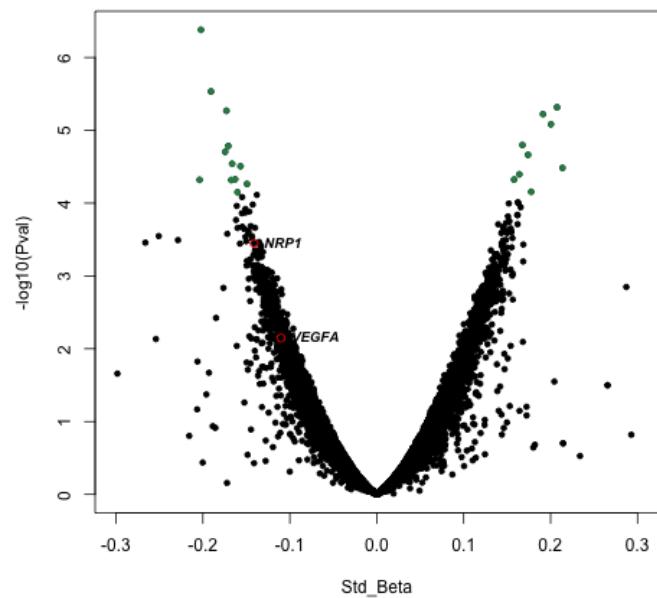
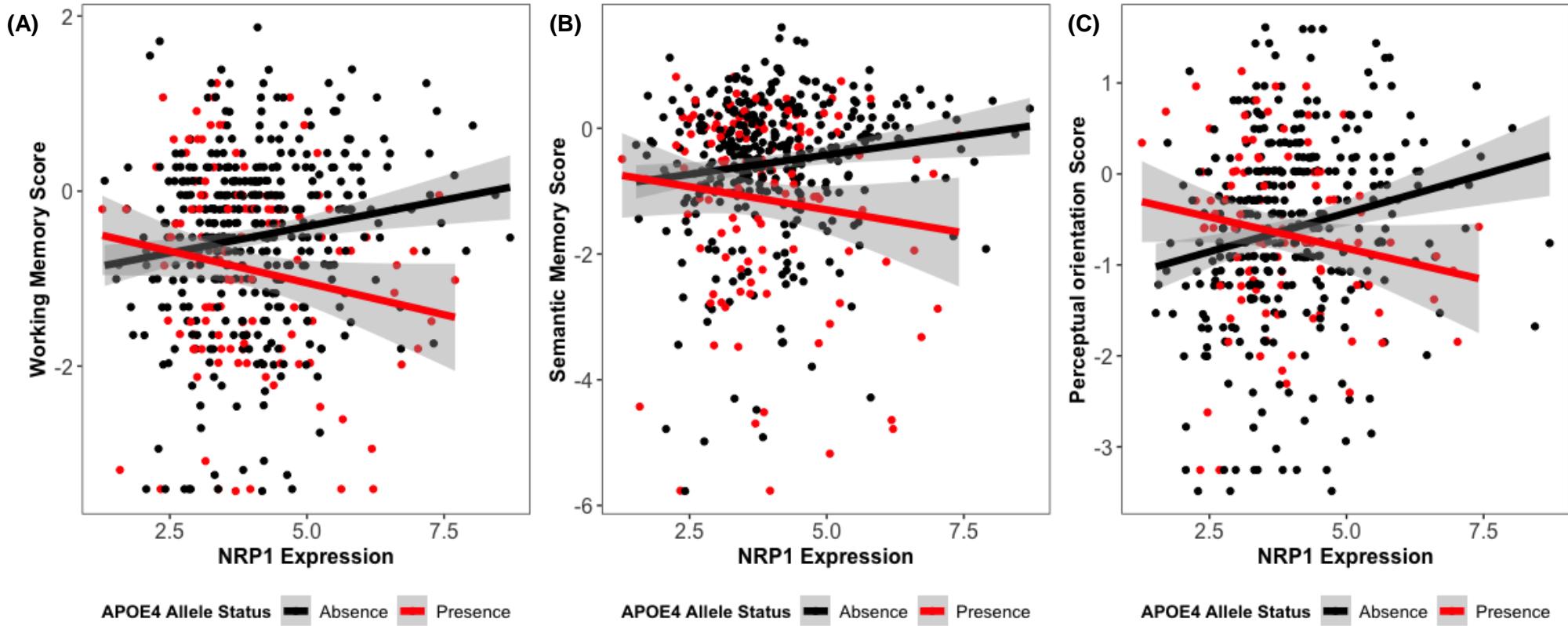


