Supplementary Material

White Matter Hyperintensity Volume and Amyloid-PET Synergistically Impact Memory Independent of Tau-PET in Older Adults Without Dementia

Supplementary Table 1. Correlation Panel of Model Predictors

		One allele	Two alleles	Sex	Education	Age	Aβ Centiloids	Pulse Pressure	WMH Volume	Braak tau-PET III/IV SUVR
One allele	*Pearson Correlation*	1	**-0.157***	0.044	-0.072	**-0.112***	**0.259***	-0.062	-0.065	**0.104***
	p		<0.001	0.287	0.082	0.006	<0.001	0.135	0.115	0.012
Two alleles	*Pearson Correlation*	**-0.157***	1	0.020	0.017	**-0.100***	**0.176***	-0.040	0.000	**0.154***
	P	<0.001		0.635	0.688	0.015	<0.001	0.329	0.991	<0.001
Sex	*Pearson Correlation*	0.044	0.020	1	**-0.104***	**-0.207***	-0.001	-0.019	-0.008	0.039
	p	0.287	0.635		0.012	<0.001	0.985	0.649	0.846	0.345
Education	*Pearson Correlation*	-0.072	0.017	**-0.104***	1	0.058	-0.056	**-0.087***	-0.066	-0.009
	p	0.082	0.688	0.012		0.159	0.177	0.034	0.113	0.824
Age	*Pearson Correlation*	**-0.112***	**-0.100***	**-0.207***	0.058	1	**0.149***	**0.284***	**0.452***	**0.090***
	p	0.006	0.015	<0.001	0.159		<0.001	<0.001	<0.001	0.029
Aβ Centiloids	*Pearson Correlation*	**0.259***	**0.176***	-0.001	-0.056	**0.149***	1	0.001	**0.126***	**0.475***
	p	<0.001	<0.001	0.985	0.177	<0.001		0.977	0.002	<0.001
Pulse Pressure	*Pearson Correlation*	-0.062	-0.040	-0.019	**-0.087***	**0.284***	0.001	1	**0.155***	0.016
	p	0.135	0.329	0.649	0.034	<0.001	0.977		<0.001	0.691
WMH Volume	*Pearson Correlation*	-0.065	0.000	-0.008	-0.066	0.**452***	**0.126***	**0.155***	1	**0.131***
	p	0.115	0.991	0.846	0.113	<0.001	0.002	<0.001		0.001
Braak tau-PET III/IV SUVR	*Pearson Correlation*	**0.104***	**0.154***	0.039	-0.009	**0.090***	**0.475***	0.016	**0.131***	1
	p	0.012	<0.001	0.345	0.824	0.029	<0.001	0.691	0.001	

The * symbol signifies that the correlation is significant (p<0.05).

Sensitivity Analyses: Including Hippocampal Volume as an Additional Predictor

When adding hippocampal volume as an additional predictor to the primary models, all findings were qualitatively similar. There remained no significant interaction between either the linear or quadratic effect of WMH and centiloids on ADNI EF (Supplementary Table 2). However, we continued to find a significant interaction between the quadratic effect of WMH and centiloids on ADNI MEM ($p=0.038$) (Supplementary Table 2). Simple slopes (SS) continued to suggest that greater Aβ burden is significantly associated with poorer executive function at average ($p=0.005$) and higher (+1 SD; $p=0.015$) levels of WMH burden, but not at low (-1 SD; $p=0.522$) levels of WMH burden. There remained no significant interaction between either the linear or quadratic effect of WMH and Braak III/IV Tau PET on ADNI MEM nor ADNI EF (Supplementary Table 3). These results suggest that the interactive effects of amyloid and white matter hyperintensity volume on memory remain, independent of hippocampal volume.

Supplementary Table 2. Model parameters of the Aβ centiloids by WMH volume interactions, controlling additionally for hippocampal volume

	Executive Function [n=581]			**Memory** [n=584]		
	Estimate	**SE**	***p***	**Estimate**	**SE**	***p***
(Intercept)	0.016	0.064	0.803	-0.233	0.061	**<0.001**
Age	-0.235	0.044	**<0 .001**	-0.052	0.043	0.219
Sex						
Male	-	-	-	-	-	-
Female	0.170	0.075	**0.023**	0.572	0.071	**<0.001**
Education	0.210	0.036	**<0.001**	0.237	0.034	**<0.001**
APOE ε4						
0 alleles	-	-	-	-	-	-
1 allele	0.046	0.083	0.580	0.003	0.078	0.972
2 alleles	-0.566	0.168	**<0.001**	-0.448	0.158	**0.005**
Pulse pressure	-0.020	0.037	0.581	-0.019	0.035	0.593
Hippocampal Volume	0.029	0.039	0.455	0.151	0.037	**<0.001**
Braak III/IV tau-PET SUVR	-0.219	0.041	**<0.001**	-0.230	0.039	**<0.001**
Aβ Centiloids	-0.063	0.051	0.214	-0.137	0.048	**0.005**
WMH volume (linear)	-0.150	0.043	**<0.001**	-0.158	0.041	**<0.001**
WMH volume (quadratic)	-0.083	0.024	**<0.001**	-0.048	0.022	**0.034**
Aβ Centiloids by WMH volume (linear)	-0.072	0.039	0.067	-0.042	0.036	0.249
Aβ Centiloids by WMH volume (quadratic)	0.012	0.029	0.690	0.056	0.027	**0.038**

PET, positron emission tomography; SUVR, standardized uptake value ratio; WMH, white matter hyperintensity.

Supplementary Table 3. Model parameters of the tau-PET by WMH volume interactions, controlling additionally for hippocampal volume

	Executive Function [n=582]			**Memory** [n=583]		
	Estimate	**SE**	***p***	**Estimate**	**SE**	***p***
(Intercept)	-0.007	0.065	0.909	-0.247	0.061	**<0.001**
Age	-0.238	0.045	**<0.001**	-0.045	0.042	0.293
Sex						
Male	-	-	-			
Female	0.184	0.075	**0.014**	0.575	0.071	**<0.001**
Education	0.209	0.036	**<0.001**	0.229	0.034	**<0.001**
APOE ε4						
0 alleles	-	-	-			
1 allele	0.049	0.083	0.557	0.002	0.078	0.976
2 alleles	-0.507	0.167	**0.002**	-0.399	0.158	**0.012**
Pulse pressure	-0.019	0.037	0.604	-0.036	0.035	0.310
Hippocampal Volume	0.031	0.039	0.430	0.150	0.037	**<0.001**
Aβ Centiloids	-0.065	0.043	0.125	-0.090	0.040	**0.026**
Braak III/IV tau-PET SUVR	-0.221	0.048	**<0.001**	-0.286	0.044	**<0.001**
WMH volume (linear)	-0.155	0.043	**<0.001**	-0.157	0.041	**<0.001**
WMH volume (quadratic)	-0.075	0.025	**0.002**	-0.044	0.023	0.058
Tau-PET by WMH volume (linear)	-0.029	0.046	0.523	0.054	0.046	0.235
Tau-PET by WMH volume (quadratic)	0.010	0.035	0.763	0.050	0.035	0.153

PET, positron emission tomography; SUVR, standardized uptake value ratio; WMH, white matter hyperintensity.