic images. This is consistent with the typical analyses of non dynamic florbetapir PET studies as employed in ADNI 2 and corresponds to an area of steady state between target (amyloid bearing) and reference regions (devoid of amyloid) as determined by dynamic PET studies originally carried out at JHU.[4] All preprocessed mean PET images were then coregistered to the corresponding structural MRI images. The MRI images were normalized to the standard

Montreal Neurologic Institute (MNI) space using the SPM8 and VBM8 toolbox for exponentiated Lie algebra algorithm[5, 6] and the transformation parameters determined by MRI spatial normalization were then applied to the coregistered PET images for PET spatial normalization. A total of 34 regions of interest (ROIs) including cortex, striatum, brainstem, and white matter were manually drawn on the MRI template using the PMOD software (PMOD Technologies Ltd., Zürich, Switzerland) in the standard MNI space. Standard uptake value ratio (SUVR) images relative to the cerebellum were calculated in the MNI space (image volume: 121x145x121, voxel size: 1.5x1.5x15 mm in x, y, z). The ROIs were subsequently applied to the SUVR images.

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Table e-1. Adjusted odds ratios (95% confidence intervals) for global cortex SUVR >1.2 (median) among those with normal cognition (n=240).

	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Age (per 10 years)	2.05 (1.23, 3.44)	1.97 (1.16, 3.33)	1.69 (0.97, 2.94)
Female versus male	1.82 (1.03, 3.18)	1.81 (1.03, 3.18)	1.29 (0.61, 2.72)
Black race versus white race	2.27 (1.30, 3.97)	2.16 (1.22, 3.82)	1.75 (0.94, 3.24)
Education level			
College, graduate, or professional school	1.00 (reference)	1.00 (reference)	1.00 (reference)
High school, GED, or vocational school	0.84 (0.46, 1.51)	0.81 (0.44, 1.47)	0.80 (0.44, 1.46)
< High school	1.01 (0.45, 2.27)	0.98 (0.43, 2.22)	0.88 (0.38, 2.02)
APOE ε4 genotype (per 1 additional ε4 allele)	1.82 (1.05, 3.15)	1.83 (1.05, 3.17)	1.91 (1.09, 3.34)

Model 1: Adjusted for age, sex, race, education, and APOE ε4 genotype
Model 2: Model 1 + hypertension and diabetes
Model 3: Model 2 + white matter hyperintensity volume and total intracranial volume

Table e-2. Adjusted odds ratios (95% confidence intervals) for global cortex SUVR >1.2 (median) among those with mild cognitive impairment (N=89)

	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Age (per 10 years)	1.59 (0.55, 4.58)	1.47 (0.49, 4.35)	1.13 (0.36, 3.63)
Female versus male	1.83 (0.61, 5.51)	1.87 (0.58, 5.98)	1.86 (0.31, 10.97)
Black race versus white race	4.38 (1.34, 14.12)	5.46 (1.47, 20.36)	6.17 (1.57, 24.18)
Education level			
College, graduate, or professional school	1.00 (reference)	1.00 (reference)	1.00 (reference)
High school, GED, or vocational school	1.00 (0.23, 4.38)	0.81 (0.18, 3.61)	0.78 (0.16, 3.64)
< High school	1.20 (0.36, 4.03)	1.39 (0.38, 5.11)	1.55 (0.38, 6.24)
APOE ε4 genotype (per 1 additional ε4 allele)	10.01 (2.52, 39.68)	16.02 (3.50, 73.23)	18.80 (3.88, 90.96)

