SUPPLEMENTARY MATERIALS

Strengths and Limitations

There are several important considerations when interpreting the present findings. First, SI was evaluated according to the suicide-related items on the MADRS, rather than via an instrument assessing SI separately from depressed mood. Nevertheless, estimation of SI from the MADRS is a well-validated approach that has been used in previous studies.[1] Second, the dependent outcome of these analyses was SI, and not suicidal behavior. The majority of previous epigenetic studies on suicide have been performed in patients who have attempted or completed suicide.[2] However, SI is known to be a predictor of more severe suicidal behavior, including future suicide attempts.[3] Moreover, irrespective of the presence of a suicide attempt, the inherent burden of SI is considerable.[4] For these reasons, it is logical to investigate the association between BDNF methylation and SI in ACS patients, but it is difficult to generalize these findings to suicidal behavior overall. Third, patients lost to follow-up were older and had worse cardiac function in this study. Death from suicide was not recorded in those lost to follow-up. These disadvantages may contribute to the results of the follow-up analyses. Finally, the present study investigated a limited number of CpG sites in BDNF exon VI, without measuring of the expression level of BDNF. This limitation may have skewed associations toward null findings, masking differences between the groups and rendering it difficult to ascertain both the functional effects of BDNF methylation and any change in the longitudinal associations between BDNF methylation and SI.

The present study also had several strengths. It was the first prospective investigation to evaluate the epigenetic factors associated with SI in ACS patients; moreover, SI and other covariates associated with SI were assessed at similar time points (within 2 weeks and 1 year after ACS) and in a large number of patients. This reduced the potential for heterogeneity associated with differences in assessment time after ACS. Finally, participants were enrolled successively from a pool of eligible patients, all of whom were hospitalized for treatment of recent ACS. This reduced the probability of selection bias and increased the generalizability of the findings.

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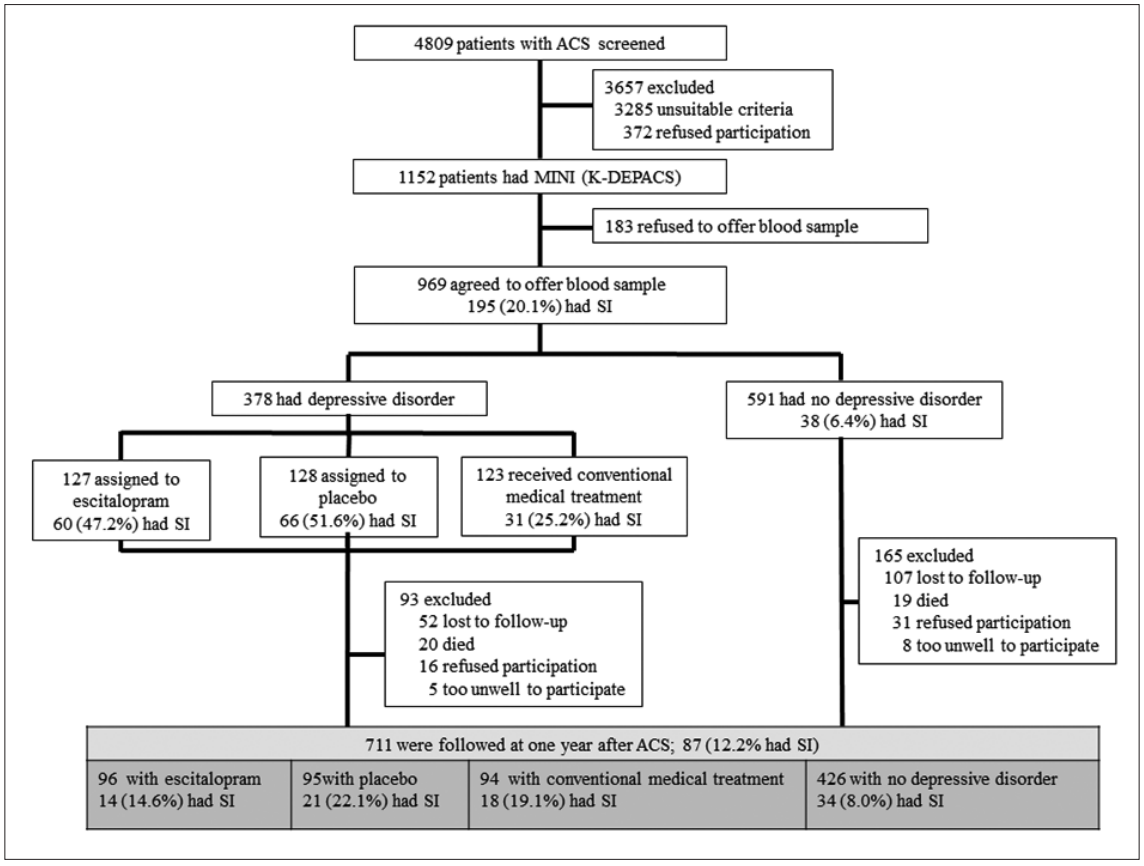
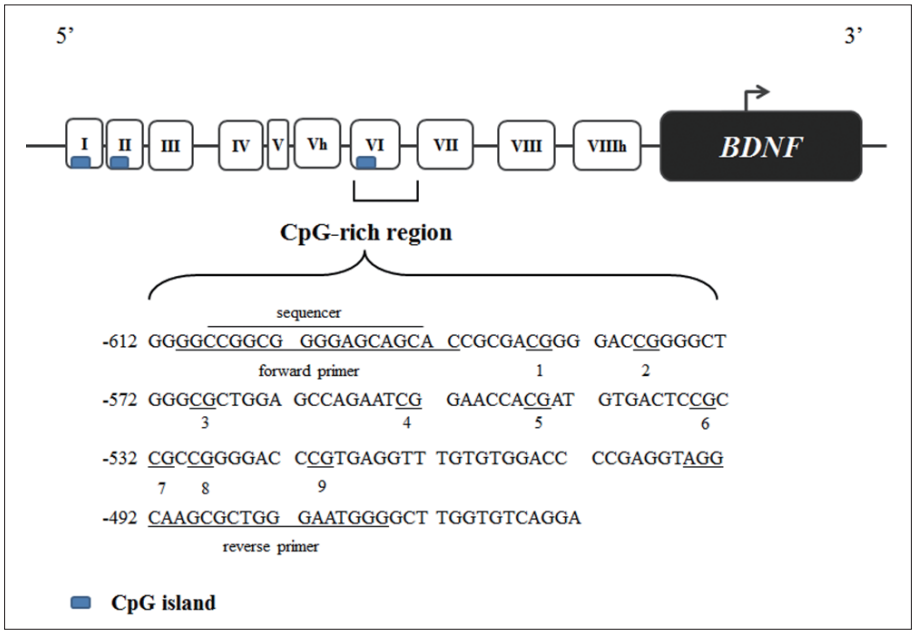
Supplementary Table 1. Baseline sociodemographic and clinical characteristics by suicidal ideation status