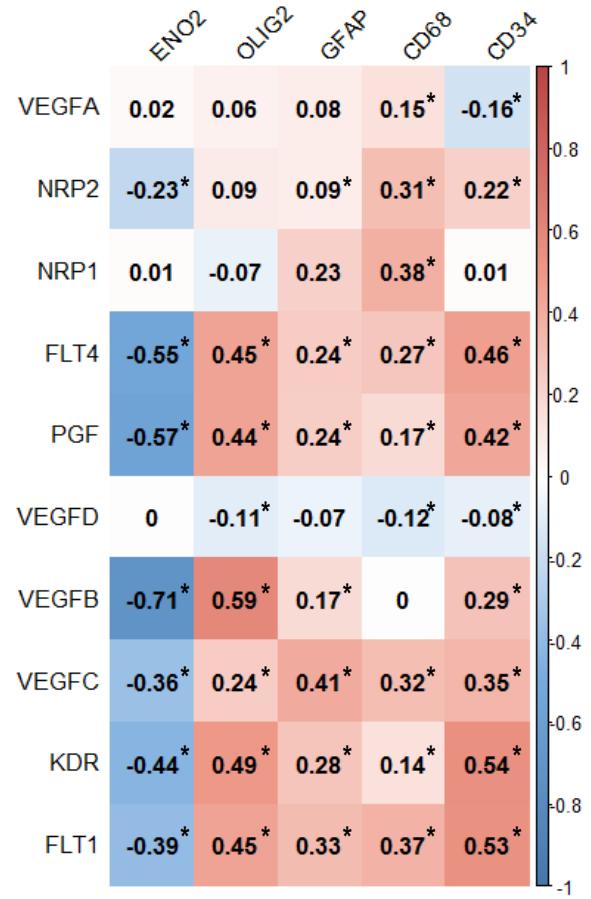
Gene interactions with APOE4 on global cognition



Supplemental Figure 1. Volcano plot of gene expression x *APOE-ε4* allele interaction results. Genes with $p.\text{fdr} < 0.1$ are colored in green.



Supplemental Figure 2. (A) *NRP1* expression associations with working memory performance at the final psychological assessment, stratified by *APOE*- ϵ 4 allele status. Overall interaction: *NRP1* x *APOE*- ϵ 4, $\beta=-0.28$, $p.fdr=0.02$; *APOE*- ϵ 4 carriers, $\beta=-0.17$, $p=0.03$; *APOE*- ϵ 4 non-carriers, $\beta=0.128$, $p=7E-04$. **(B)** *NRP1* expression associations with cross-sectional semantic memory, stratified by *APOE*- ϵ 4 allele status. Overall interaction: *NRP1* x *APOE*- ϵ 4, $\beta=-0.31$, $p.fdr=0.03$; *APOE*- ϵ 4 carriers, $\beta=-0.19$, $p=0.096$; *APOE*- ϵ 4 non-carriers, $\beta=0.12$, $p=0.006$. **(C)** *NRP1* expression associations with endpoint perceptual orientation scores, stratified by *APOE*- ϵ 4 allele status. Overall interaction: *NRP1* x *APOE*- ϵ 4, $\beta=-0.28$, $p.fdr=0.028$; *APOE*- ϵ 4 carriers, $\beta=-0.11$, $p=0.19$; *APOE*- ϵ 4 non-carriers, $\beta=0.17$, $p=2E-04$.



Supplemental Figure 3. Correlation matrix for VEGF family gene expression and cell-type marker expression. *ENO2*, neurons; *OLIG2*, oligodendrocytes; *GFAP*, astrocytes; *CD34*, endothelial cells; *CD38*, microglia. *P<0.05, Pearson's correlation

Supplementary Table 1. VEGF associations with APOE genotype

Gene	β	SE	P
<i>FLT4</i>	0.10	0.06	0.09
<i>FLT1</i>	0.62	0.38	0.10
<i>NRP1</i>	-0.19	0.13	0.14
<i>KDR</i>	0.05	0.04	0.23
<i>PGF</i>	0.18	0.16	0.26
<i>VEGFC</i>	0.02	0.03	0.50
<i>VEGFD</i>	0.02	0.03	0.57
<i>VEGFA</i>	0.31	1.00	0.75
<i>NRP2</i>	-0.01	0.07	0.86
<i>VEGFB</i>	-0.40	2.67	0.88

