

Supplemental Data

Imaging microglial activation and amyloid burden in amnesic mild cognitive impairment

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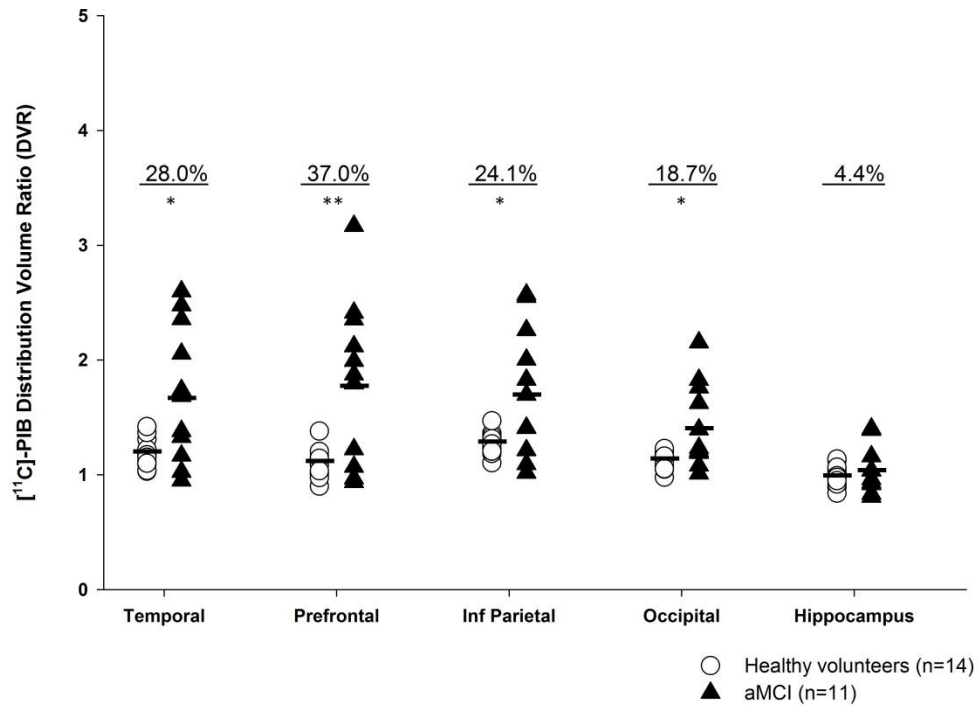


Figure 1. [¹¹C]-PIB Distribution Value Ratio (DVR) in regions of interest. aMCI participants (n=11) had higher [¹¹C]-PIB binding in all regions except hippocampus. The cerebellum was used as a reference region. *p≤0.05, **p<0.01