	Baseline sample (N=969)			Follow-up sample (N=711)		
	No suicidal ideation (N=774)	Suicidal ideation (N=195)	p-value†	No suicidal ideation (N=624)	Suicidal ideation (N=87)	p-value†
Socio-demographic characteristics						
Age, mean (SD) years	58.0 (11.3)	58.9 (10.6)	0.315	57.6 (10.7)	57.4 (11.1)	0.855
Sex, N (%) female	201 (26.0)	68 (34.9)	0.013*	163 (26.1)	33 (37.9)	0.021*
Education, mean (SD) year	10.0 (4.7)	9.1 (4.4)	0.012*	10.0 (4.6)	9.2 (4.8)	0.118
Living alone, N (%) yes	71 (9.2)	21 (10.8)	0.497	49 (7.9)	11 (12.6)	0.132
Housing, N (%) rented	109 (14.1)	41 (21.0)	0.017*	102 (16.3)	20 (23.0)	0.124
Currently unemployed, N (%)	279 (36.0)	89 (45.6)	0.014*	213 (34.1)	38 (43.7)	0.081
Depression characteristics, N (%)						
Previous depression	19 (2.5)	15 (7.7)	<0.001*	24 (3.8)	6 (6.9)	0.247
Family history of depression	15 (1.9)	8 (4.1)	0.108	14 (2.2)	6 (6.9)	0.026*
DSM-IV depression	221 (28.6)	157 (80.5)	<0.001*	232 (37.2)	53 (60.9)	<0.001*
Cardiac risk factors, N (%)						
Previous ACS	30 (3.9)	9 (4.6)	0.639	25 (4.0)	6 (6.9)	0.255
Family history of ACS	24 (3.1)	7 (3.6)	0.729	18 (2.9)	6 (6.9)	0.103
Hypertension	360 (46.5)	98 (50.3)	0.349	282 (45.2)	42 (48.3)	0.588
Diabetes mellitus	144 (18.6)	47 (24.1)	0.085	118 (18.9)	24 (27.6)	0.058
Hypercholesterolemia	384 (49.6)	102 (52.3)	0.501	333 (53.4)	50 (57.5)	0.472
Obesity	341 (44.1)	74 (37.9)	0.123	280 (44.9)	35 (40.2)	0.414
Current smoker	297 (38.4)	69 (35.4)	0.442	247 (39.6)	33 (37.9)	0.768
Current cardiac status						
Killip class >1, N (%)	132 (17.1)	36 (18.5)	0.643	101 (16.2)	13 (14.9)	0.767
LVEF, mean (SD) %	61.2 (11.4)	61.1 (10.8)	0.911	61.4 (11.0)	59.7 (11.8)	0.183
Heart rate, mean (SD) beat/min	74.7 (12.1)	76.1 (15.8)	0.230	75.1 (12.7)	74.5 (13.7)	0.710
Troponin I, mean (SD) mg/dL	9.5 (15.0)	11.5 (14.7)	0.092	10.2 (15.7)	10.9 (17.4)	0.724
CK-MB, mean (SD) mg/dL	16.8 (38.2)	19.7 (33.3)	0.333	18.1 (39.1)	16.6 (35.5)	0.736
Intervention group, N (%)						
Escitalopram				82 (35.3)	14 (26.4)	0.404/0.001*
Placebo				74 (31.9)	21 (39.6)	
Non-participants				76 (32.8)	18 (34.0)	

*statistical significance after Bonferroni's correction, †p-values were determined using t-tests or χ^2 tests as appropriate. HAMD: Hamilton Depression Rating Scale, ACS: acute coronary syndrome, LVEF: left ventricular ejection fraction, CK-MB: Creatine kinase-MB



Supplementary Figure 1. Flow diagram for the recruitment process. ACS: acute coronary syndrome, MINI: Mini-International Neuropsychiatric Interview, SI: suicidal ideation, K-DEPACS: Korean DEPression in Acute Coronary Syndrome study, EsDEPACS: Escitalopram for DEPression in Acute Coronary Syndrome study.



Supplementary Figure 2. Brain-derived neurotrophic factor (BDNF) exon VI cytosine-guanine (CpG) regions analyzed for methylation percentage. The CpGs are underlined and numbered. Forward and backward primers are shown, as well as sequencers. The genetic sequence is calculated from the transcriptional start site. CpG islands were determined as sequences of at least 200 pairs of bases with a GC percentage greater than 50%.