

Supplementary Material

The Combined Effect of *APOE* and *BDNF* Val66Met Polymorphisms on Spatial Navigation in Older Adults

Supplementary Table 1. Correlation matrix

Correlation matrix of spatial navigation performance, hippocampal and cortical volumes in the participants with amnesic mild cognitive impairment													
	Egocentric navigation	Allocentric navigation	Delayed navigation	Left hippocampal volume	Right hippocampal volume	Left entorhinal volume	Right entorhinal volume	Left inferior parietal volume	Right inferior parietal volume	Left posterior cingulate volume	Right posterior cingulate volume	Left precuneus volume	Right precuneus volume
Egocentric navigation ^a	1												
Allocentric navigation ^a	0.62***	1											
Delayed navigation ^a	0.48***	0.71***	1										
Left hippocampal volume ^a	-0.28*	-0.28*	-0.30*	1									
Right hippocampal volume ^a	-0.32**	-0.39***	-0.33**	0.82***	1								
Left entorhinal volume ^a	0.03	0.04	-0.12	0.44***	0.36**	1							
Right entorhinal volume ^a	-0.17	-0.21	-0.27*	0.41***	0.48***	0.44***	1						
Left inferior parietal volume ^a	0.10	0.11	-0.08	0.23	0.29*	0.18	0.24*	1					
Right inferior parietal volume ^a	-0.12	-0.07	-0.23	0.37**	0.49***	0.23*	0.22	0.61***	1				
Left posterior cingulate volume ^a	-0.02	0.19	0.27*	-0.06	-0.03	-0.09	-0.28*	0.23	0.22	1			
Right posterior cingulate volume ^a	-0.03	0.06	0.11	0.08	0.26*	0.09	-0.20	0.27*	0.45***	0.53***	1		
Left precuneus volume ^a	-0.11	-0.03	-0.07	0.28*	0.36**	0.08	-0.09	0.54***	0.47***	0.25*	0.42***	1	
Right precuneus volume ^a	-0.23	-0.18	-0.10	0.25*	0.45***	-0.09	-0.04	0.43***	0.53***	0.32**	0.41***	0.66***	1

* Correlation is significant at the 0.05 level (2-tailed); ** Correlation is significant at the 0.01 level (2-tailed); *** Correlation is significant at the 0.001 level (2-tailed).

Values in bold indicate significant correlations after Bonferroni correction for multiple comparisons ($p < 0.005$). ^aValues in standard deviation units calculated from the overall mean and SD of the sample.

Supplementary Table 2. Group-wise comparisons of hippocampal and cortical volumes of cognitively unimpaired participants

