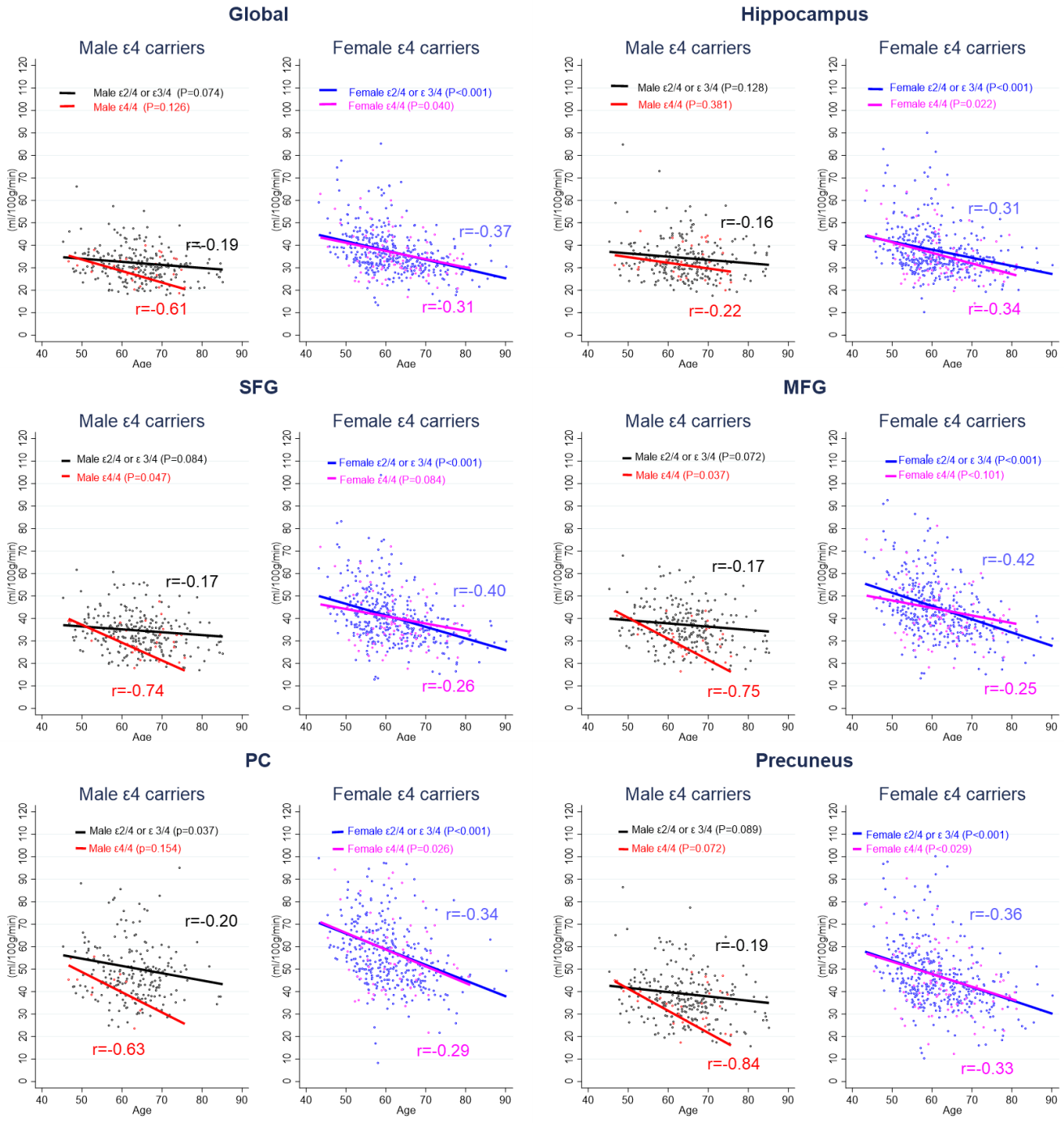
SUPPLEMENTARY MATERIALS



Supplementary Figure 1. Cerebral perfusion trajectories among *APOE* ε4 carriers by sex and *APOE* isoform
SFG=Superior frontal gyrus, MFG=middle frontal gyrus, PC=Posterior cingulate
Notes. There were 132 male ε2/4 or ε3/4 carriers, 225 female ε2/4 or ε3/4 carriers, 22 male ε4/4 carriers, and 46 female ε4/4 carriers.