Supplementary Table 2. VEGF x APOE expression on Cognition

Gene	Cross-Sectional				Longitudinal			
	β	SE	P	p.fdr	β	SE	P	p.fdr
VEGFC	-8.37E-04	4.67E-04	0.07	0.47	-9.40E-05	4.96E-05	0.06	0.54
NRP2	-2.13E-04	1.28E-04	0.10	0.47	-2.03E-05	1.37E-05	0.14	0.54
FLT1	-3.61E-05	2.44E-05	0.14	0.47	-2.59E-06	2.47E-06	0.29	0.67
FLT4	-1.77E-04	2.01E-04	0.38	0.78	-2.04E-05	2.13E-05	0.34	0.67
NRP1	-6.60E-05	8.76E-05	0.45	0.78	-1.31E-05	9.36E-06	0.16	0.54
VEGFB	1.89E-06	2.82E-06	0.50	0.78	1.02E-07	2.97E-07	0.73	0.81
PGF	2.82E-05	4.81E-05	0.56	0.78	2.69E-06	5.21E-06	0.61	0.76
VEGFD	-1.16E-04	2.53E-04	0.65	0.78	-6.48E-06	2.72E-05	0.81	0.81
VEGFA	-6.15E-06	1.61E-05	0.70	0.78	-1.47E-06	1.76E-06	0.40	0.67
KDR	-4.27E-05	2.52E-04	0.87	0.87	-1.62E-05	2.71E-05	0.55	0.76

Supplementary Table 3. APOE- ϵ 4 stratified VEGF expression associations with AD Diagnosis

Gene	Interaction				APOE- ϵ 4 Carriers				APOE- ϵ 4 Non-Carriers			
	β	SE	P	p.fdr	β	SE	P	p.fdr	β	SE	P	p.fdr
<i>NRP1</i>	0.77	0.27	3.70E-03	0.037	0.45	0.24	0.06	0.24	-0.31	0.12	0.01	0.03
<i>NRP2</i>	-1.11	0.44	0.01	0.06	-0.86	0.40	0.03	0.24	0.19	0.20	0.35	0.58
<i>VEGFA</i>	0.07	0.04	0.08	0.17	0.07	0.04	0.08	0.24	-0.01	0.01	0.65	0.73
<i>PGF</i>	-0.29	0.16	0.08	0.17	-0.07	0.14	0.59	0.85	0.18	0.09	0.047	0.16
<i>VEGFB</i>	-0.02	0.01	0.07	0.17	1.76E-03	0.01	0.84	0.86	0.02	0.01	6.66E-04*	0.01
<i>FLT1</i>	0.08	0.09	0.38	0.64	0.14	0.08	0.10	0.24	0.02	0.04	0.52	0.73
<i>FLT4</i>	-0.29	0.45	0.53	0.66	0.07	0.39	0.86	0.86	0.42	0.23	0.07	0.17
<i>VEGFD</i>	-0.55	0.82	0.50	0.66	-0.57	0.72	0.43	0.72	0.20	0.41	0.62	0.73
<i>KDR</i>	-0.21	0.70	0.76	0.85	0.28	0.68	0.68	0.85	0.08	0.33	0.80	0.80
<i>VEGFC</i>	0.10	1.21	0.93	0.93	0.93	1.14	0.41	0.72	0.49	0.47	0.30	0.58

Boldface signifies $P \leq 0.05$. *denotes results that were significant after adjusting for all models tested for main outcomes (cognition, diagnosis)

Supplementary Table 4. VEGF x APOE- ϵ 4 interactions on working memory performance

Gene	Interaction				APOE- ϵ 4 Carriers				APOE- ϵ 4 Non-Carriers			
	β	SE	P	p.fdr	β	SE	P	p.fdr	β	SE	P	p.fdr
<i>NRP1</i>	-0.29	0.08	2.46E-04	2.46E-03	-0.17	0.08	0.03	0.26	0.13	0.04	6.87E-04	0.01
<i>VEGFA</i>	-0.03	0.01	0.02	0.09	-0.02	0.01	0.05	0.26	0.01	4.73E-03	0.29	0.60
<i>KDR</i>	0.49	0.26	0.06	0.19	0.42	0.27	0.12	0.30	-0.10	0.12	0.42	0.60
<i>VEGFB</i>	0.01	0.00	0.16	0.40	5.93E-04	3.94E-03	0.88	0.93	-4.86E-03	1.80E-03	0.01	0.04
<i>FLT4</i>	-0.16	0.16	0.31	0.53	-0.26	0.16	0.10	0.30	-0.08	0.08	0.36	0.60
<i>FLT1</i>	-0.03	0.03	0.32	0.53	-0.03	0.02	0.21	0.42	-3.49E-03	0.01	0.79	0.79
<i>NRP2</i>	-0.04	0.15	0.81	0.94	0.02	0.15	0.89	0.93	0.06	0.07	0.42	0.60
<i>PGF</i>	-0.01	0.06	0.85	0.94	-0.04	0.06	0.57	0.93	-0.01	0.03	0.72	0.79
<i>VEGFD</i>	0.12	0.30	0.68	0.94	-0.03	0.29	0.93	0.93	-0.16	0.15	0.27	0.60
<i>VEGFC</i>	-0.02	0.38	0.96	0.96	-0.14	0.40	0.73	0.93	-0.06	0.17	0.72	0.79

Boldface signifies P≤0.05.