(I) Groupcode	(J) Groupcode	Mean difference (I-J)	<i>p</i>	95% Confidence interval for difference	
				Lower bound	Upper bound
<i>Left hippocampal volume^a</i>					
$\epsilon 4^+/\text{BDNF}^{\text{Met}}$	$\epsilon 4^+/\text{BDNF}^{\text{Val/Val}}$	-0.348	0.998	-2.466	1.770
	$\epsilon 4^-/\text{BDNF}^{\text{Met}}$	-0.135	1.000	-2.568	2.297
	$\epsilon 4^-/\text{BDNF}^{\text{Val/Val}}$	0.633	0.962	-1.501	2.768
$\epsilon 4^+/\text{BDNF}^{\text{Val/Val}}$	$\epsilon 4^-/\text{BDNF}^{\text{Met}}$	0.213	1.000	-1.475	1.901
	$\epsilon 4^-/\text{BDNF}^{\text{Val/Val}}$	0.982	0.211	-0.285	2.248
$\epsilon 4^-/\text{BDNF}^{\text{Met}}$	$\epsilon 4^-/\text{BDNF}^{\text{Val/Val}}$	0.769	0.777	-0.934	2.472
<i>Right hippocampal volume^a</i>					
$\epsilon 4^+/\text{BDNF}^{\text{Met}}$	$\epsilon 4^+/\text{BDNF}^{\text{Val/Val}}$	-0.085	1.000	-1.978	1.808
	$\epsilon 4^-/\text{BDNF}^{\text{Met}}$	-0.224	1.000	-2.398	1.950
	$\epsilon 4^-/\text{BDNF}^{\text{Val/Val}}$	0.802	0.828	-1.105	2.710
$\epsilon 4^+/\text{BDNF}^{\text{Val/Val}}$	$\epsilon 4^-/\text{BDNF}^{\text{Met}}$	-0.138	1.000	-1.647	1.370
	$\epsilon 4^-/\text{BDNF}^{\text{Val/Val}}$	0.888	0.200	-0.244	2.020
$\epsilon 4^-/\text{BDNF}^{\text{Met}}$	$\epsilon 4^-/\text{BDNF}^{\text{Val/Val}}$	1.026	0.355	-0.496	2.548
<i>Left entorhinal volume^a</i>					
$\epsilon 4^+/\text{BDNF}^{\text{Met}}$	$\epsilon 4^+/\text{BDNF}^{\text{Val/Val}}$	-0.186	1.000	-1.932	1.560
	$\epsilon 4^-/\text{BDNF}^{\text{Met}}$	-0.853	0.820	-2.858	1.152
	$\epsilon 4^-/\text{BDNF}^{\text{Val/Val}}$	0.391	0.991	-1.369	2.151
$\epsilon 4^+/\text{BDNF}^{\text{Val/Val}}$	$\epsilon 4^-/\text{BDNF}^{\text{Met}}$	-0.667	0.728	-2.058	0.725
	$\epsilon 4^-/\text{BDNF}^{\text{Val/Val}}$	0.577	0.584	-0.467	1.621
$\epsilon 4^-/\text{BDNF}^{\text{Met}}$	$\epsilon 4^-/\text{BDNF}^{\text{Val/Val}}$	1.244	0.108	-0.160	2.648
<i>Right entorhinal volume^a</i>					
$\epsilon 4^+/\text{BDNF}^{\text{Met}}$	$\epsilon 4^+/\text{BDNF}^{\text{Val/Val}}$	-1.074	0.485	-2.854	0.707
	$\epsilon 4^-/\text{BDNF}^{\text{Met}}$	-0.959	0.747	-3.004	1.086
	$\epsilon 4^-/\text{BDNF}^{\text{Val/Val}}$	-0.713	0.862	-2.507	1.082
$\epsilon 4^+/\text{BDNF}^{\text{Val/Val}}$	$\epsilon 4^-/\text{BDNF}^{\text{Met}}$	0.115	1.000	-1.304	1.534
	$\epsilon 4^-/\text{BDNF}^{\text{Val/Val}}$	0.361	0.929	-0.704	1.426
$\epsilon 4^-/\text{BDNF}^{\text{Met}}$	$\epsilon 4^-/\text{BDNF}^{\text{Val/Val}}$	0.246	0.998	-1.186	1.678
<i>Left inferior parietal volume^a</i>					
$\epsilon 4^+/\text{BDNF}^{\text{Met}}$	$\epsilon 4^+/\text{BDNF}^{\text{Val/Val}}$	0.393	0.998	-1.958	2.744
	$\epsilon 4^-/\text{BDNF}^{\text{Met}}$	-0.131	1.000	-2.831	2.570
	$\epsilon 4^-/\text{BDNF}^{\text{Val/Val}}$	0.613	0.981	-1.757	2.983
$\epsilon 4^+/\text{BDNF}^{\text{Val/Val}}$	$\epsilon 4^-/\text{BDNF}^{\text{Met}}$	-0.524	0.971	-2.397	1.350
	$\epsilon 4^-/\text{BDNF}^{\text{Val/Val}}$	0.220	0.999	-1.186	1.626
$\epsilon 4^-/\text{BDNF}^{\text{Met}}$	$\epsilon 4^-/\text{BDNF}^{\text{Val/Val}}$	0.744	0.867	-1.147	2.635
<i>Right inferior parietal volume^a</i>					
$\epsilon 4^+/\text{BDNF}^{\text{Met}}$	$\epsilon 4^+/\text{BDNF}^{\text{Val/Val}}$	0.303	1.000	-2.350	2.956
	$\epsilon 4^-/\text{BDNF}^{\text{Met}}$	-0.007	1.000	-3.054	3.040
	$\epsilon 4^-/\text{BDNF}^{\text{Val/Val}}$	0.702	0.979	-1.972	3.376
$\epsilon 4^+/\text{BDNF}^{\text{Val/Val}}$	$\epsilon 4^-/\text{BDNF}^{\text{Met}}$	-0.310	0.999	-2.424	1.805
	$\epsilon 4^-/\text{BDNF}^{\text{Val/Val}}$	0.400	0.983	-1.187	1.986
$\epsilon 4^-/\text{BDNF}^{\text{Met}}$	$\epsilon 4^-/\text{BDNF}^{\text{Val/Val}}$	0.709	0.935	-1.424	2.843
<i>Left posterior cingulate volume^a</i>					
$\epsilon 4^+/\text{BDNF}^{\text{Met}}$	$\epsilon 4^+/\text{BDNF}^{\text{Val/Val}}$	0.079	1.000	-2.438	2.597