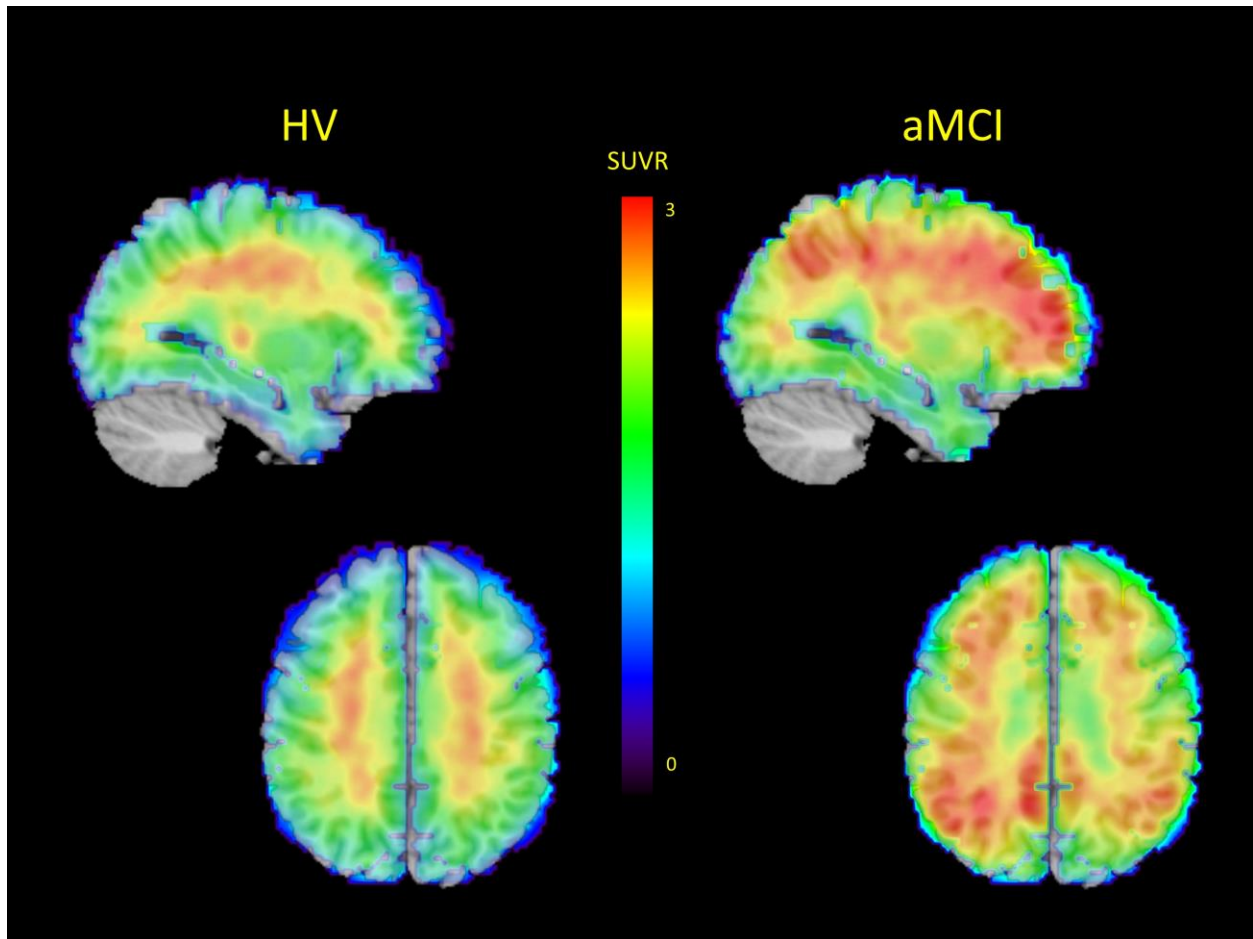


Figure 2. Parametric images of [¹¹C]-PIB standardized uptake value ratios (SUVR) overlaid on T1-weighted magnetic resonance imaging (MRI) template. The cerebellum was used as a reference region. Voxel threshold was set to $p < 0.05$ (FWE corrected).