Supplementary Table 5. VEGF x APOE- ϵ 4 interactions on semantic memory performance

Gene	Interaction				APOE- ϵ 4 Carriers				APOE- ϵ 4 Non-Carriers			
	β	SE	P	p.fdr	β	SE	P	p.fdr	β	SE	P	p.fdr
<i>NRP1</i>	-0.31	0.10	3.35E-03	0.03	-0.19	0.12	0.10	0.24	0.13	0.05	0.01	0.03
<i>VEGFA</i>	-0.04	0.01	0.01	0.04	-0.03	0.02	0.04	0.21	0.01	0.01	0.37	0.62
<i>KDR</i>	0.74	0.34	0.03	0.09	0.81	0.39	0.04	0.21	0.10	0.15	0.48	0.69
<i>FLT4</i>	-0.37	0.21	0.07	0.19	-0.40	0.22	0.08	0.24	-0.04	0.10	0.73	0.73
<i>VEGFD</i>	0.48	0.37	0.20	0.33	0.36	0.41	0.38	0.64	-0.17	0.18	0.32	0.62
<i>VEGFB</i>	0.01	4.98E-03	0.19	0.33	0.00	0.01	0.97	0.97	-0.01	0.00	0.00	0.03
<i>FLT1</i>	-0.04	0.03	0.25	0.35	-0.04	0.04	0.29	0.58	0.01	0.02	0.73	0.73
<i>NRP2</i>	0.06	0.19	0.76	0.84	0.12	0.21	0.56	0.70	0.08	0.09	0.33	0.62
<i>VEGFC</i>	0.20	0.50	0.69	0.84	0.06	0.58	0.91	0.97	-0.08	0.21	0.71	0.73
<i>PGF</i>	-0.01	0.08	0.92	0.92	-0.07	0.09	0.45	0.65	-0.05	0.04	0.16	0.54

Boldface signifies P≤0.05.

Supplementary Table 6. VEGF x APOE- ϵ 4 interactions on perceptual orientation

Gene	Interaction				APOE- ϵ 4 Carriers				APOE- ϵ 4 Non-Carriers			
	β	SE	P	p.fdr	β	SE	P	p.fdr	β	SE	P	p.fdr
<i>NRP1</i>	-0.28	0.09	2.77E-03	0.03	-0.11	0.08	0.19	0.63	0.17	0.04	1.58E-04	1.58E-03
<i>NRP2</i>	-0.13	0.16	0.44	0.82	0.07	0.14	0.60	0.96	0.21	0.08	0.01	0.04
<i>FLT4</i>	-0.24	0.19	0.20	0.82	-0.23	0.16	0.15	0.63	0.01	0.10	0.92	0.96
<i>VEGFD</i>	-0.15	0.33	0.65	0.82	-0.05	0.28	0.87	0.96	0.07	0.17	0.67	0.95
<i>VEGFB</i>	2.70E-03	4.41E-03	0.54	0.82	-3.05E-03	3.89E-03	0.43	0.96	-4.50E-03	2.12E-03	0.03	0.11
<i>VEGFC</i>	-0.22	0.47	0.64	0.82	-0.30	0.42	0.49	0.96	0.01	0.20	0.96	0.96
<i>KDR</i>	0.28	0.30	0.35	0.82	0.43	0.27	0.11	0.63	0.19	0.14	0.17	0.33
<i>FLT1</i>	-0.02	0.03	0.60	0.82	4.73E-03	0.03	0.86	0.96	0.02	0.02	0.11	0.27
<i>VEGFA</i>	-4.01E-03	0.01	0.75	0.83	3.88E-03	0.01	0.72	0.96	0.01	0.01	0.20	0.33
<i>PGF</i>	0.01	0.07	0.87	0.87	6.78E-04	0.06	0.99	0.99	-0.01	0.03	0.76	0.95

Boldface signifies P≤0.05.