$\epsilon 4^+ / BDNF^{Val/Val}$	$\epsilon 4^- / BDNF^{Met}$	-0.092	1.000	-2.983	2.800
	$\epsilon 4^- / BDNF^{Val/Val}$	0.750	0.963	-1.788	3.287
	$\epsilon 4^- / BDNF^{Met}$	-0.171	1.000	-2.178	1.835
	$\epsilon 4^- / BDNF^{Val/Val}$	0.670	0.788	-0.835	2.176
$\epsilon 4^- / BDNF^{Met}$	$\epsilon 4^- / BDNF^{Val/Val}$	0.842	0.835	-1.183	2.866
	<i>Right posterior cingulate volume^a</i>				
$\epsilon 4^+ / BDNF^{Met}$	$\epsilon 4^+ / BDNF^{Val/Val}$	0.444	0.996	-1.882	2.771
	$\epsilon 4^- / BDNF^{Met}$	0.678	0.982	-1.994	3.350
	$\epsilon 4^- / BDNF^{Val/Val}$	1.443	0.460	-0.901	3.788
$\epsilon 4^+ / BDNF^{Val/Val}$	$\epsilon 4^- / BDNF^{Met}$	0.233	1.000	-1.621	2.088
	$\epsilon 4^- / BDNF^{Val/Val}$	0.999	0.286	-0.392	2.391
	$\epsilon 4^- / BDNF^{Met}$	0.766	0.845	-1.105	2.637
<i>Left precuneus volume^a</i>					
$\epsilon 4^+ / BDNF^{Met}$	$\epsilon 4^+ / BDNF^{Val/Val}$	0.242	1.000	-2.444	2.929
	$\epsilon 4^- / BDNF^{Met}$	-0.751	0.986	-3.837	2.334
	$\epsilon 4^- / BDNF^{Val/Val}$	0.841	0.953	-1.867	3.548
$\epsilon 4^+ / BDNF^{Val/Val}$	$\epsilon 4^- / BDNF^{Met}$	-0.993	0.755	-3.135	1.148
	$\epsilon 4^- / BDNF^{Val/Val}$	0.598	0.894	-1.008	2.205
	$\epsilon 4^- / BDNF^{Met}$	1.592	0.259	-0.569	3.752
<i>Right precuneus volume^a</i>					
$\epsilon 4^+ / BDNF^{Met}$	$\epsilon 4^+ / BDNF^{Val/Val}$	0.209	1.000	-2.741	3.159
	$\epsilon 4^- / BDNF^{Met}$	-0.208	1.000	-3.597	3.180
	$\epsilon 4^- / BDNF^{Val/Val}$	0.676	0.990	-2.298	3.649
$\epsilon 4^+ / BDNF^{Val/Val}$	$\epsilon 4^- / BDNF^{Met}$	-0.417	0.997	-2.769	1.934
	$\epsilon 4^- / BDNF^{Val/Val}$	0.467	0.978	-1.298	2.231
	$\epsilon 4^- / BDNF^{Met}$	0.884	0.894	-1.489	3.256

Analysis of covariance adjusted for age, gender and education. Mean differences are in standard deviation units.

^aAdjusted for estimated total intracranial volume.

$\epsilon 4^+ / BDNF^{Met}$, *APOE* $\epsilon 4$ and *BDNF* Met carriers' group; $\epsilon 4^+ / BDNF^{Val/Val}$, *APOE* $\epsilon 4$ carriers and *BDNF* Met noncarriers' group; $\epsilon 4^- / BDNF^{Met}$, *APOE* $\epsilon 4$ noncarriers and *BDNF* Met carriers' group; $\epsilon 4^- / BDNF^{Val/Val}$, *APOE* $\epsilon 4$ and *BDNF* Met noncarriers' group.

Supplementary Table 3. Correlation matrix

Correlation matrix of spatial navigation performance and hippocampal and cortical volumes in the cognitively unimpaired participants													
	Egocentric navigation	Allocentric navigation	Delayed navigation	Left hippocampal volume	Right hippocampal volume	Left entorhinal volume	Right entorhinal volume	Left inferior parietal volume	Right inferior parietal volume	Left posterior cingulate volume	Right posterior cingulate volume	Left precuneus volume	Right precuneus volume
Egocentric navigation ^a	1												
Allocentric navigation ^a	0.34**	1											
Delayed navigation ^a	-0.01	0.52***	1										
Left hippocampal volume ^a	-0.08	-0.09	0.07	1									
Right hippocampal volume ^a	-0.17	-0.13	0.09	0.59***	1								
Left entorhinal volume ^a	0.13	-0.17	-0.01	0.39***	0.40***	1							
Right entorhinal volume ^a	-0.09	-0.10	-0.02	0.38***	0.23	0.39***	1						
Left inferior parietal volume ^a	-0.07	-0.06	0.04	0.16	0.12	0.19	0.05	1					
Right inferior parietal volume ^a	-0.17	-0.15	-0.06	0.24	0.27*	0.11	0.03	0.62***	1				
Left posterior cingulate volume ^a	0.22	0.13	0.02	0.21	0.27*	-0.00	0.00	0.25	0.19	1			
Right posterior cingulate volume ^a	0.04	-0.01	-0.08	-0.17	-0.03	-0.08	-0.40***	0.23	0.17	0.25	1		
Left precuneus volume ^a	-0.03	-0.13	-0.11	0.18	0.35**	0.31*	-0.10	0.49***	0.47***	0.22	0.31*	1	
Right precuneus volume ^a	-0.06	-0.18	-0.15	0.18	0.31*	0.31*	0.16	0.33*	0.29*	0.27*	0.00	0.73***	1

* Correlation is significant at the 0.05 level (2-tailed); ** Correlation is significant at the 0.01 level (2-tailed); *** Correlation is significant at the 0.001 level (2-tailed).

Values in bold indicate significant correlations after Bonferroni correction for multiple comparisons ($p < 0.005$). ^aValues in standard deviation units calculated from the overall mean and SD of the sample.