Supplementary Material

PATTERNS OF WHITE MATTER HYPERINTENSITIES ASSOCIATED WITH COGNITION IN MIDDLE-AGED COGNITIVELY HEALTHY INDIVIDUALS

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Table S1. Correlation between global WMH load and cognition

	Rho [95% CI]	*p*
Cognitive z-score composites		
Memory	-0.07 [-0.151 - 0.012]	0.04
Executive Function	-0.07 [-0.151 - 0.012]	0.04
Memory Binding Test		
Total Free Recall	-0.05 [-0.132 - 0.033]	0.12
Total Delayed Free Recall	-0.07 [-0.151 - 0.012]	0.05
Total Paired Recall	-0.05 [-0.132 - 0.033]	0.13
Total Delayed Paired Recall	-0.07 [-0.151 - 0.012]	0.04
Paired Recall Pairs	-0.06 [-0.142 - 0.022]	0.07
Pairs in Delayed Free Recall	-0.08 [-0.161 – 0.002]	0.02
Semantic Proactive Interference	-0.08 [-0.161 – 0.002]	0.02
Subtests of WAIS-IV		
Digit Span Forward	-0.01[-0.092 – 0.072]	0.43
Digit Span Backward	-0.09 [-0.171 - -0.008]	0.01
Digit Span Sequencing	0.03 [-0.052 - 0.112]	0.28
Coding	-0.06 [-0.142 - 0.022]	0.09
Visual Puzzles	-0.01 [-0.092 - 0.072]	0.39
Matrix Reasoning	-0.05 [-0.132 - 0.033]	0.12
Similarities	-0.06 [-0.142 - 0.022]	0.07

Adjusted by age, education, sex, number of APOE-ε4 alleles and MTA.
WMH also adjusted by TIV.

Table S1. Correlation between global WMH load and cognition correcting by age, education, sex, number of APOE-ε4 alleles, TIV and MTA. Abbreviations: TIV, total intracranial volume; MTA, medial temporal atrophy.
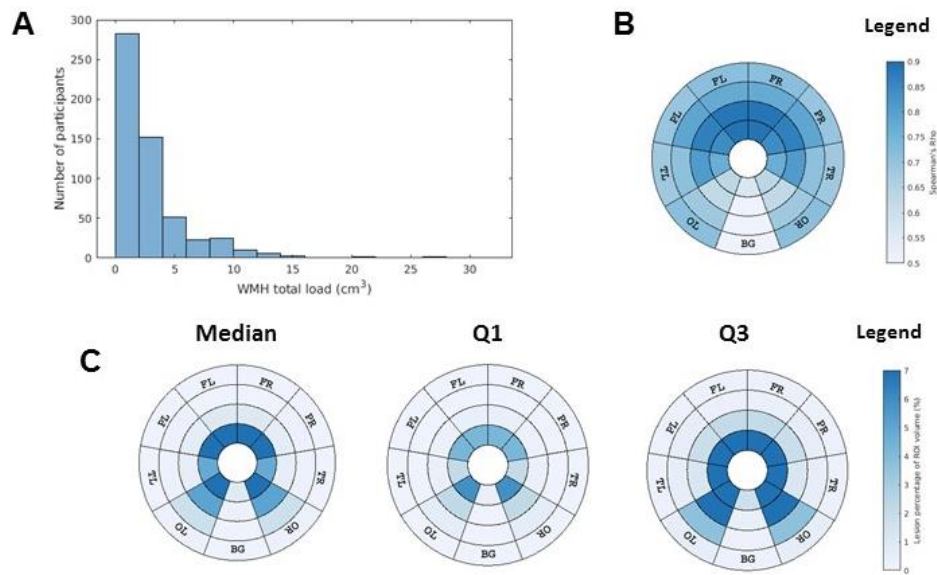
Table S2. Correlation between global WMH load and cognition		
	Rho [95% CI]	***p***
Cognitive z-score composites		
Memory	-0.07 [-0.151 – 0.012]	0.04
Executive Function	-0.07 [-0.151 - 0.012]	0.05
Memory Binding Test		
Total Free Recall	-0.05 [-0.132 - 0.033]	0.11
Total Delayed Free Recall	-0.07 [-0.151 - 0.012]	0.04
Total Paired Recall	-0.05 [-0.132 - 0.033]	0.13
Total Delayed Paired Recall	-0.07 [-0.151 – 0.102]	0.03
Paired Recall Pairs	-0.06 [-0.142 - 0.022]	0.06
Pairs in Delayed Free Recall	-0.09 [-0.171 - -0.008]	0.02
Semantic Proactive Interference	-0.08 [-0.161 – 0.002]	0.03
Subtests of WAIS-IV		
Digit Span Forward	-0.01[-0.092 – 0.072]	0.40
Digit Span Backward	-0.09 [-0.171 - -0.008]	0.02
Digit Span Sequencing	0.04 [-0.042 - 0.122]	0.21
Coding	-0.06 [-0.142 - 0.022]	0.08
Visual Puzzles	-0.01 [-0.092 - 0.072]	0.38
Matrix Reasoning	-0.05 [-0.132 - 0.033]	0.13
Similarities	-0.05 [-0.132 - 0.033]	0.13
Adjusted by age, education, sex, number of APOE-ε4 alleles and CAIDE risk score. WMH also adjusted by TIV.		