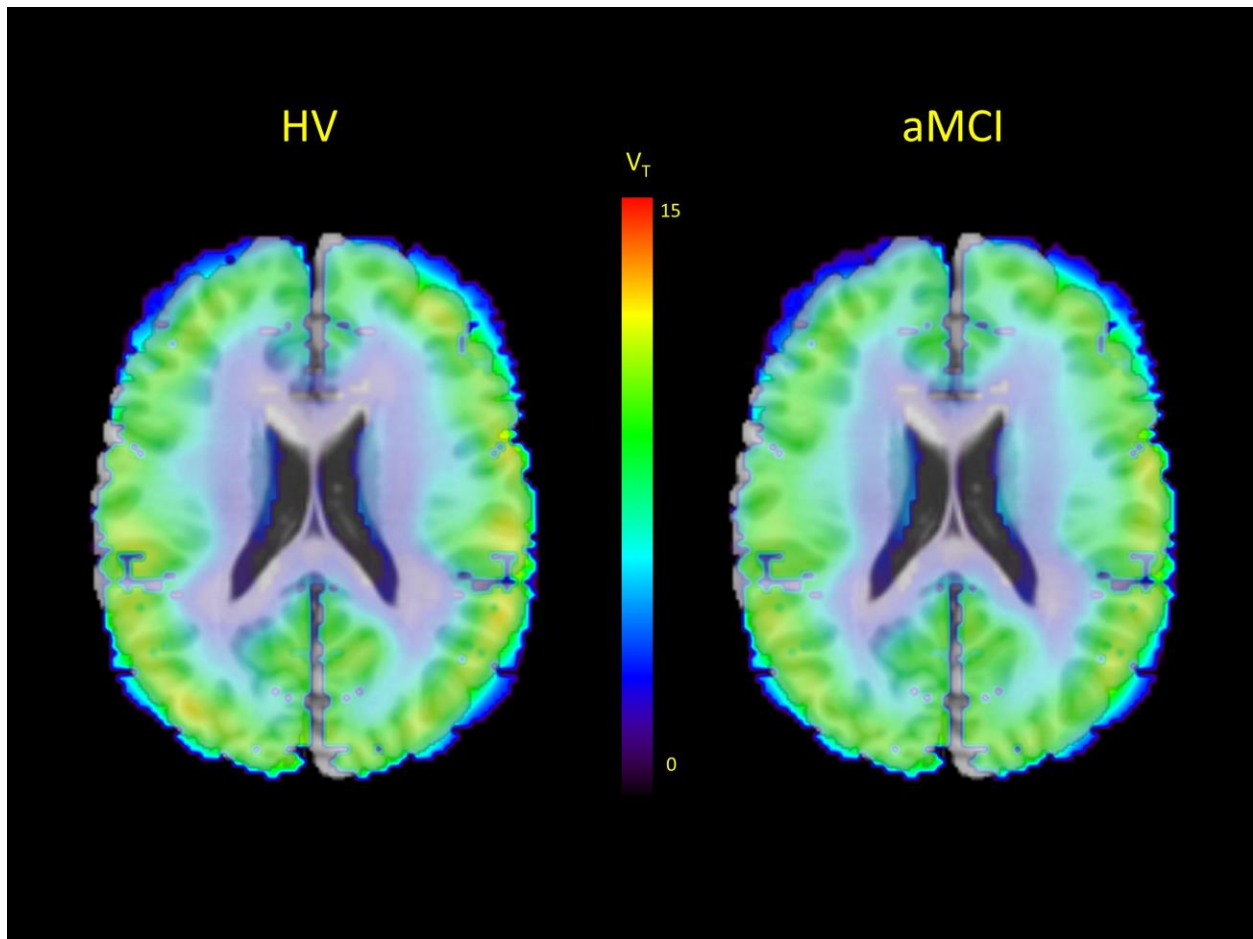


Figure 3. Parametric images of [^{18}F]-FEPPA total distribution volume (V_T) overlaid on T1-weighted magnetic resonance imaging (MRI) template. Voxel threshold was set to $p < 0.05$ (FWE corrected).

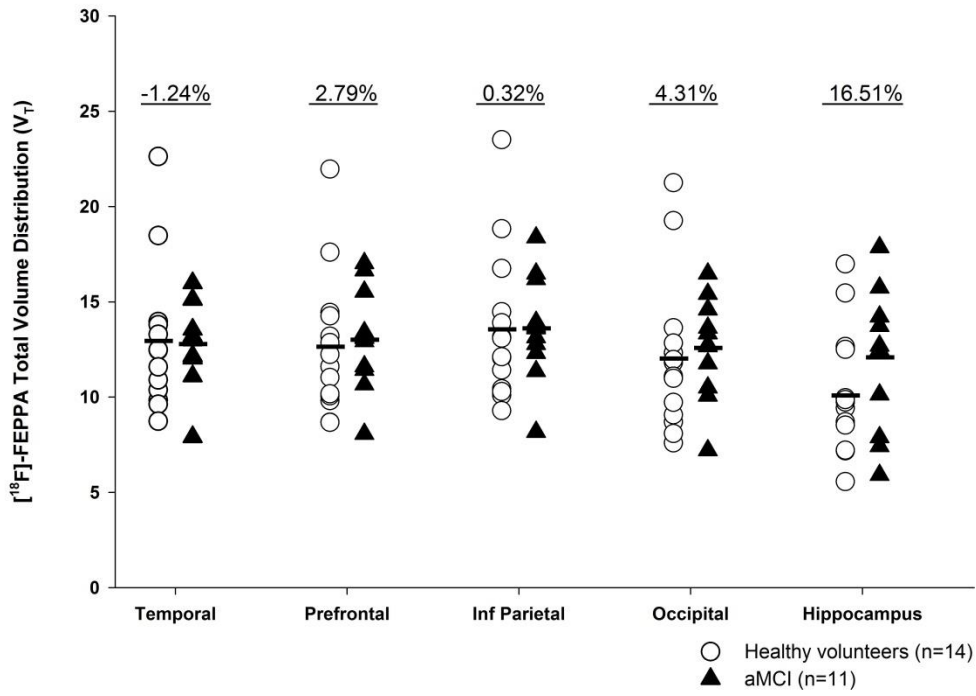


Figure 4. $[^{18}\text{F}]\text{-FEPPA}$ Total Volume Distribution (V_T) in regions of interest. No significant differences were observed between aMCI participants (n=11) and healthy volunteers (n=14).

