

**Appendix 1** to Steiger H, Booij L, Kahan E, et al. A longitudinal, epigenome-wide study of DNA methylation in anorexia nervosa: results in actively ill, partially weight-restored, long-term remitted and non-eating-disordered women. *J Psychiatry Neurosci* 2019.

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**Table S1.** Inter-rater agreement statistics for comorbid diagnoses. †

<i>Disorder</i>	<i>% inter-rater agreement</i>	<i>Prevalence Index</i>	<i>Bias Index</i>	<i>KAPPA Coefficient (K)</i>	<i>Prevalence and Bias adjusted coefficient (PABAK)</i>	<i>N</i>
MDE	96%	0.80	-0.04	0.78	<b>0.92</b>	25
Dysthymia	96%	0.92	0.04	*	<b>0.92</b>	24
PD	92%	0.84	0	0.46	<b>0.84</b>	25
Agoraphobia	92%	0.92	0	-0.04	<b>0.84</b>	25
SAD	100%	0.92	0	1.00	<b>1</b>	25
GAD	96%	0.79	-0.04	0.78	<b>0.92</b>	24
OCD	100%	0.92	0	1.00	<b>1</b>	24
Substance Dependence	100%	1	0	*	<b>1</b>	24
Substance Abuse	100%	1	0	*	<b>1</b>	24
PTSD	100%	0.87	0	1.00	<b>1</b>	15
OCPD	100%	0.30	0	1.00	<b>1</b>	23
BPD	96%	0.96	0.04	*	<b>0.91</b>	23

**Table S1.** MDE = Major Depressive Episode; PD = Panic Disorder (with or without agoraphobia); SAD = Social Anxiety Disorder; GAD = Generalized Anxiety Disorder; OCD = Obsessive Compulsive Disorder; PTSD=Posttraumatic Stress Disorder; OCPD = Obsessive Compulsive Personality Disorder; BPD = Borderline Personality Disorder.

† Prevalence and Bias adjusted Coefficients (PABAK) (indicated in bold) are used for interpretation due to the imbalanced distribution of the marginal totals (i.e. high Prevalence Index and small Bias index). Prevalence Index, Bias Index and the KAPPA and PABAK coefficients are calculated according to formulas in Byrt et al<sup>1</sup> and Flight & Julious<sup>2</sup>.

\* kappa cannot be calculated because the variable tested is a constant.

In each of the inter-rater analyses; the sample consists of approximately 54% AN-active; 21% AN-remitted and 25% NED.

<sup>1</sup> Byrt T, Bishop J, Carlin JB. Bias, prevalence and kappa. *J Clin Epidemiol* 1993;46(5):423-9.

<sup>2</sup> Flight L, Julious SA. The disagreeable behaviour of the kappa statistic. *Pharm Stat* 2015;14(1):74-78.

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Table S2

Probes (and corresponding genes) on which methylation levels differ significantly ( $Q < .01$ ) in ANOVA and pairwise comparisons of AN-Active vs. AN-Remitted vs. NED. (See footnote 1 below)

CpG	Gene	Name	Function	ANOVA	AN-Active vs. NED		AN-Active vs. AN-Remitted	
				Q-value	Effec t	Q value	Effec t	Q value
cg172725 49	EML6	echinoderm microtubule associated protein like 6		3.17E-07	0.058 9	1.29E-05	- 0.058 1	1.11E-05
cg003238 42	ZNF60 8	zinc finger protein 608		3.17E-07	0.046 8	8.32E-05	- 0.047 5	3.52E-05
cg069830 52	LRRC 8D	leucine rich repeat containing 8 VRAC subunit D		8.66E-07	0.042 5	8.32E-05	- 0.039 8	0.000141
cg040428 61	HTR2 B	5- hydroxytrypta mine receptor 2B	This gene encodes one of the several different receptors for 5- hydroxytryptamine (serotonin). Serotonin is a biogenic hormone that functions as a neurotransmitter, a hormone, and a mitogen.	8.66E-07	0.040 3	0.00760	- 0.070 8	8.47E-07
cg043952 30	MCF2 L	MCF.2 cell line derived transforming sequence like	This gene encodes a guanine nucleotide exchange factor that plays a role in the Rho/Rac signaling pathways.	8.66E-07			- 0.109	1.21E-07
cg144222 40	FTSJD 2	cap methyltransfera se 1		2.16E-06	0.057 6	9.33E-05	- 0.049 1	0.000609
cg251971 94	CCDC 48	EF-hand and coiled-coil domain containing 1		2.70E-06	0.051 9	0.00194	- 0.056 0	0.000109