Supplementary Table 1. Association between age-related cerebral perfusion change and time-varying cardiometabolic measurements

	Gray matter[a]	**Hippocampus**[a]	**Superior frontal gyrus**[a]	**Middle frontal gyrus**[a]	**Posterior cingulate**[a]	**Precuneus**[a]
Systolic blood pressure (n=881)	-0.08 (-0.10, -0.05)**	-0.08 (-0.12, -0.05)**	-0.08 (-0.11, -0.04)**	-0.09 (-0.13, -0.05)**	-0.13 (-0.19, -0.08)**	-0.09 (-0.13, -0.04)**
Body mass index (n=881)	-0.34 (-0.43, -0.25)**	-0.34 (-0.44, -2.06)**	-3.09 (-3.62, -2.56)**	-0.44 (-0.55, -0.32)**	-0.58 (-0.76, -0.41)**	-0.47 (-0.61, -0.34)**
Blood glucose (n=822)	-0.07 (-0.10, -0.04)**	-0.06 (-0.10, -0.03)**	-0.09 (-0.12, -0.05)**	-0.10 (-0.13, -0.06)**	-0.12 (-0.18, -0.06)**	-0.11 (-0.15, -0.07)**
Total cholesterol (n=883)	-1.07 (-1.57, -2.02)**	-0.96 (-1.54, -0.38)**	-1.18 (-1.76, -0.59)**	0.00 (0.00, 0.01)	0.01 (0.00, 0.02)	0.01 (0.00, 0.01)

[a] β-coefficients and 95% confidence intervals in models were adjusted for birth cohort, sex, APOE ε4 status, education, parental history of dementia, smoking status, intracranial volume, post-labeling delay, and head coil.

†$0.05<P<0.1$; *$0.01<P<0.05$; **$P<0.01$.

Supplementary Table 2. Association of cerebral perfusion with age, sex, and *APOE* ε4 status among participants with a 2025 ms post-labeling delay cerebral perfusion (n=876)

	Total Gray matter[a]	**Hippocampus[a]**	**Superior frontal gyrus[a]**	**Middle frontal gyrus[a]**	**Posterior cingulate[a]**	**Precuneus[a]**
Linear model, 5-yrs						
Age, 5-year	-1.11**	-0.98**	-1.32**	-1.54**	-2.46**	-2.14**
	(-1.47, -0.74)	(-1.35, -0.61)	(-1.74, -0.91)	(-2.01, -1.07)	(-3.26, -1.67)	(-2.76, -1.62)
Categorical age						
Age groups						
40-49	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
50-59	-2.84**	-3.00**	-2.80**	-3.01**	-5.76**	-4.95**
	(-4.66, -1.02)	(-5.06, -0.95)	(-4.78, -0.82)	(-5.15, -0.87)	(-9.16, -2.36)	(-7.63, -2.26)
60-69	-3.82**	-3.89**	-4.26**	-4.59**	-7.99**	-7.40**
	(-5.86, -1.78)	(-6.14, -1.63)	(-6.50, -2.01)	(-7.05, -2.13)	(-12.00, -3.99)	(-10.57, -4.23)
≥70	-5.69**	-5.61**	-6.28**	-6.96**	-11.68**	-10.46**
	(-8.09, -3.28)	(-8.20, -3.02)	(-8.99, -3.58)	(-9.96, -3.96)	(-16.66, -6.69)	(-14.43, -6.50)
Annual change rate of cerebral perfusion (Slope)						
Male *APOE non*-ε4	-1.44**	-1.35**	-1.60**	-1.92**	-2.83**	-2.33**
	(-2.07, -0.80)	(-2.02, -0.67)	(-2.30, -0.89)	(-2.71, -1.13)	(-4.19, -1.46)	(-3.39, -1.26)
Male *APOE* ε4	-0.56	-0.35	-0.77†	-0.85†	-1.47	-0.96
	(-1.38, 0.27)	(-1.23, 0.53)	(-1.68, 0.14)	(-1.87, 0.17)	(-3.14, 0.20)	(-2.26, 0.34)
Female *APOE non*-ε4	-1.16**	-1.01**	-1.33**	-1.55**	-2.41**	-2.30**
	(-1.66, -0.67)	(-1.52, -0.49)	(-1.88, -0.77)	(-2.17, -0.93)	(-3.47, -1.35)	(-3.12, -1.47)
Female *APOE* ε4	-1.97**	-1.91**	-2.27**	-2.79**	-4.37**	-4.00**
	(-3.13, -0.81)	(-3.15, -0.67)	(-3.55, -1.00)	(-4.21, -1.36)	(-6.77, -1.98)	(-5.86, -2.13)