Table 1. [¹⁸F]-FEPPA Standardized Uptake Value Ratios (SUVR). The standard uptake value between 90-120 minutes in an ROI was normalized to the standard uptake value of the cerebellum between 90-120 minutes. The ratio for each ROI, along with the percent difference is shown.

A. Before partial volume correction

Region	HV (n=14)		aMCI (n=11)		% Diff between HV and aMCI	t	p
	mean	SD	mean	SD			
Temporal	0.99	0.08	0.97	0.07	-1.92	-0.647	0.524
Prefrontal	0.92	0.08	0.93	0.08	1.43	0.419	0.679
Inf Parietal	1.03	0.09	1.01	0.05	-1.37	-0.479	0.636
Occipital	0.95	0.09	0.97	0.07	2.72	0.793	0.436
Hippocampus	0.74	0.08	0.77	0.11	4.55	0.865	0.396

B. After partial volume correction

Region	HV (n=14)		aMCI (n=11)		% Diff between HV and aMCI	t	p
	mean	SD	mean	SD			
Temporal	1.15	0.14	1.20	0.12	4.77	1.046	0.307
Prefrontal	1.32	0.15	1.39	0.11	5.41	1.324	0.199
Inf Parietal	1.41	0.21	1.47	0.14	4.01	0.682	0.453
Occipital	1.37	0.17	1.49	0.25	8.58	0.176	0.177
Hippocampus	0.78	0.14	0.88	0.19	12.04	0.533	0.174

Table 2. Regional [^{18}F]-FEPPA V_T for HV and aMCI participants when stratified by PIB status. An average of 1.20 DVR in the cortical regions was used as a cut-off. No significant differences were observed between groups.

Region	HV (n=14)		aMCI (n=11)		% Difference between HV PIB- and aMCI PIB+
	PIB- (n=11)	PIB+ (n=3)	PIB- (n=3)	PIB+ (n=8)	
Temporal	13.32 \pm 0.97	11.10 \pm 1.78	10.29 \pm 1.82	13.89 \pm 1.20	4.28
Prefrontal	13.22 \pm 0.98	10.12 \pm 1.80	10.44 \pm 1.84	14.12 \pm 1.21	6.81
Inferior Parietal	14.08 \pm 1.05	11.19 \pm 1.93	10.94 \pm 1.98	14.76 \pm 1.30	4.83
Occipital	12.35 \pm 1.08	10.38 \pm 1.99	10.02 \pm 2.04	13.71 \pm 1.34	11.01
Hippocampus	10.35 \pm 1.03	8.60 \pm 1.91	9.27 \pm 1.96	13.34 \pm 1.28	28.89