Table S2. Correlation between global WMH load and cognition correcting by age, education, sex, number of APOE-ε4 alleles, TIV and CAIDE. Abbreviations: TIV, total intracranial volume; CAIDE, Cardiovascular Risk Factors, Aging, and Incidence of Dementia.

**Table S3. Correlation between global WMH load and cognition**

	Rho [95% CI]	*p*
Cognitive z-score composites		
Memory	-0.08 [-0.161 – 0.002]	0.03
Executive Function	-0.07 [-0.151 - 0.012]	0.05
Memory Binding Test		
Total Free Recall	-0.05 [-0.132 - 0.033]	0.11
Total Delayed Free Recall	-0.07 [-0.151 - 0.012]	0.05
Total Paired Recall	-0.06 [-0.142 - 0.022]	0.09
Total Delayed Paired Recall	-0.08 [-0.161 – 0.002]	0.03
Paired Recall Pairs	-0.07 [-0.151 - 0.012]	0.05
Pairs in Delayed Free Recall	-0.09 [-0.171 - -0.008]	0.01
Semantic Proactive Interference	-0.08 [-0.161 – 0.002]	0.03
Subtests of WAIS-IV		
Digit Span Forward	-0.01[-0.092 – 0.072]	0.40
Digit Span Backward	-0.09 [-0.171 - -0.008]	0.02
Digit Span Sequencing	0.02 [-0.062 - 0.102]	0.31
Coding	-0.06 [-0.142 - 0.022]	0.08
Visual Puzzles	-0.01 [-0.092 - 0.072]	0.38
Matrix Reasoning	-0.05 [-0.132 - 0.033]	0.13
Similarities	-0.05 [-0.132 - 0.033]	0.11

Adjusted by age, education, sex, number of APOE-ε4 alleles and Goldberg depression subscale. WMH also adjusted by TIV.

Table S3. Correlation between global WMH load and cognition correcting by age, education, sex, number of APOE-ε4 alleles, TIV and Goldberg depression subscale. Abbreviations: TIV, total intracranial volume.

Figure S1. A) Frequency Distribution of WMH load for all the participants in the analyses (N=561) B) Correlation between global and regional WMH lesion C) WMH percentage of ROI volume in each region.