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Table S2 *continued*

CpG	Gene	Name	Function	ANOVA	AN-Active vs. NED		AN-Active vs. AN-Remitted	
				Q-value	Effec t	Q value	Effec t	Q value
cg190033 37	KRT1 7	keratin 17	This gene encodes the type I intermediate filament chain keratin 17, expressed in nail bed, hair follicle, sebaceous glands, and other epidermal appendages.	3.81E-06			0.046 0	8.51E-06
cg113228 79	GATS L1	GATS protein like 2		4.92E-06			- 0.084 4	3.78E-06
cg006683 37	NRXN 2	neurexin 2	The products of the encoded genes function as cell adhesion molecules and receptors in the vertebrate nervous system.	7.81E-06			- 0.101	8.47E-07
cg230111 94	SORB S1	sorbin and SH3 domain containing 1	This gene encodes a CBL-associated protein which functions in the signaling and stimulation of insulin. Mutations in this gene may be associated with human disorders of insulin resistance	1.03E-05	0.060 0	0.00933	- 0.083 3	3.69E-06
cg092975 14	CAM KK2	calcium/calmodulin dependent protein kinase kinase 2	This gene has its strongest expression in the brain and influences signalling cascades involved with learning and memory, neuronal differentiation and migration, neurite outgrowth, and synapse formation.	1.03E-05			0.075 5	5.30E-06
cg046896 76	PRKY	protein kinase, Y-linked, pseudogene		1.03E-05			0.066 1	1.11E-05

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cg081063 19	ZFAN D3	zinc finger AN1-type containing 3		1.19E-05	0.047 7	0.00963	- 0.064 6	3.57E-05
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Table S2 *continued*

CpG	Gene	Name	Function	<u>ANOVA</u>	<u>AN-Active vs. NED</u>		<u>AN-Active vs. AN-Remitted</u>	
				Q-value	Effec t	Q value	Effec t	Q value
cg262324 51	LETM 2	leucine zipper and EF-hand containing transmembrane protein 2		1.19E-05			- 0.034 5	5.30E-06
cg032336 24	MSI2	musashi RNA binding protein 2	The encoded protein is a transcriptional regulator that targets genes involved in development and cell cycle regulation.	1.98E-05	0.050 0	0.000553	- 0.051 8	9.12E-05
cg028001 00	AUTS 2	AUTS2, activator of transcription and developmental regulator	This gene has been implicated in neurodevelopment and as a candidate gene for numerous neurological disorders, including autism spectrum disorders, intellectual disability, and developmental delay.	2.15E-05			- 0.058 3	3.57E-05
cg014894 41	MAPK 8IP3	mitogen- activated protein kinase 8 interacting protein 3		2.15E-05			0.047 2	7.51E-05

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cg082554 75	CDT1	chromatin licensing and DNA replication factor 1	The protein encoded by this gene is involved in the formation of the pre- replication complex that is necessary for DNA replication. The encoded protein can bind geminin, which prevents replication and may function to prevent this protein from initiating replication at inappropriate origins.	2.75E-05	- 0.055 1	0.00386	0.054 6	0.000292
cg009686 16	CUED C1	CUE domain containing 1		2.94E-05	0.034 9	0.00375	- 0.035 1	0.000785

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA	AN-Active vs. NED		AN-Active vs. AN-Remitted	
				Q-value	Effec t	Q value	Effec t	Q value
cg187340 95	NOSIP	nitric oxide synthase interacting protein	The protein encoded by this gene may modulate the activity and localization of nitric oxide synthase and thus nitric oxide production.	2.94E-05	0.028 0	0.000645	- 0.022 6	0.00236
cg201248 77	KPNA 1	karyopherin subunit alpha 1	The protein encoded by this gene belongs to the importin alpha family, and is involved in nuclear protein import.	4.76E-05	0.030 6	0.00552	- 0.037 7	0.000129
cg060963 36	PSMD 1	proteasome 26S subunit, non- ATPase 1	This gene encodes the largest non-ATPase subunit of the 19S regulator lid, which is responsible for substrate recognition and binding.	5.30E-05			- 0.054 1	1.11E-05
cg178791 01	FAM5 3B	family with sequence similarity 53 member B		6.14E-05			0.034 1	0.000127

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cg204818 24	RNF3 9	ring finger protein 39		6.33E-05			0.079 9	1.11E-05
cg059920 79	SIT1	signaling threshold regulating transmembrane adaptor 1		6.53E-05			- 0.024 8	0.000548
cg146664 04	MCF2 L2	MCF.2 cell line derived transforming sequence-like 2		6.90E-05	0.026 5	0.00334	- 0.026 8	0.000488