Supplementary Table 7. VEGF x APOE-ε4 interactions on episodic memory and perceptual speed

Gene	Episodic Memory				Perceptual Speed			
	β	SE	P	p.fdr	β	SE	P	p.fdr
VEGFA	-0.03	0.01	0.03	0.16	-4.31E-03	0.01	0.75	0.90
NRP1	-0.22	0.10	0.03	0.16	-0.15	0.10	0.15	0.74
VEGFB	0.01	4.56E-03	0.08	0.19	0.00	4.32E-03	0.78	0.90
FLT1	-0.06	0.03	0.06	0.19	-0.02	0.03	0.51	0.90
KDR	0.51	0.32	0.11	0.22	0.18	0.31	0.55	0.90
NRP2	0.24	0.18	0.19	0.27	0.02	0.18	0.90	0.90
FLT4	-0.27	0.20	0.18	0.27	-0.11	0.19	0.55	0.90
PGF	0.02	0.07	0.77	0.96	0.01	0.07	0.90	0.90
VEGFD	0.01	0.37	0.98	0.98	0.64	0.35	0.07	0.68
VEGFC	0.01	0.49	0.98	0.98	0.20	0.47	0.68	0.90

Supplementary Table 8. VEGF x APOE- ϵ 4 interactions on AD-related pathology

Note: Used square root of continuous variables (amyloid, tangles, nft, neuritic plaques)

Gene	Amyloid				Tangles				NFT				Neuritic Plaques			
	β	SE	DF	P	β	SE	DF	P	β	SE	DF	P	β	SE	DF	P
<i>FLT1</i>	-0.04	0.03	514	0.17	0.02	0.03	514	0.58	-3.0E-03	0.01	518	0.74	7.3E-04	0.01	518	0.95
<i>KDR</i>	-0.24	0.28	516	0.38	-0.39	0.31	516	0.20	-0.09	0.09	520	0.34	-0.01	0.13	520	0.91
<i>NRP1</i>	0.06	0.09	514	0.53	-0.01	0.10	514	0.90	-0.02	0.03	518	0.57	0.04	0.04	518	0.35
<i>VEGFA</i>	0.01	0.01	514	0.58	-0.01	0.01	514	0.31	-3.3E-03	3.8E-03	518	0.40	4.6E-03	0.01	518	0.39
<i>PGF</i>	0.03	0.07	513	0.66	0.10	0.07	513	0.18	0.01	0.02	517	0.76	0.01	0.03	517	0.81
<i>VEGFB</i>	-2.3E-03	4.1E-03	515	0.58	0.01	4.4E-03	515	0.23	5.3E-04	1.4E-03	519	0.70	6.5E-04	1.8E-03	519	0.72
<i>FLT4</i>	0.07	0.18	513	0.70	0.19	0.19	513	0.32	-0.02	0.06	517	0.79	0.03	0.08	517	0.73
<i>NRP2</i>	-0.05	0.17	515	0.79	-0.19	0.18	515	0.30	-0.10	0.05	519	0.07	-0.08	0.07	519	0.29
<i>VEGFC</i>	-0.13	0.42	514	0.75	-0.37	0.46	514	0.42	-0.17	0.14	518	0.21	-0.01	0.19	518	0.97
<i>VEGFD</i>	0.02	0.33	516	0.96	0.21	0.36	516	0.56	0.08	0.11	520	0.47	3.9E-03	0.15	520	0.98

Supplementary Table 9. VEGF x APOE- ϵ 4 interactions on nonAD-related pathology

Gene	TDP-43				CAA				Atherosclerosis				Arteriolosclerosis			
	β	SE	DF	P	β	SE	DF	P	β	SE	DF	P	β	SE	DF	P
<i>FLT4</i>	0.28	0.15	462	0.059	-0.42	0.31	503	0.17	-0.05	0.30	511	0.87	0.06	0.31	512	0.85
<i>VEGFB</i>	4.7E-03	3.4E-03	465	0.17	4.4E-03	0.01	505	0.54	-7.9E-04	0.01	513	0.91	-4.9E-03	0.01	514	0.49
<i>NRP2</i>	-0.17	0.13	464	0.19	-0.05	0.29	505	0.88	-0.40	0.28	513	0.15	-0.31	0.28	514	0.27
<i>FLT1</i>	0.02	0.02	463	0.32	4.9E-03	0.05	504	0.92	-3.7E-03	0.05	512	0.94	0.03	0.05	513	0.55
<i>NRP1</i>	0.04	0.07	463	0.53	-0.08	0.15	504	0.61	-0.05	0.14	512	0.72	0.01	0.16	513	0.92
<i>PGF</i>	0.03	0.05	462	0.54	0.14	0.11	503	0.21	-0.04	0.11	511	0.68	-0.22	0.11	512	0.05
<i>VEGFA</i>	1.1E-03	0.01	463	0.90	0.03	0.02	504	0.12	-0.01	0.02	512	0.57	0.01	0.02	513	0.48
<i>VEGFC</i>	-0.02	0.32	463	0.95	-0.83	0.73	504	0.25	1.10	0.72	512	0.13	0.91	0.76	513	0.23
<i>VEGFD</i>	0.01	0.27	465	0.96	0.01	0.57	506	0.99	3.6E-03	0.55	514	0.99	0.18	0.59	515	0.76
<i>KDR</i>	-0.01	0.23	465	0.97	-0.07	0.48	506	0.88	0.19	0.46	514	0.68	-0.08	0.50	515	0.87