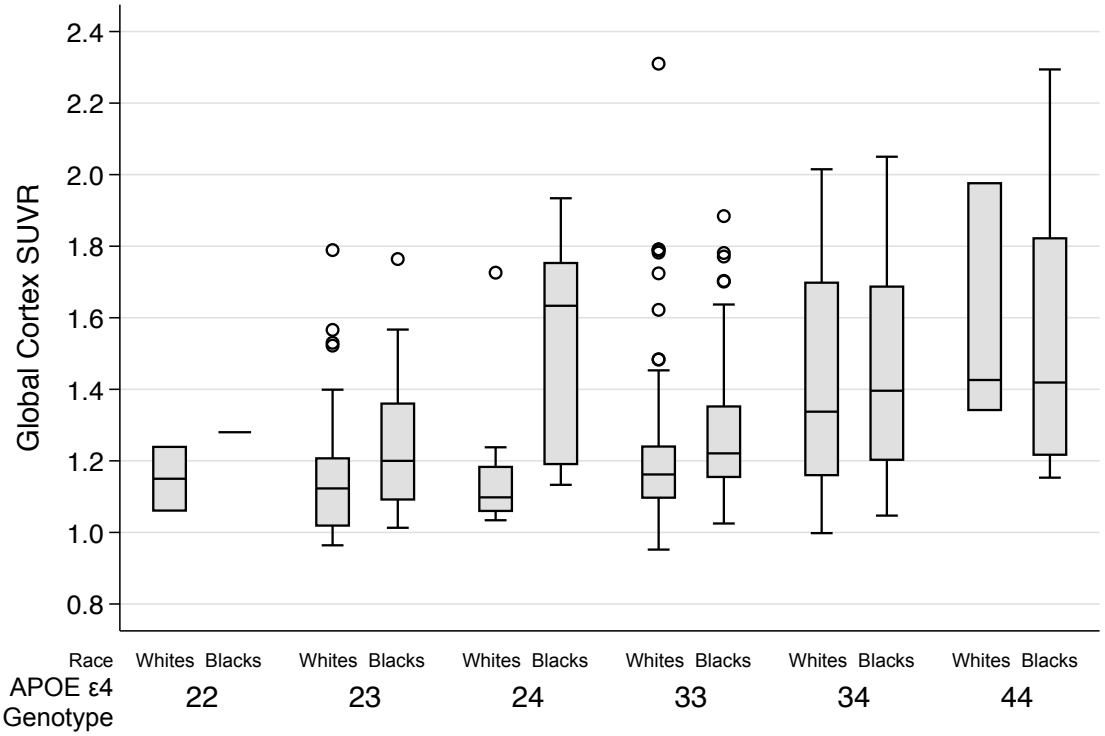
Model 1: Adjusted for age, sex, race, education, and APOE ε4 genotype
Model 2: Model 1 + hypertension and diabetes
Model 3: Model 2 + white matter hyperintensity volume and total intracranial volume

Table e-3. Adjusted odds ratios (95% confidence intervals) for global SUVR >1.1 and for global SUVR >1.11.

	SUVR>1.1 OR (95% CI)	SUVR>1.11 OR (95% CI)
Age (per 10 years)	0.77 (0.44, 1.34)	0.65 (0.38, 1.12)
Female versus male	2.20 (1.00, 4.80)	2.22 (1.03, 4.79)
Black race versus white race	3.35 (1.68, 6.68)	3.22 (1.64, 6.30)
Education level		
College, graduate, or professional school	1.00 (reference)	1.00 (reference)
High school, GED, or vocational school	1.31 (0.71, 2.32)	1.15 (0.63, 2.10)
< High school	1.41 (0.57, 3.51)	1.26 (0.52, 3.05)
APOE ε4 genotype (per 1 additional ε4 allele)	1.67 (0.89, 3.13)	1.53 (0.84, 2.79)

Model 3: Adjusted for age, sex, race, education, APOE ε4 genotype, hypertension, diabetes, white matter hyperintensity volume and estimated total intracranial volume

Figure e-1. Unadjusted box plots of global cortex SUVR by race and APOE ε4 genotype, across all genotypes*.



*Genotypes are listed as the pair of numbers representing the two alleles (e.g. 22 is ε2/ε2; 24 is ε2/ε4).