FR: frontal right, FL: frontal left, TR: temporal right, TL: temporal left, PR: parietal right, PL: parietal left, OR: occipital right, OL: occipital left, BG: basal ganglia, Q1: first interquartile and Q3: third interquartile.
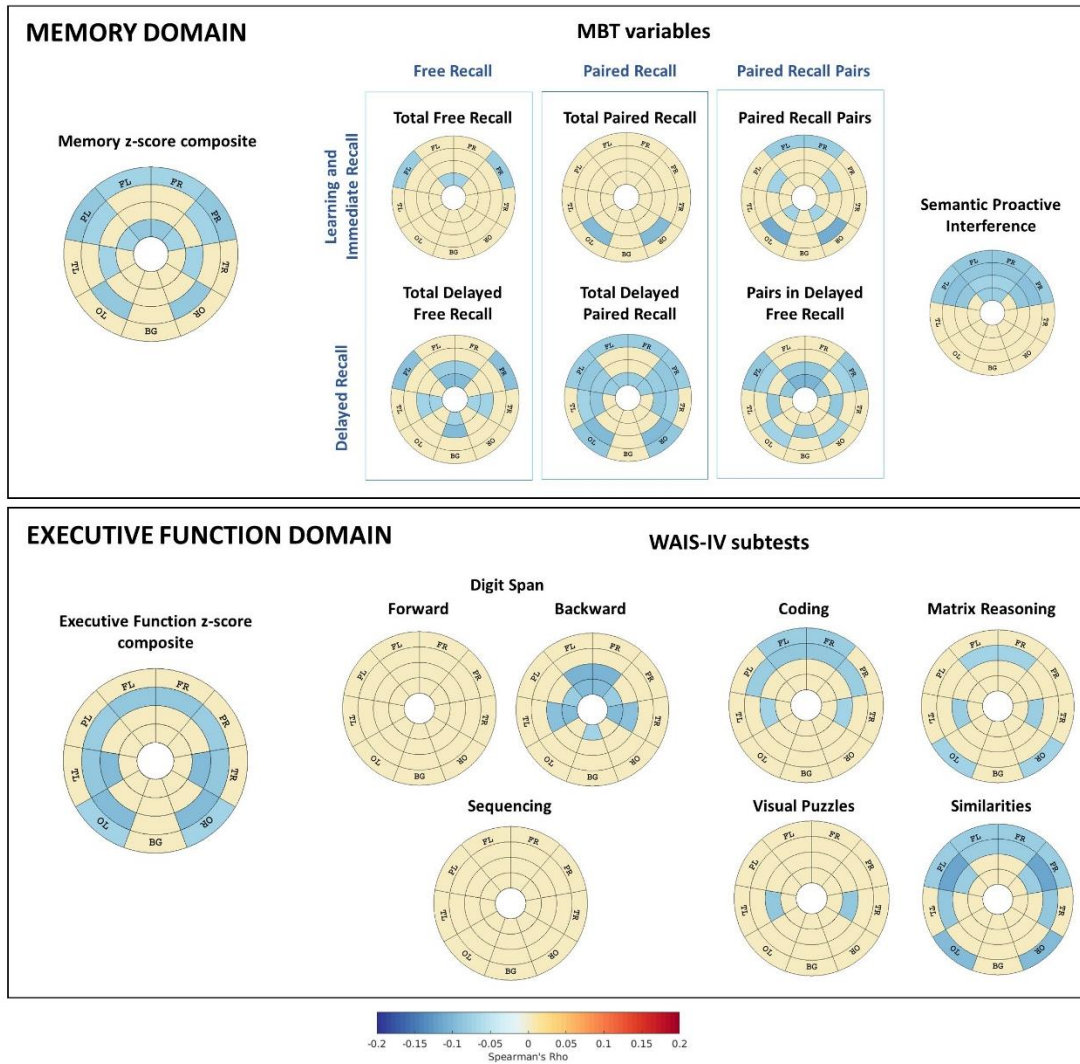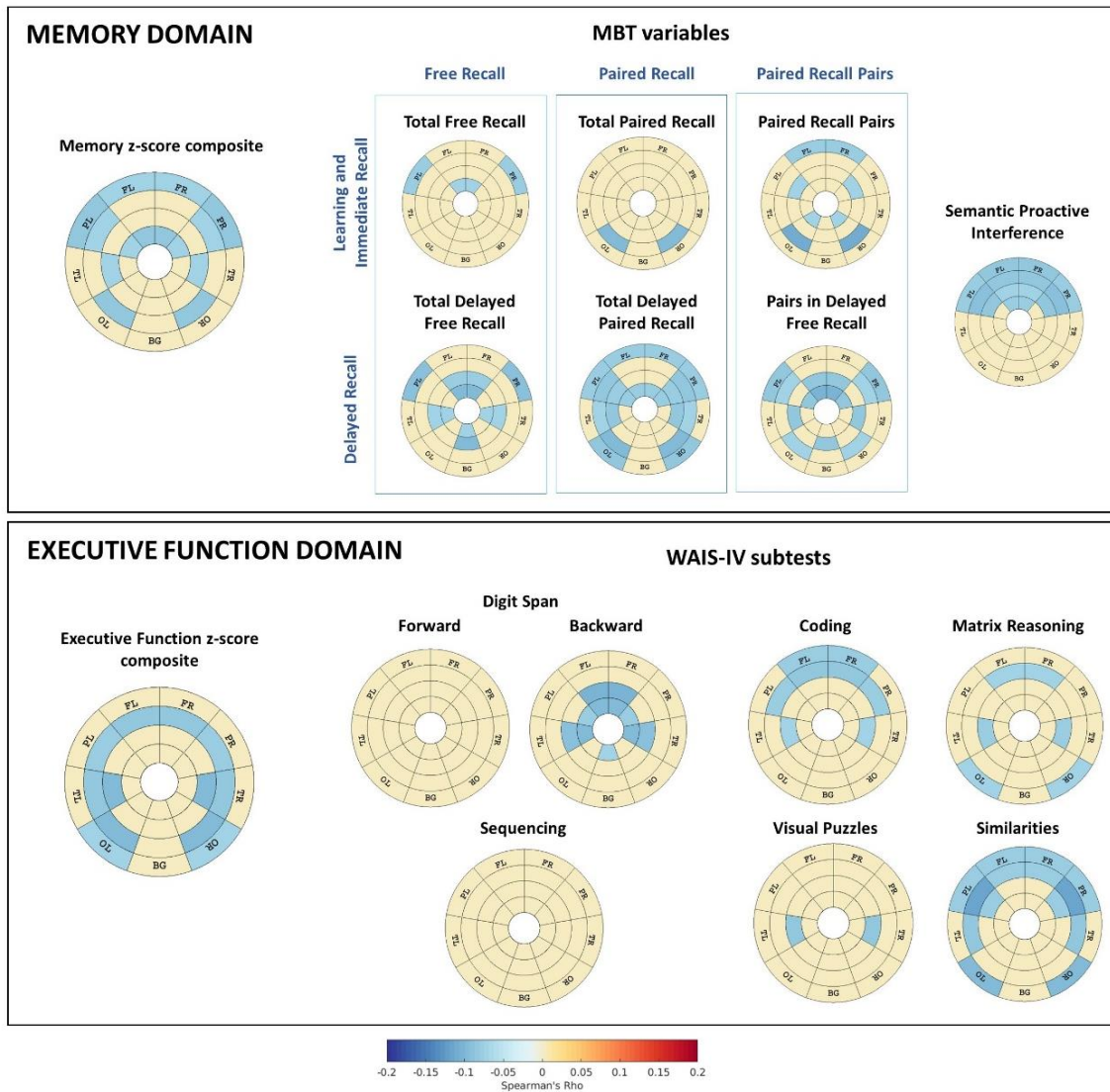
Fig. S2: Regional patterns of correlation between cognition and WMH correcting by age, education, sex, number of APOE-ε4 alleles, TIV and MTA. Effect sizes of these correlation measures by Spearman's Rho are shown in those areas that presented statistical significant association (p<0.05). All the other regions are depicted in beige. Cognition and WMH were adjsuted by age, sex, education, number of *APOE-ε4* alleles and MTA. WMH were also adjusted by TIV.