Supplementary Table 9 cont. VEGF x APOE-ε4 interactions on nonAD-related pathology

Gene	Hippocampal Sclerosis				Gross infarcts				Microinfarcts			
	β	SE	DF	P	β	SE	DF	P	β	SE	DF	P
<i>FLT1</i>	0.16	0.10	514	0.099	0.07	0.06	519	0.28	0.02	0.06	519	0.69
<i>KDR</i>	1.53	0.94	516	0.101	-0.18	0.71	521	0.80	0.23	0.61	521	0.70
<i>FLT4</i>	0.75	0.61	513	0.22	0.08	0.42	518	0.86	0.29	0.37	518	0.44
<i>PGF</i>	0.15	0.21	513	0.47	0.10	0.16	518	0.52	-0.07	0.14	518	0.62
<i>VEGFC</i>	-0.97	1.47	514	0.51	-0.50	1.00	519	0.62	1.26	0.88	519	0.15
<i>VEGFD</i>	0.65	1.29	516	0.62	-1.29	0.86	521	0.13	-0.38	0.69	521	0.59
<i>NRP2</i>	-0.26	0.60	515	0.66	0.16	0.39	520	0.68	0.21	0.35	520	0.55
<i>VEGFA</i>	-0.02	0.04	514	0.67	3.1E-03	0.03	519	0.91	0.01	0.02	519	0.84
<i>NRP1</i>	-0.09	0.33	514	0.79	0.04	0.22	519	0.85	-0.02	0.20	519	0.91
<i>VEGFB</i>	-1.7E-03	0.01	515	0.90	-0.01	0.01	520	0.59	1.7E-03	0.01	520	0.84

Supplementary Table 10. VEGFA and NRP1 isoform x APOE-ε4 interactions on cross-sectional global cognition

Isoform	Protein-coding	β	SE	P.fdr	Isoform	Protein-coding	β	SE	P.fdr
VEGFA-212	No	-1.37	0.37	0.007	<i>NRP1-214</i>	Yes	1.17	0.61	0.10
VEGFA-211	No	-1.07	0.36	0.028	<i>VEGFA-201</i>	Yes	-0.55	0.30	0.13
NRP1-202	Yes	-4.42	1.53	0.028	<i>NRP1-210</i>	Yes	-0.53	0.40	0.29
NRP1-201	Yes	-0.37	0.13	0.028	<i>VEGFA-218</i>	Yes	-1.86	1.48	0.32
VEGFA-205	Yes	-0.05	0.02	0.028	<i>VEGFA-222</i>	Yes	-0.27	0.27	0.47
VEGFA-216	No	-0.22	0.08	0.030	<i>NRP1-212</i>	Yes	0.96	1.24	0.56
VEGFA-207	Yes	-3.32	1.28	0.033	<i>VEGFA-204</i>	Yes	-0.22	0.29	0.56
NRP1-208	Yes	-9.13	3.55	0.033	<i>VEGFA-209</i>	Yes	-0.11	0.15	0.56
NRP1-209	Yes	-1.12	0.44	0.033	<i>NRP1-203</i>	Yes	3.40	4.88	0.57
NRP1-205	Yes	-1.79	0.72	0.033	<i>VEGFA-206</i>	Yes	0.10	0.16	0.60
VEGFA-214	No	-0.37	0.15	0.041	<i>NRP1-207</i>	Yes	-0.06	0.11	0.60
VEGFA-215	No	-0.08	0.03	0.053	<i>VEGFA-225</i>	Yes	-0.05	0.48	0.95
NRP1-204	Yes	1.90	0.98	0.10	<i>NRP1-213</i>	Yes	-0.15	2.80	0.96

Boldface signifies corrected P.fdr≤0.05.

P.fdr column contains p-values corrected for 26 tests using the false discovery rate (FDR).

Supplementary Table 11. Cross-sectional VEGF x APOE-ε4 interactions on global cognition adjusted for cell-type effects

Note: ENO2 was used as the marker for neurons, CD68 for microglia, OLIG2 for oligodendrocytes, GFAP for astrocytes, and CD34 for endothelial cells.