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA Q-value	AN-Active vs. NED		AN-Active vs. AN-Remitted	
					Effec t	Q value	Effec t	Q value
cg276313 89	MICA L2	microtubule associated monooxygenas e, calponin and LIM domain containing 2	The protein encoded by this gene is involved in cytoskeletal dynamics. The encoded protein is a regulator of the SRF signaling pathway.	7.43E-05	0.041 8	0.00781	- 0.044 2	0.000201
cg097965 83	CDH2 3	cadherin related 23	The encoded protein is thought to be involved in stereocilia organization and hair bundle formation.	9.11E-05			- 0.057 7	2.58E-05
cg241019 45	HFM1	HFM1, ATP dependent DNA helicase homolog	The protein encoded by this gene is thought to be an ATP-dependent DNA helicase.	9.12E-05	0.057 3	0.00941	- 0.080 8	0.000122
cg040369 20	C11orf 41	KIAA1549 like		0.000105			- 0.041 8	0.000864
cg172029 48	NAT9	N- acetyltransferas e 9 (putative)		0.000108			0.063 9	5.30E-06



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cg157324 22	CASC 1	cancer susceptibility 1		0.000132		0.088 7	7.72E-05
cg275528 57	SEMA 6B	semaphorin 6B	The protein encoded by this gene may be involved in both peripheral and central nervous system development.	0.000170		0.034 0	0.000564
cg167023 62	MGA T5	mannosyl (alpha-1,6-)- glycoprotein beta-1,6-N- acetyl- glucosaminyltr ansferase	The encoded protein is one of the most important enzymes involved in the regulation of the biosynthesis of glycoprotein oligosaccharides.	0.000174		- 0.052 1	0.00115

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA	AN-Active vs. NED	AN-Active vs. AN-Remitted	
				Q-value	Effec t	Q value	Effec t
cg074807 62	PLCH 1	phospholipase C eta 1	PLCH1 is involved in the cleaving of phosphatidylinositol 4,5-bisphosphate to generate second messengers IP3 and DAG.	0.000182		- 0.049 7	0.000469
cg262934 23	MRPS 27	mitochondrial ribosomal protein S27	Mammalian mitochondrial ribosomal proteins are encoded by nuclear genes and help in protein synthesis within the mitochondrion.	0.000216		- 0.060 5	0.000108
cg128990 65	GP1B B	glycoprotein Ib platelet beta subunit	The encoded part of the GPIb-V-IX system that constitutes the receptor for von Willebrand factor (VWF), and mediates platelet adhesion in the arterial circulation.	0.000221		- 0.068 9	6.74E-05



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cg235102 58	TBCD	tubulin folding cofactor D	Cofactor D is one of four proteins involved in the pathway leading to correctly folded beta- tubulin from folding intermediates.	0.000221			0.038 5	0.000149
cg040725 45	INS- IGF2	INS-IGF2 readthrough		0.000239			0.068 2	4.01E-05
cg018105 93	KIAA 1967	cell cycle and apoptosis regulator 2		0.000261	0.054 1	0.00230	- 0.043 3	0.00649
cg243125 20	STAT 3	signal transducer and activator of transcription 3	The encoded protein mediates the expression of a variety of genes in response to cell stimuli, and thus plays a key role in many cellular processes such as cell growth and apoptosis.	0.000268			- 0.058 3	0.000118

Table S2 *continued*

CpG	Gene	Name	Function	<u>ANOVA</u>	<u>AN-Active vs. NED</u>		<u>AN-Active vs. AN-Remitted</u>	
				Q-value	Effec t	Q value	Effec t	Q value
cg220912 36	RPTO R	regulatory associated protein of MTOR complex 1	This gene encodes a component of a signaling pathway that regulates cell growth in response to nutrient and insulin levels.	0.000268	0.027 8	0.00707	- 0.025 1	0.00639
cg118006 35	DOK1	docking protein 1	The encoded protein is a scaffold protein that helps form a platform for the assembly of multiprotein signaling complexes.	0.000290			0.030 3	0.000308

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cg001298 11	DSE	dermatan sulfate epimerase	The protein encoded by this gene is a tumor-rejection antigen. This antigen possesses tumor epitopes capable of inducing HLA-A24-restricted and tumor-specific cytotoxic T lymphocytes in cancer patients.	0.000310	0.058 0	0.00597	- 0.054 2	0.00239
cg180712 02	LOC1 00292 680	long intergenic non-protein coding RNA 942		0.000343	0.049 1	0.00933	- 0.049 1	0.00235
cg137188 27	MIR19 9B	microRNA 199b	microRNAs are short non-coding RNAs that are involved in post-transcriptional regulation of gene expression in multicellular organisms by affecting both the stability and translation of mRNAs.	0.000351			0.024 3	0.000606
cg047546 52	MED1 2L	mediator complex subunit 12 like	The protein encoded by this gene is part of the Mediator complex, which is involved in transcriptional coactivation of nearly all RNA polymerase II-dependent genes.	0.000387	0.041 9	0.00570		