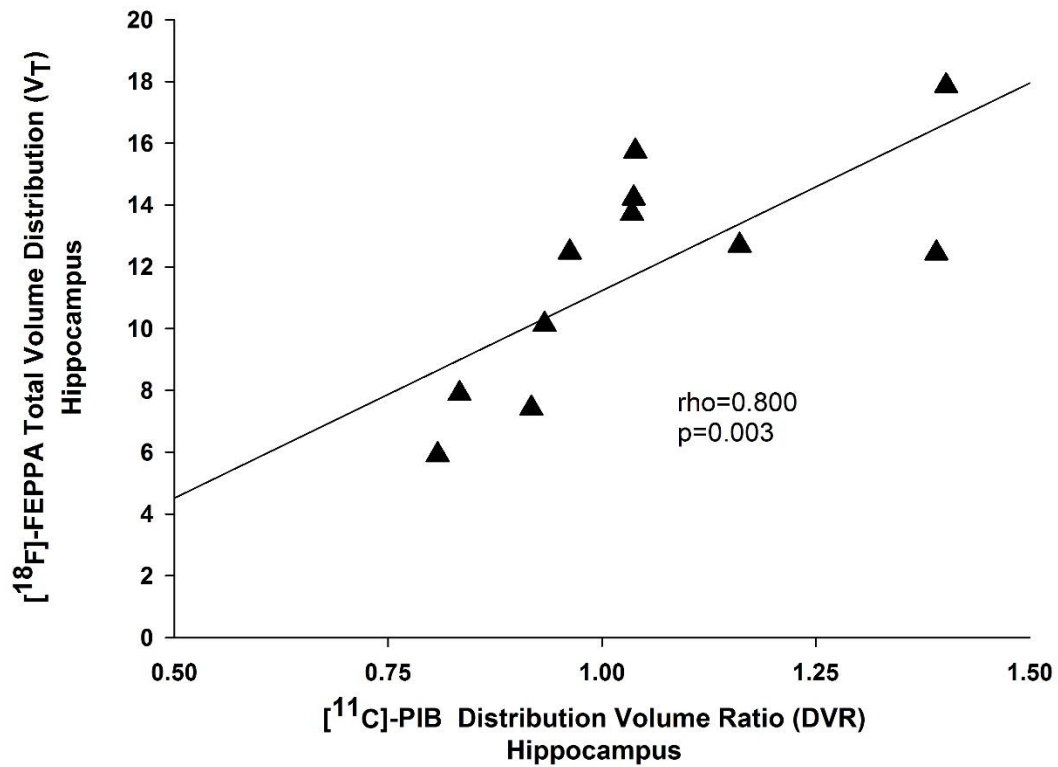


Figure 5. Regional associations between [¹⁸F]-FEPPA and [¹¹C]-PIB binding in hippocampus of aMCI participants (n=11) before partial volume correction. The correlation in the hippocampus survived after Bonferroni correction for multiple comparisons.

Table 4. Correlation analyses between [¹¹C]-PIB DVR and neuropsychological score. Spearman's rank coefficient (rho).

A. Correlations before partial volume error correction.

Cognitive Measure MCI (n=7)	MEMORY						LANGUAGE			
	RBANS Immediate Memory		RBANS Delayed Memory		Logical Memory Delayed (n=11)		RBANS Language		Verbal Fluency (n=11)	
DVR	rho	p	rho	p	rho	p	rho	p	rho	p
Temporal	0.071	0.879	-0.054	0.908	-0.635	0.036	-0.143	0.760	0.369	0.264
Prefrontal	0.000	1.000	0.432	0.333	-0.584	0.059	0.143	0.760	0.205	0.545
Inf Parietal	0.286	0.535	-0.108	0.818	-0.667	0.025	-0.036	0.939	0.446	0.169
Occipital	0.393	0.383	-0.180	0.699	-0.584	0.059	-0.071	0.879	0.310	0.354
Hippocampus	-0.071	0.879	0.162	0.728	-0.557	0.075	-0.071	0.879	-0.005	0.989

Cognitive Measure MCI (n=7)	GENERAL COGNITION				ATTENTION		VISUOSPATIAL			
	MMSE		MoCA		RBANS Attention (n=7)		TMT Task A		RBANS Visuospatial (n=7)	
DVR	rho	p	rho	p	rho	p	rho	p	rho	p
Temporal	-0.302	0.367	-0.169	0.619	0.055	0.908	0.018	0.958	0.342	0.452
Prefrontal	-0.181	0.594	-0.330	0.322	0.109	0.816	-0.127	0.709	0.252	0.585
Inf Parietal	-0.149	0.663	-0.046	0.894	0.218	0.638	-0.018	0.958	0.523	0.229
Occipital	-0.306	0.360	-0.078	0.820	0.273	0.554	0.045	0.894	0.414	0.355
Hippocampus	-0.167	0.623	-0.549	0.080	-0.582	0.170	0.009	0.979	-0.198	0.670

Cognitive Measure MCI (n=7)	EXECUTIVE FUNCTION							
	TMT Task B		Stroop Test Color Task (n=8)		Stroop Test Color Word Task (n=8)		Letter Number Span (n=7)	
DVR	rho	p	rho	p	rho	p	rho	p
Temporal	-0.191	0.574	0.109	0.797	-0.333	0.420	0.315	0.491
Prefrontal	-0.218	0.519	0.109	0.797	-0.167	0.693	0.315	0.491
Inf Parietal	-0.282	0.401	0.218	0.604	-0.357	0.385	0.315	0.491
Occipital	-0.127	0.709	0.218	0.604	-0.190	0.651	0.512	0.240
Hippocampus	-0.045	0.894	-0.343	0.406	-0.310	0.456	-0.335	0.463