Part 1: Correction for ENO2 levels

Gene	Cross-sectional Results			Cross-sectional Results - ENO2 Covariate			Cross-sectional Results - Adjusted for ENO2		
	β	SE	P.fdr	β	SE	P.fdr	β	SE	P.fdr
NRP1	-0.29	0.08	0.004	-0.29	0.08	0.003	-0.29	0.08	0.004
VEGFA	-0.03	0.01	0.026	-0.03	0.01	0.016	-0.03	0.01	0.026
FLT1	-0.06	0.03	0.12	-0.06	0.03	0.09	-0.07	0.03	0.041
FLT4	-0.24	0.16	0.30	-0.25	0.16	0.32	-0.43	0.20	0.07
VEGFB	0.01	0.004	0.30	0.01	0.00	0.34	0.01	0.01	0.23
KDR	0.29	0.26	0.43	0.29	0.25	0.42	0.31	0.28	0.46
VEGFD	0.24	0.31	0.62	0.28	0.30	0.51	0.23	0.30	0.57
PGF	-0.02	0.06	0.81	-0.03	0.06	0.75	-0.07	0.08	0.48
VEGFC	-0.14	0.39	0.81	-0.13	0.39	0.75	-0.21	0.42	0.68
NRP2	0.02	0.15	0.88	0.05	0.15	0.75	0.02	0.16	0.91

Boldface signifies corrected P.fdr≤0.05.

P.fdr column contains p-values corrected for 10 tests using the false discovery rate (FDR).

Part 2: Adjusting for expression of other cell-type markers

	Cross-sectional Results			Cross-sectional Results - OLIG2, GFAP, CD68, and CD34 Covariates			Cross-sectional Results - Adjusted for OLIG2			Cross-sectional Results - Adjusted for GFAP			Cross-sectional Results - Adjusted for CD68			Cross-sectional Results - Adjusted for CD34		
Gene	β	SE	P.fdr	β	SE	P.fdr	β	SE	P.fdr	β	SE	P.fdr	β	SE	P.fdr	β	SE	P.fdr
<i>NRP1</i>	-0.29	0.08	0.004	-0.30	0.08	0.003	-0.29	0.08	0.004	-0.30	0.09	0.005	-0.25	0.08	0.028	-0.29	0.08	0.003
<i>VEGFA</i>	-0.03	0.01	0.026	-0.03	0.01	0.031	-0.03	0.01	0.027	-0.02	0.01	0.13	-0.02	0.01	0.14	-0.03	0.01	0.011
<i>FLT1</i>	-0.06	0.03	0.12	-0.07	0.03	0.057	-0.08	0.03	0.036	-0.04	0.03	0.31	-0.04	0.03	0.30	-0.06	0.03	0.18
<i>FLT4</i>	-0.24	0.16	0.30	-0.22	0.17	0.43	-0.29	0.18	0.24	-0.14	0.17	0.68	-0.13	0.17	0.63	-0.27	0.19	0.28
<i>VEGFB</i>	0.01	0.004	0.30	0.01	0.00	0.43	0.01	0.00	0.24	0.01	0.00	0.31	0.01	0.00	0.30	0.01	0.00	0.22
<i>KDR</i>	0.29	0.26	0.43	0.19	0.27	0.73	0.34	0.28	0.39	0.39	0.26	0.31	0.32	0.26	0.44	0.45	0.29	0.23
<i>VEGFD</i>	0.24	0.31	0.62	0.15	0.31	0.79	0.25	0.30	0.60	0.22	0.31	0.68	0.18	0.31	0.70	0.22	0.31	0.68
<i>PGF</i>	-0.02	0.06	0.81	-0.04	0.07	0.73	-0.04	0.07	0.66	0.01	0.06	0.82	0.00	0.06	1.00	-0.02	0.07	0.84
<i>VEGFC</i>	-0.14	0.39	0.81	-0.13	0.42	0.85	-0.13	0.40	0.83	0.24	0.41	0.69	0.08	0.41	0.93	0.10	0.43	0.84
<i>NRP2</i>	0.02	0.15	0.88	0.01	0.16	0.97	0.02	0.15	0.87	0.04	0.16	0.82	0.15	0.16	0.58	0.03	0.15	0.84

Supplementary Table 12. Longitudinal *VEGF* x *APOE-ε4* interactions on global cognition adjusted for cell-type effects

Note: ENO2 was used as the marker for neurons, CD68 for microglia, OLIG2 for oligodendrocytes, GFAP for astrocytes, and CD34 for endothelial cells.