Table S2 *continued*

CpG	Gene	Name	Function	<u>ANOVA</u>	<u>AN-Active vs. NED</u>	<u>AN-Active vs. AN-Remitted</u>	
				Q-value	Effec t	Q value	Effec t
cg256158 90	LIMA 1	LIM domain and actin binding 1	This gene encodes a cytoskeleton-associated protein that inhibits actin filament depolymerization and cross-links filaments in bundles.	0.000393		0.056 8	0.000212

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cg045407 12	CBFA 2T3	CBFA2/RUNX 1 translocation partner 3	This gene encodes a member of the myeloid translocation gene family which interact with which recruits a range of corepressors which helps to facilitate transcriptional repression. This gene is also a putative breast tumor suppressor.	0.000393	0.028 1	0.00386		
cg128723 57	RAB3 2	RAB32, member RAS oncogene family	The protein encoded by this gene aids in mitochondrial fission. The encoded protein also appears to be involved in autophagy and melanosome secretion.	0.000397	0.045 7	0.00570	- 0.046 3	0.00110
cg260973 81	HSPA 1L	heat shock protein family A (Hsp70) member 1 like	This gene encodes a 70kDa heat shock protein. In conjunction with other heat shock proteins, this protein stabilizes existing proteins against aggregation and mediates the folding of newly translated proteins in the cytosol and in organelles.	0.000397			0.072 4	0.00148
cg006693 30	C2orf8 5	receptor transporter protein 5 (putative)		0.000470	0.027 8	0.000801		

Table S2 *continued*

CpG	Gene	Name	Function	<u>ANOVA</u>	<u>AN-Active vs.</u>	<u>AN-Active vs.</u>	
				Q-value	<u>NED</u>	<u>AN-Remitted</u>	
				Effec t	Q value	Effec t	
cg270006 90	PACSI N1	protein kinase C and casein kinase substrate in neurons 1		0.000477		- 0.037 7	0.000107

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cg235971 62	JAZF1	JAZF zinc finger 1	This gene encodes a nuclear protein with three C2H2-type zinc fingers, and functions as a transcriptional repressor.	0.000532	0.044 3	0.00386		
cg130077 01	DLC1	DLC1 Rho GTPase activating protein	This gene functions as a tumor suppressor gene in a number of common cancers, including prostate, lung, colorectal, and breast cancer.	0.000532		-	0.000428	0.039 4
cg006921 73	ZYG1 1B	zyg-11 family member B, cell cycle regulator		0.000543		-	0.000428	0.044 0
cg076585 08	SLC26 A1	solute carrier family 26 member 1	This gene is a member of a family of sulfate/anion transporter genes.	0.000547		0.045 8	0.000760	
cg045240 40	CREB 3L3	cAMP responsive element binding protein 3 like 3	The encoded protein acts as a transcription factor activated by cyclic AMP stimulation. The encoded has been linked to acute inflammatory response, hepatocellular carcinoma, triglyceride metabolism, and hepcidin expression.	0.000579		-	0.000896	0.039 3
cg158325 77	C1orf5 3	chromosome 1 open reading frame 53		0.000581		-	0.000176	0.091 7

Table S2 *continued*

CpG	Gene	Name	Function	<u>ANOVA</u>	<u>AN-Active vs.</u>	<u>AN-Active vs.</u>		
				Q-value	<u>NED</u>	<u>AN-Remitted</u>		
				Effec t	Q value	Effec t		
cg032386 87	ZNF48 7	zinc finger protein 487		0.000601		-	0.000240	0.053 9

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cg086532 92	FAM1 11A	family with sequence similarity 111 member A		0.000682			-	0.00167
							0.037 2	
cg225811 87	IQGA P2	IQ motif containing GTPase activating protein 2	The encoded protein helps to regulate cell morphology and motility. It also acts as a tumor suppressor and has been found to play a role in regulating innate antiviral responses.	0.000684	0.048	0.00386	0	
cg126541 99	RPTO R	regulatory associated protein of MTOR complex 1	This gene encodes a component of a signaling pathway that regulates cell growth in response to nutrient and insulin levels.	0.000738			-	0.00141
							0.035 8	
cg243955 45	CUL4 B	cullin 4B	The encoded protein forms a complex that functions as an E3 ubiquitin ligase and catalyzes the polyubiquitination of specific protein substrates in the cell.	0.000740			-	0.000455
							0.063 6	
cg191615 59	CUX1	cut like homeobox 1	The protein encoded by this gene is a member of the homeodomain family of DNA binding proteins. It may regulate gene expression, morphogenesis, and differentiation and it may also play a role in the cell cycle progression. Several alternatively spliced transcript variants encoding different isoforms have been identified	0.000752	0.036	0.00954	-	0.00404
					7		0.035 6	