Abbreviations: FR, frontal right; FL, frontal left; TR, temporal right; TL: temporal left; PR, parietal right; PL, parietal left; OR, occipital right; OL, occipital left; BG, basal ganglia; WMH, white matter hyperintensities; MTA, medial temporal atrophy; TIV, total intracranial volume.
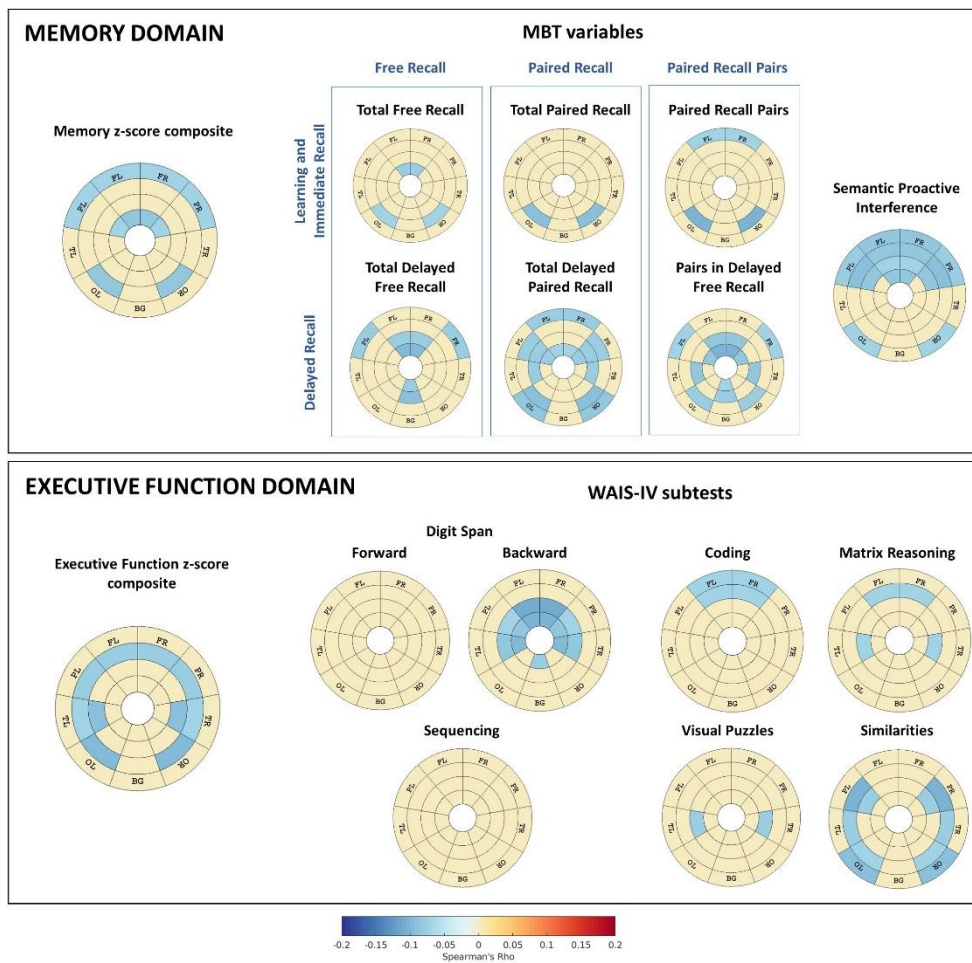
Fig. S3: Regional patterns of correlation between cognition and WMH correcting by age, education, sex, number of APOE-ε4 alleles, TIV and CAIDE-I. Effect sizes of these correlation measures by Spearman's Rho are shown in those areas that presented statistical significant association (p<0.05). All the other regions are depicted in beige. Cognition and WMH were adjsuted by age, sex, education, number of *APOE-ε4* alleles and CAIDE-I. WMH were also adjusted by TIV.

Abbreviations: FR, frontal right; FL, frontal left; TR, temporal right; TL: temporal left; PR, parietal right; PL, parietal left; OR, occipital right; OL, occipital left; BG, basal ganglia; WMH, white matter hyperintensities; CAIDE, Cardiovascular Risk Factors; TIV, total intracranial volume.

Fig. S4: Regional patterns of correlation between cognition and WMH correcting by age, education, sex, number of APOE-ε4 alleles, TIV and Goldberg depression subscale. Effect sizes of these correlation measures by Spearman's Rho are shown in those areas that presented statistical significant association (p<0.05). All the other regions are depicted in beige. Cognition and WMH were adjsuted by age, sex, education, number of *APOE-ε4* alleles and Goldberg depression subscale. WMH were also adjusted by TIV.

Abbreviations: FR, frontal right; FL, frontal left; TR, temporal right; TL: temporal left; PR, parietal right; PL, parietal left; OR, occipital right; OL, occipital left; BG, basal ganglia; WMH, white matter hyperintensities; CAIDE, Cardiovascular Risk Factors; TIV, total intracranial volume.