B. Correlations after partial volume error correction

Cognitive Measure MCI (n=7)	MEMORY						LANGUAGE			
	RBANS Immediate Memory		RBANS Delayed Memory		Logical Memory Delayed (n=11)		RBANS Language		Verbal Fluency (n=11)	
DVR	rho	p	rho	p	rho	p	rho	p	rho	p
Temporal	0.071	0.879	-0.054	0.908	-0.635	0.036	0.143	0.760	0.369	0.264
Prefrontal	0.000	1.000	0.432	0.333	-0.584	0.059	0.143	0.760	0.205	0.545
Inf Parietal	0.071	0.879	-0.054	0.908	-0.676	0.022	-0.143	0.760	0.456	0.159
Occipital	0.393	0.383	-0.180	0.699	-0.525	0.097	-0.071	0.879	0.287	0.392
Hippocampus	-0.321	0.482	0.414	0.355	-0.621	0.041	0.000	1.000	0.118	0.729

Cognitive Measure MCI (n=7)	GENERAL COGNITION				ATTENTION		VISUOSPATIAL			
	MMSE		MoCA		RBANS Attention (n=7)		TMT Task A		RBANS Visuospatial (n=7)	
DVR	rho	p	rho	p	rho	p	rho	p	rho	p
Temporal	-0.302	0.367	-0.169	0.619	0.055	0.908	0.018	0.958	0.342	0.452
Prefrontal	-0.181	0.594	-0.330	0.322	0.109	0.816	-0.127	0.709	0.252	0.585
Inf Parietal	-0.204	0.547	-0.124	0.717	0.055	0.908	0.000	1.000	0.342	0.452
Occipital	-0.330	0.322	-0.027	0.936	0.273	0.554	0.055	0.873	0.414	0.355
Hippocampus	-0.176	0.604	-0.572	0.066	-0.346	0.448	-0.100	0.770	0.072	0.878

Cognitive Measure MCI (n=7)	EXECUTIVE FUNCTION							
	TMT Task B		Stroop Test Color Task (n=8)		Stroop Test Color Word Task (n=8)		Letter Number Span (n=7)	
DVR	rho	p	rho	p	rho	p	rho	p
Temporal	0.191	0.574	0.109	0.797	-0.333	0.420	0.315	0.491
Prefrontal	-0.218	0.519	0.109	0.797	-0.167	0.693	0.315	0.491
Inf Parietal	-0.273	0.417	0.109	0.797	-0.405	0.320	0.315	0.491
Occipital	-0.118	0.729	0.218	0.604	-0.190	0.651	0.512	0.240
Hippocampus	-0.191	0.574	-0.171	0.685	-0.333	0.420	-0.256	0.579

Table 5. Correlation analyses between [¹⁸F]-FEPPA V_T and neuropsychological score. Spearman's rank coefficient (rho).

A. Correlations before partial volume error correction.

Cognitive Measure MCI (n=7)	MEMORY						LANGUAGE			
	RBANS Immediate Memory		RBANS Delayed Memory		Logical Memory Delayed (n=11)		RBANS Language		Verbal Fluency (n=11)	
V _T	rho	p	rho	p	rho	p	rho	p	rho	p
Temporal	-0.214	0.645	0.198	0.670	-0.406	0.215	0.321	0.482	0.542	0.085
Prefrontal	-0.071	0.879	0.234	0.613	-0.365	0.269	0.464	0.294	0.533	0.091
Inf Parietal	-0.071	0.879	0.631	0.129	-0.219	0.517	0.714	0.071	0.415	0.205
Occipital	-0.214	0.645	0.324	0.478	-0.320	0.338	0.393	0.383	0.483	0.132
Hippocampus	0.357	0.432	0.054	0.908	-0.584	0.059	0.321	0.482	0.005	0.989