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CpG	Gene	Name	Function	ANOVA	AN-Active vs. NED		AN-Active vs. AN-Remitted	
				Q-value	Effec t	Q value	Effec t	Q value
cg178337 46	STAT 3	signal transducer and activator of transcription 3	The encoded protein mediates the expression of a variety of genes in response to cell stimuli, and thus plays a key role in many cellular processes such as cell growth and apoptosis.	0.000806	-	-	0.049 7	0.000579
cg252022 61	SNX2 7	sorting nexin family member 27	This gene encodes a member of the sorting nexin family, which is involved in endocytosis of plasma membrane receptors and protein trafficking through these compartments.	0.000840	0.043 0	0.00462	- 0.039 8	0.00647
cg152783 74	GPR1 33	adhesion G protein-coupled receptor D1	The adhesion G-protein-coupled receptors (GPCRs), transduce extracellular signals through heterotrimeric G proteins.	0.000852	- 0.036 5	0.00645	0.035 4	0.00545
cg136552 50	RAPG EF1	Rap guanine nucleotide exchange factor 1	The encoded protein is involved in a signaling cascade that may be involved in apoptosis, integrin-mediated signal transduction, and cell transformation.	0.000942	-	-	0.032 3	0.00224
cg050596 07	PITPN C1	phosphatidylinositol transfer protein, cytoplasmic 1	The encoded cytoplasmic protein plays a role in cell signaling and lipid metabolism by facilitating the transfer of phosphatidylinositol between membrane compartments.	0.000942	-	-	0.040 5	0.00158

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cg196798 65	RERE	arginine-glutamic acid dipeptide repeats	The encoded protein co-localizes with a transcription factor in the nucleus, and its overexpression triggers apoptosis.	0.000952	-	0.00188
					0.0225	

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA	AN-Active vs. NED		AN-Active vs. AN-Remitted	
				Q-value	Effec t	Q value	Effec t	Q value
cg136309 62	IER3	immediate early response 3	This gene functions in the protection of cells from Fas- or tumor necrosis factor type alpha-induced apoptosis.	0.000952	-	6.52E-05	0.0741	
cg065822 66	DOK7	docking protein 7	The encoded protein functions in aneural activation of muscle-specific receptor kinase, which is required for postsynaptic differentiation, and in the subsequent clustering of the acetylcholine receptor in myotubes.	0.000956	-	0.000139	0.0999	
cg044302 04	STK36	serine/threonine kinase 36	This human protein is a positive regulator of the GLI zinc-finger transcription factors.	0.00103	-	0.00288	0.0299	
cg177072 95	C4orf3	chromosome 4 open reading frame 33		0.00106	-	0.000326	0.0391	
cg091447 69	AP2B1	adaptor related protein complex 2 beta 1 subunit	The protein encoded by this gene is one of two large chain components of the assembly protein complex 2, which serves to link clathrin to receptors in coated vesicles.	0.00108	0.0240	0.00941	-	0.00888
							0.0196	

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cg084849 92	CBFA 2T3	CBFA2/RUNX 1 translocation partner 3	This gene encodes a member of the myeloid translocation gene family which interact with which recruits a range of corepressors which helps to facilitate transcriptional repression. This gene is also a putative breast tumor suppressor.	0.00109	- 0.060 6	0.000284
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Table S2 *continued*

CpG	Gene	Name	Function	<u>ANOVA</u>	<u>AN-Active vs.</u> <u>NED</u>	<u>AN-Active vs.</u> <u>AN-Remitted</u>
				Q-value	Effec t	Q value
cg247515 51	KCNJ 15	potassium voltage-gated channel subfamily J member 15	The protein encoded by this gene is an integral membrane protein and inward-rectifier type potassium channel.	0.00111	- 0.048 6	0.00106
cg099580 65	CAM K1D	calcium/calmod ulin dependent protein kinase ID	The encoded protein is has been associated with multiple processes including regulation of granulocyte function, activation of CREB-dependent gene transcription, aldosterone synthesis, differentiation and activation of neutrophil cells, and apoptosis of erythroleukemia cells.	0.00114	- 0.043 7	0.00193
cg187157 93	PLIN4	perilipin 4	Members of the perilipin family, such as PLIN4, coat intracellular lipid storage droplets.	0.00114	- 0.056 6	0.000149



