SUPPLEMENTAL MATERIAL

Supplementary Table I. Baseline Characteristics of Stroke/TIA Study Samples based on BDNF quartiles

Clinical Characteristics	Entire Sample N=3440	Q1 BDNF N=847	Q2-Q3-Q4 BDNF N=2593	p
Women,%	56%	50%	59%	**<0.001**
Age, years*	65±11	66±11	64±11	**<0.001**
Systolic Blood Pressure, mmHg*	130±20	130±21	129±20	0.214
Anti-hypertensive medication, %	36%	37%	36%	0.506
Current smokers, %	11%	9%	12%	**0.015**
Diabetes mellitus, %	12%	14%	12%	0.070
Prevalent cardiovascular disease, %	14%	16%	13%	0.066
Atrial fibrillation, %	3.8%	5.8%	3.2%	**<0.001**

* mean+SD.

Supplementary Table II. Baseline Characteristics of NP Study Samples based on BDNF quartiles

Clinical Characteristics	Entire Sample N=2104	Q1 BDNF N=498	Q2-Q3-Q4 BDNF N=1606	p
Women,%	55%	48%	57%	**<0.001**
Age, years*	61±9	62±10	61±9	**<0.001**
Systolic Blood Pressure, mm Hg*	126±19	127±19	126±18	0.161
Anti-hypertensive medication, %	31%	32%	30%	0.354
Current smokers, %	11%	9%	12%	0.067
Diabetes mellitus, %	11%	15%	10%	**0.007**
Prevalent cardiovascular disease, %	10%	12%	9%	0.077
Atrial fibrillation, %	3%	3%	2%	0.233
Total cholesterol, mg/dl	201±37	195±36	203±37	**<0.001**
Total homocysteine, μmol/L	7.8 [6.5,9.5]	7.7 [6.3,9.7]	7.8 [6.6,9.5]	0.584
College Degree	39%	42%	38%	0.095
Depression (CES-D score)**	3 [1,7]	3 [1,7]	3 [1,7]	0.805
Physical activity index (PAI) **	37 [33,41]	36 [34,41]	37 [33,41]	0.920
**Brain MRI Measures**				
WMHI (Log)	-3.0 ± 1.0	-2.9 ± 1.1	-3.1 ± 1.0	**0.001**
Extensive WMH	12%	14%	11%	0.142
**Cognitive Measures**				
VRd	8.1±3.4	7.7±3.4	8.3±3.3	**0.002**
TrB-TrA**	0.67 [0.45,0.98]	0.72 [0.48,1.07]	0.65 [0.43,0.97]	**0.042**

* mean+SD.
** Comparison made using log-transformed measures

Supplementary Table III. Baseline Characteristics of MRI Study Samples based on BDNF quartiles

Clinical Characteristics	Entire Sample N=1863	Q1 BDNF N=440	Q2-Q3-Q4 BDNF N=1423	p
Women,%	55%	48%	57%	**0.002**
Age, years*	61±9	62±10	61±9	**0.001**
Systolic Blood Pressure, mm Hg*	126±19	127±19	125±18	0.069
Anti-hypertensive medication, %	30%	30%	30%	0.908
Current smokers, %	11%	8%	12%	**0.039**
Diabetes mellitus, %	12%	14%	11%	**0.037**
Prevalent cardiovascular disease, %	9%	11%	9%	0.095
Atrial fibrillation, %	2%	3%	2%	0.120
Total cholesterol, mg/dl	201±37	195±36	203±37	**<0.001**
Total homocysteine, µmol/L	7.8 [6.5,9.5]	7.7 [6.3,9.7]	7.8 [6.6,9.5]	0.621
College Degree	39%	42%	39%	0.210
Depression (CES-D score)**	3 [1,7]	3 [1,7]	3 [1,7]	0.951
Physical activity index (PAI) **	37 [33,41]	37 [34,41]	37 [33,41]	0.794
Brain MRI Measures				
WMHI (Log)	-3.0 ± 1.0	-2.9 ± 1.1	-3.1 ± 1.0	**0.001**
Extensive WMH	12%	14%	11%	0.142
Cognitive Measures				
VRd	8.2±3.3	7.8±3.4	8.4±3.3	**0.002**
TrB-TrA**	0.67 [0.45-0.98]	0.73 [0.50-1.08]	0.65 [0.43-0.95]	**0.015**

*mean+SD.
** Comparison made using log-transformed measures

Supplementary Table IV. Association of serum BDNF and logVEGF and risk of stroke/ only

Case/N			All Stroke (151/3513)*	
			HR [95% CI]	P
BDNF	**Per SD**	**Model A**	0.91[0.77-1.08]	0.28
		Model B	0.93[0.78-1.10]	0.38
	Q1	**Model A**	1.00	REF
	Q2		0.96 [0.64-1.45]	0.86
	Q3		**0.58 [0.36-0.94]**	**0.028**
	Q4		0.82 [0.53-1.31]	0.43
	Q1vsQ2-Q4	**Model A**	1.26 [0.89-1.78]	0.20
		Model B	1.23[0.87-1.75]	0.24
logVEGF	**Per SD**	**Model A**	**1.22[1.03-1.43]**	**0.019**
		Model B	**1.23[1.05-1.46]**	**0.013**

Model A: adjusted for age and sex
Model B: adjusted for systolic blood pressure, prevalent CVD, diabetes mellitus, atrial fibrillation, current smoking
*Study Sample 1b; over a 10-year follow-up period we observed 151 incident strokes
(129 ischemic, 21 hemorrhagic and one definite stroke of uncertain etiology

Supplementary Table V. Additional effect of serum BDNF and VEGF on risk of stroke/TIA

†Model B		HR [95% CI]	P	NRI [95%CI]	C-Statistics
BDNF	Q1 vs Q2-Q4	**1.47[1.09-2.00]**	**0.012**	**0.199 [0.023-0.384]**	0.79 [0.76-0.81]
Log(VEGF)	Per SD	**1.21[1.04-1.40]**	**0.012**	**0.234 [0.067-0.401]**	0.79 [0.76-0.82]
Model with both markers included					
BDNF	Q1 vs Q2-Q4	**1.62[1.20-2.20]**	**0.002**	**0.274 [0.090-0.449]**	0.79 [0.76-0.82]
Log(VEGF)	Per SD	**1.25[1.08-1.45]**	**0.003**		

†Model B: Model A additionally adjusted for SBP, CVD, DM, AF and SMK

Note: the interaction between log(VEGF) and Q1-BDNF has p=0.465.