Cognitive Measure MCI (n=7)	GENERAL COGNITION				ATTENTION		VISUOSPATIAL			
	MMSE		MoCA		RBANS Attention (n=7)		TMT Task A		RBANS Visuospatial (n=7)	
V _T	rho	p	rho	p	rho	p	rho	p	rho	p
Temporal	-0.079	0.818	-0.320	0.337	0.055	0.908	-0.418	0.201	0.360	0.427
Prefrontal	-0.060	0.860	-0.256	0.447	0.218	0.638	-0.364	0.272	0.396	0.379
Inf Parietal	0.232	0.492	-0.252	0.455	0.273	0.554	-0.655	0.029	0.450	0.310
Occipital	-0.214	0.528	-0.220	0.516	0.109	0.816	-0.682	0.021	0.559	0.192
Hippocampus	0.181	0.594	-0.334	0.315	-0.291	0.527	0.000	1.000	0.180	0.699

Cognitive Measure MCI (n=7)	EXECUTIVE FUNCTION							
	TMT Task B		Stroop Test Color Task (n=8)		Stroop Test Color Word Task (n=8)		Letter Number Span (n=7)	
V _T	rho	p	rho	p	rho	p	rho	p
Temporal	-0.309	0.355	0.436	0.280	0.167	0.693	0.118	0.801
Prefrontal	-0.245	0.467	0.546	0.162	0.357	0.385	0.217	0.641
Inf Parietal	-0.382	0.247	0.655	0.078	0.476	0.233	0.118	0.801
Occipital	-0.455	0.160	0.546	0.162	0.167	0.693	-0.079	0.867
Hippocampus	0.009	0.979	-0.078	0.854	-0.214	0.610	-0.571	0.180

B. Correlations after partial volume error correction.

Cognitive Measure MCI (n=7)	MEMORY						LANGUAGE			
	RBANS Immediate Memory		RBANS Delayed Memory		Logical Memory Delayed (n=11)		RBANS Language		Verbal Fluency (n=11)	
V_T	rho	p	rho	p	rho	p	rho	p	rho	p
Temporal	-0.536	0.215	0.090	0.848	-0.356	0.282	-0.179	0.703	0.469	0.145
Prefrontal	-0.357	0.432	0.595	0.159	-0.292	0.383	0.500	0.253	0.551	0.079
Inf Parietal	-0.464	0.294	0.703	0.078	-0.365	0.269	0.429	0.337	0.433	0.184
Occipital	-0.536	0.215	0.252	0.585	-0.457	0.158	-0.071	0.879	0.396	0.228
Hippocampus	-0.429	0.337	0.360	0.427	-0.639	0.034	0.000	1.000	0.150	0.659

Cognitive Measure MCI (n=7)	GENERAL COGNITION				ATTENTION		VISUOSPATIAL			
	MMSE		MoCA		RBANS Attention (n=7)		TMT Task A		RBANS Visuospatial (n=7)	
V_T	rho	p	rho	p	rho	p	rho	p	rho	p
Temporal	-0.200	0.556	-0.430	0.187	-0.418	0.350	-0.345	0.298	-0.234	0.613
Prefrontal	0.111	0.744	-0.348	0.295	-0.091	0.846	-0.518	0.102	0.198	0.670
Inf Parietal	0.079	0.818	-0.481	0.135	-0.145	0.756	-0.473	0.142	0.108	0.818
Occipital	-0.149	0.663	-0.467	0.148	-0.109	0.816	-0.491	0.125	0.234	0.613
Hippocampus	-0.116	0.734	-0.650	0.030	-0.746	0.054	0.109	0.750	-0.468	0.289

Cognitive Measure MCI (n=7)	EXECUTIVE FUNCTION							
	TMT Task B		Stroop Test Color Task (n=8)		Stroop Test Color Word Task (n=8)		Letter Number Span (n=7)	
V_T	rho	p	rho	p	rho	p	rho	p
Temporal	-0.300	0.370	-0.031	0.942	-0.095	0.823	0.177	0.704
Prefrontal	-0.509	0.110	0.296	0.476	0.143	0.736	-0.118	0.801
Inf Parietal	-0.355	0.285	0.187	0.657	0.048	0.911	-0.118	0.801
Occipital	-0.364	0.272	0.109	0.797	-0.238	0.570	0.020	0.967
Hippocampus	0.064	0.853	-0.483	0.225	-0.357	0.385	-0.335	0.463