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cg268278 76	KLK4	kallikrein related peptidase 4	Kallikreins are a subgroup of serine proteases having diverse physiological functions, and may be implicated in carcinogenesis.	0.00117			- 0.049 1	0.000534
cg040840 52	ALDH 9A1	aldehyde dehydrogenase 9 family member A1	The encoded enzyme catalyzes the dehydrogenation of gamma-aminobutyraldehyde to gamma-aminobutyric acid (GABA).	0.00117			0.074 5	0.000395
cg138245 00	VTI1A	vesicle transport through interaction with t-SNAREs 1A	The protein encoded by this gene functions in intracellular trafficking. This family member is involved in vesicular transport between endosomes and the trans-Golgi network.	0.00117	0.054 6	0.00386		

Table S2 *continued*

CpG	Gene	Name	Function	<u>ANOVA</u>	<u>AN-Active vs.</u>	<u>AN-Active vs.</u>	Effec t	Q value
				Q-value	NED	AN-Remitted		
cg129590 48	RELT	RELT, TNF receptor	The encoded receptor is capable of stimulating T-cell proliferation in the presence of CD3 signaling, which suggests its regulatory role in immune response.	0.00117			- 0.027 1	0.00109
cg137500 61	CD3G	CD3g molecule	The encoded protein forms part of a complex that plays an important role in coupling antigen recognition to several intracellular signal-transduction pathways.	0.00118			- 0.020 1	0.00241

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cg214429 98	VGLL 4	vestigial like family member 4		0.00126			0.022 8	0.00138
cg108919 51	STAG 1	stromal antigen 1	This gene encodes a component of cohesin, a multisubunit protein complex that provides sister chromatid cohesion along the length of a chromosome from DNA replication through prophase and prometaphase.	0.00126			- 0.047 5	0.000455
cg179883 20	ZNRF 2	zinc and ring finger 2		0.00126			- 0.083 4	0.000193
cg276524 59	ARHG AP1	Rho GTPase activating protein 1	This gene encodes a member of a large family of proteins that activate Rho-type guanosine triphosphate (GTP) metabolizing enzymes.	0.00126	0.039 5	0.00963		
cg134605 56	ABHD 2	abhydrolase domain containing 2	The encoded protein catalyzes the hydrolysis of endocannabinoid arachidonoylglycerol from the cell membrane.	0.00126			- 0.028 9	0.00223

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA Q-value	AN-Active vs. NED		AN-Active vs. AN-Remitted	
					Effec t	Q value	Effec t	Q value
cg274572 90	VPS54	VPS54, GARP complex subunit	This gene encodes for a protein that in yeast forms part of a trimeric vacuolar-protein-sorting complex that is required for retrograde transport of proteins from prevacuoles to the late Golgi compartment.	0.00133			- 0.087 5	0.000356

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cg266760 34	RTKN	rhotekin	Rho proteins regulate many important cellular processes, including cytokinesis, transcription, smooth muscle contraction, cell growth and transformation.	0.00140			- 0.049 2	0.000141
cg097468 17	EBF3	early B-cell factor 3	The encoded protein inhibits cell survival through the regulation of genes involved in cell cycle arrest and apoptosis.	0.00140			- 0.094 9	0.000455
cg135496 38	RPTOR	regulatory associated protein of MTOR complex 1	This gene encodes a component of a signaling pathway that regulates cell growth in response to nutrient and insulin levels.	0.00146	0.037 6	0.00570		
cg007860 84	CCR9	C-C motif chemokine receptor 9	Chemokines and their receptors are key regulators of the thymocytes migration and maturation in normal and inflammation conditions.	0.00149			- 0.023 1	0.00681
cg020433 29	FNDC3A	fibronectin type III domain containing 3A		0.00149			- 0.024 9	0.00707

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA	AN-Active vs. NED		AN-Active vs. AN-Remitted	
				Q-value	Effec t	Q value	Effec t	Q value
cg244818 82	PDE7B	phosphodiesterase 7B	This gene encodes a cAMP-specific phosphodiesterase, a member of the cyclic nucleotide phosphodiesterase family.	0.00151			- 0.029 0	0.000743
cg116303 92	GPR171	G protein-coupled receptor 171		0.00155			- 0.043 1	0.00874