Part 1: Adjusting for *ENO2* expression

Gene	Longitudinal Results			Longitudinal Results - <i>ENO2</i> Covariate			Longitudinal Results - Adjusted for <i>ENO2</i>		
	β	SE	P.fdr	β	SE	P.fdr	β	SE	P.fdr
<i>NRP1</i>	-0.02	0.01	0.44	-0.02	0.01	0.46	-0.01	0.01	0.57
<i>KDR</i>	0.04	0.03	0.44	0.04	0.03	0.46	0.04	0.03	0.57
<i>VEGFB</i>	0.001	4.16E-04	0.44	5.9E-04	4.2E-04	0.46	4.0E-04	6.1E-04	0.64
<i>VEGFA</i>	-0.002	0.001	0.44	-1.6E-03	1.2E-03	0.46	-1.5E-03	1.2E-03	0.57
<i>VEGFD</i>	0.04	0.03	0.57	0.04	0.03	0.56	0.03	0.03	0.57
<i>NRP2</i>	0.01	0.02	0.82	0.01	0.02	0.83	0.01	0.02	0.73
<i>VEGFC</i>	0.02	0.04	0.87	0.02	0.04	0.86	1.1E-03	0.05	0.98
<i>FLT4</i>	-0.01	0.02	0.90	-0.01	0.02	0.90	-0.03	0.02	0.57
<i>FLT1</i>	-4.65E-04	0.003	0.92	-4.3E-04	2.9E-03	0.93	-2.1E-03	3.2E-03	0.64
<i>PGF</i>	0.001	0.01	0.92	6.1E-04	0.01	0.93	-0.01	0.01	0.57

Part 2: Adjusting for expression of other cell-type markers

	Longitudinal Results			Longitudinal Results - <i>OLIG2</i> , <i>GFAP</i> , <i>CD68</i> , and <i>CD34</i> Covariates			Longitudinal Results - Adjusted for <i>OLIG2</i>			Longitudinal Results - Adjusted for <i>GFAP</i>		
Gene	β	SE	P.fdr	β	SE	P.fdr	β	SE	P.fdr	β	SE	P.fdr
<i>NRP1</i>	-0.02	0.01	0.44	-0.02	0.01	0.64	-0.01	0.01	0.49	-0.02	0.01	0.53
<i>KDR</i>	0.04	0.03	0.44	0.04	0.03	0.64	0.05	0.03	0.49	0.05	0.03	0.53
<i>VEGFB</i>	0.001	4.16E-04	0.44	5.7E-04	4.4E-04	0.64	7.3E-04	5.2E-04	0.49	5.6E-04	4.2E-04	0.53
<i>VEGFA</i>	-0.002	0.001	0.44	-1.3E-03	1.2E-03	0.64	-1.5E-03	1.2E-03	0.49	-1.2E-03	1.2E-03	0.53
<i>VEGFD</i>	0.04	0.03	0.57	0.03	0.03	0.64	0.04	0.03	0.56	0.04	0.03	0.53
<i>NRP2</i>	0.01	0.02	0.82	0.01	0.02	0.73	0.01	0.02	0.71	0.01	0.02	0.62
<i>VEGFC</i>	0.02	0.04	0.87	0.03	0.05	0.73	0.02	0.05	0.71	0.05	0.05	0.53
<i>FLT4</i>	-0.01	0.02	0.90	-1.4E-03	0.02	0.94	-0.01	0.02	0.71	-1.3E-03	0.02	0.95
<i>FLT1</i>	-4.65E-04	0.003	0.92	-8.3E-04	3.2E-03	0.94	-1.8E-03	3.3E-03	0.71	7.8E-04	3.0E-03	0.88
<i>PGF</i>	0.001	0.01	0.92	-6.4E-04	0.01	0.94	-2.1E-03	0.01	0.79	2.8E-03	0.01	0.87

Part 3: Adjusting for expression of other cell-type markers

Gene	Longitudinal Results			Longitudinal Results - Adjusted for CD68			Longitudinal Results - Adjusted for CD34		
	β	SE	P.fdr	β	SE	P.fdr	β	SE	P.fdr
<i>NRP1</i>	-0.02	0.01	0.44	-0.01	0.01	0.49	-0.01	0.01	0.37
<i>KDR</i>	0.04	0.03	0.44	0.04	0.03	0.49	0.05	0.03	0.37
<i>VEGFB</i>	0.001	4.16E-04	0.44	6.2E-04	4.2E-04	0.49	6.7E-04	4.4E-04	0.37
<i>VEGFA</i>	-0.002	0.001	0.44	-1.2E-03	1.2E-03	0.51	-1.7E-03	1.2E-03	0.37
<i>VEGFD</i>	0.04	0.03	0.57	0.04	0.03	0.51	0.03	0.03	0.62
<i>NRP2</i>	0.01	0.02	0.82	0.02	0.02	0.49	0.01	0.02	0.71
<i>VEGFC</i>	0.02	0.04	0.87	0.04	0.05	0.54	0.04	0.05	0.64
<i>FLT4</i>	-0.01	0.02	0.90	-6.3E-04	0.02	0.98	-0.01	0.02	0.94
<i>FLT1</i>	-4.65E-04	0.003	0.92	6.9E-05	3.0E-03	0.98	-2.6E-04	3.3E-03	0.94
<i>PGF</i>	0.001	0.01	0.92	2.2E-03	0.01	0.94	6.0E-04	0.01	0.94