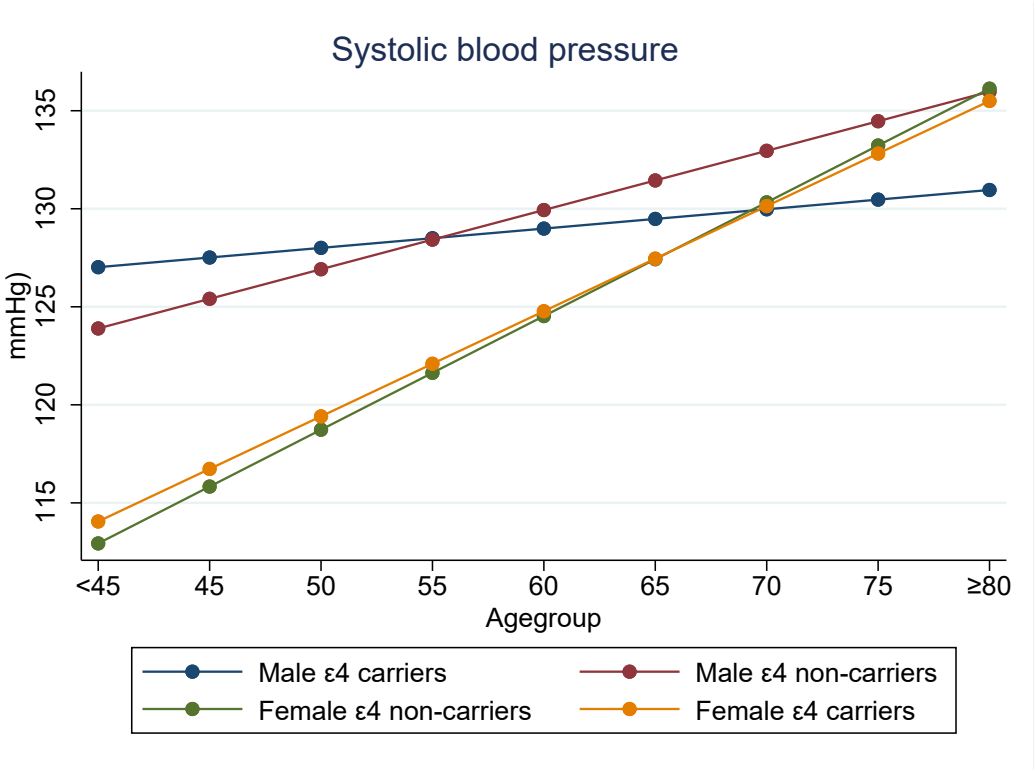
[a]The β-coefficients and 95% confidence intervals in the models were adjusted for birth cohort, sex, *APOE* ε4 status, education, parental history of dementia, smoking status, intracranial volume, and head coil. †0.05<*P*<0.1; *0.01<*P*<0.05; **P<0.01.

Supplementary Table 3. Non-linear associations of cerebral perfusion with age, sex, and *APOE* ε4 (n=950)

	Gray matter[a]	**Hippocampus**[a]	**Superior frontal gyrus**[a]	**Middle frontal gyrus**[a]	**Posterior cingulate**[a]	**Precuneus**[a]
Quadratic model						
Age, year	-1.47**	-1.61**	-1.56**	-1.61**	-2.75**	-2.20**
	(-2.29, -0.66)	(-2.54, -0.67)	(-2.51, -0.60)	(-2.63, -0.59)	(-4.32, -1.18)	(-3.39, -1.00)
Age square	0.01*	0.01*	0.01†	0.01†	0.01*	0.01†
	(0.00, 0.01)	(0.00, 0.02)	(-0.00, 0.01)	(0.00, 0.01)	(0.00, 0.03)	(0.00, 0.02)
Interaction, Sex						
Quadratic model						
Age×Sex	-1.02	-0.48	-1.69†	-1.54	-1.88	-1.73
	(-2.65, 0.60)	(-2.33, 1.36)	(-3.59, 0.22)	(-3.58, 0.49)	(-5.01, 1.25)	(-4.11, 0.65)
Age square ×Sex	0.01	0.00	0.01	0.01	0.01	0.01
	(-0.01, 0.01)	(-0.01, 0.02)	(-0.00, 0.03)	(-0.01, 0.03)	(-0.01, 0.04)	(-0.01, 0.03)
Interaction, *APOE* ε4						
Quadratic model						
Age×ε4	-1.35†	-1.43	-1.37	-1.33	-2.95†	-1.81
	(-2.90, 0.20)	(-3.20, 0.34)	(-3.19, 0.45)	(-3.27, 0.62)	(-5.94, 0.04)	(-4.09, 0.46)
Age square ×ε4	0.01†	0.01	0.01	0.01	0.02*	0.02
	(-0.00, 0.02)	(-0.00, 0.03)	(-0.00, 0.03)	(0.00, 0.03)	(0.00, 0.05)	(0.00, 0.03)

[a] β-coefficients and 95% confidence intervals in models were adjusted for birth cohort, sex, APOE ε4 status, education, parental history of dementia, smoking status, intracranial volume, post-labeling delay, and head coil.

$^{\dagger}0.05<P<0.1$; $^{*}0.01<P<0.05$; $^{**}P<0.01$.



Supplementary Figure 2. The association between systolic blood pressure and age by *APOE* ε4 status and sex (n=876)