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cg082179 10	TME M37	transmembrane protein 37		0.00158			- 0.061 6	0.000749
cg054871 34	STAT 3	signal transducer and activator of transcription 3	The encoded protein mediates the expression of a variety of genes in response to cell stimuli, and thus plays a key role in many cellular processes such as cell growth and apoptosis.	0.00165			- 0.051 5	0.000683
cg011020 73	GATA 2	GATA binding protein 2	The encoded protein plays an essential role in regulating transcription of genes involved in the development and proliferation of hematopoietic and endocrine cell lineages.	0.00166			0.045 8	0.00207
cg267326 15	CILP2	cartilage intermediate layer protein 2		0.00166			0.057 8	0.00822
cg018912 60	VPRE B1	V-set pre-B cell surrogate light chain 1	The encoded protein is thought to regulate Ig gene rearrangements in the early steps of B-cell differentiation.	0.00166			- 0.031 3	0.000796
cg001336 24	EFCA B4B	calcium release activated channel regulator 2A		0.00179	0.050 1	0.00933		

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA Q-value	AN-Active vs. NED		AN-Active vs. AN-Remitted	
					Effec t	Q value	Effec t	Q value

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cg042650 51	LRP5	LDL receptor related protein 5	The encoded protein plays a key role in skeletal homeostasis and many bone density related diseases are caused by mutations in this gene.	0.00180			0.051 1	0.00103
cg040572 19	ABCC 1	ATP binding cassette subfamily C member 1	This full transporter is a member of the MRP subfamily which is involved in multi-drug resistance.	0.00182			- 0.064 6	0.00108
cg129993 66	NOD1	nucleotide binding oligomerization domain containing 1	The encoded protein plays a role in innate immunity by acting as a pattern-recognition receptor (PRR) that binds bacterial peptidoglycans and initiates inflammation. This protein has also been implicated in the immune response to viral and parasitic infection.	0.00183	0.047 5	0.00894		
cg135914 08	CHST 11	carbohydrate sulfotransferase 11	The protein encoded by this gene catalyzes the transfer of sulfate to position 4 of the N-acetylgalactosamine residue of chondroitin. Chondroitin sulfate constitutes the predominant proteoglycan present in cartilage, and is distributed on the surfaces of many cells and extracellular matrices.	0.00187	0.036 7	0.00933		
cg064921 44	SRD5 A2	steroid 5 alpha- reductase 2	This gene encodes a microsomal protein expressed at high levels in androgen-sensitive tissues such as the prostate.	0.00193			- 0.075 6	0.000945

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Table S2 *continued*

CpG	Gene	Name	Function	ANOVA	AN-Active vs. NED		AN-Active vs. AN-Remitted	
				Q-value	Effec t	Q value	Effec t	Q value
cg20857301	SKA1	spindle and kinetochore associated complex subunit 1		0.00194			0.0489	0.00188
cg03631078	ZBTB20	zinc finger and BTB domain containing 20	This gene acts as a transcriptional repressor and plays a role in many processes including neurogenesis, glucose homeostasis, and postnatal growth.	0.00194			-0.0450	0.000579
cg12353636	PCDH21	cadherin related family member 1	The encoded protein is a photoreceptor-specific cadherin that plays a role in outer segment disc morphogenesis.	0.00196	0.0598	0.00386		
cg26979339	RIC8B	RIC8 guanine nucleotide exchange factor B		0.00200			-0.0957	0.000752
cg20486651	RPS6KA2	ribosomal protein S6 kinase A2	This gene encodes a member of the RSK (ribosomal S6 kinase) family of serine/threonine kinases. The activity of this protein has been implicated in controlling cell growth and differentiation.	0.00201			-0.0643	0.00261
cg11058932	TSGA13	testis specific 13		0.00201			-0.0378	0.00379
cg25740640	LOC10190939	TPT1 antisense RNA 1		0.00201			-0.0445	0.000954

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cg100952 47	ANKIB 1	ankyrin repeat and IBR domain containing 1	0.00201	0.030 9	0.00933	- 0.028 9	0.00867
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Table S2 *continued*

CpG	Gene	Name	Function	ANOVA	AN-Active vs. NED		AN-Active vs. AN-Remitted	
				Q-value	Effec t	Q value	Effec t	Q value
cg235172 79	MAN EA	mannosidase endo-alpha	MANEA catalyzes the release of mono-, di-, and triglucosylmannose oligosaccharides by cleaving the alpha-1,2- mannosidic bond that links them to high-mannose glycans.	0.00206			- 0.050 3	0.00264
cg018809 29	CRIM 1	cysteine rich transmembrane BMP regulator 1	The encoded protein may play a role in tissue development.	0.00207			- 0.032 7	0.00416
cg087524 31	KLHD C4	kelch domain containing 4		0.00210			- 0.066 4	0.000385
cg023467 37	ARHG AP26	Rho GTPase activating protein 26	The protein encoded by this gene is a GTPase activating protein that binds to focal adhesion kinase and mediates the activity of the GTP binding proteins RhoA and Cdc42.	0.00211			- 0.032 1	0.000502
cg160391 57	B2M	beta-2- microglobulin	The encoded antimicrobial protein displays antibacterial activity in amniotic fluid.	0.00212	0.023 1	0.00645		
cg178705 20	GTDC 1	glycosyltransfe rase like domain containing 1		0.00212	0.044 1	0.00552		

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cg138211 76	TRIB1	tribbles pseudokinase 1		0.00212	0.031	0.00760	0	
cg070792 31	DNAH 3	dynein axonemal heavy chain 3	The encoded protein is an axonemal dynein heavy chain. It is involved in producing force for ciliary beating by using energy from ATP hydrolysis.	0.00212			- 0.031 3	0.00109

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA	AN-Active vs. NED		AN-Active vs. AN-Remitted	
				Q-value	Effec t	Q value	Effec t	Q value
cg171925 99	PRKA G2	protein kinase AMP-activated non-catalytic subunit gamma 2	AMPK is an important energy-sensing enzyme that monitors cellular energy status and functions by inactivating key enzymes involved in regulating de novo biosynthesis of fatty acid and cholesterol. This gene is a member of the AMPK gamma subunit family.	0.00214	0.041 2	0.00941		
cg011248 10	IFT88	intraflagellar transport 88	The encoded protein is involved in cilium biogenesis.	0.00215			- 0.036 5	0.000410
cg232562 35	TCP10	t-complex 10		0.00216			- 0.055 5	0.000129
cg157208 32	C1orf3 5	chromosome 1 open reading frame 35		0.00217	- 0.076 9	0.00963		
cg203387 54	RNF1 38	ring finger protein 138	The protein encoded by this gene is involved in protein-DNA and protein-protein interactions.	0.00225			- 0.041 4	0.00190



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cg018839 89	KLF7	Kruppel like factor 7	This protein may contribute to the progression of type 2 diabetes by inhibiting insulin expression and secretion in pancreatic beta-cells and by deregulating adipocytokine secretion in adipocytes.	0.00234	- 0.048 6	0.00242
cg255590 69	COL1 1A2	collagen type XI alpha 2 chain	This gene encodes one of the two alpha chains of type XI collagen, a minor fibrillar collagen.	0.00234	0.059 6	0.00108

Table S2 *continued*

CpG	Gene	Name	Function	<u>ANOVA</u>	<u>AN-Active vs.</u> <u>NED</u>	<u>AN-Active vs.</u> <u>AN-Remitted</u>
				Q-value	Effec t	Q value
cg078798 25	AUTS 2	AUTS2, activator of transcription and developmental regulator	This gene has been implicated in neurodevelopment and as a candidate gene for numerous neurological disorders, including autism spectrum disorders, intellectual disability, and developmental delay.	0.00234	- 0.036 3	0.00136
cg196617 05	TRPM 1	transient receptor potential cation channel subfamily M member 1	The encoded protein may play a role in melanin synthesis.	0.00234	- 0.036 1	0.00588
cg146417 57	C21orf 96	RUNX1 intronic transcript 1		0.00234	0.025 2	0.00804

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cg076618 35	ACSF 3	acyl-CoA synthetase family member 3	This gene encodes a member of the acyl-CoA synthetase family of enzymes that activate fatty acids by catalyzing the formation of a thioester linkage between fatty acids and coenzyme A.	0.00236	-	0.00178	0.054 6
cg001633 72	MYC	MAX dimerization protein 1	The MYC/MAX/MAD transcription factors mediate cellular proliferation, differentiation and apoptosis.	0.00242	-	0.00954	0.051 2
cg047493 16	WDF Y4	WDFY family member 4		0.00242	-	0.00198	0.062 2
cg006869 26	GRK7	G protein- coupled receptor kinase 7	The encoded protein has been shown to phosphorylate cone opsins and initiate their deactivation.	0.00244	-	0.00122	0.040 9

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA Q-value	AN-Active vs. NED Effec t	Q value	AN-Active vs. AN-Remitted Effec t	Q value
cg017639 90	RGPD 4	RANBP2-like and GRIP domain containing 4		0.00246			0.049 9	0.000668
cg219365 52	BAHC C1	BAH domain and coiled-coil containing 1		0.00257			0.038 1	0.00168
cg004766 53	LRCH 1	leucine rich repeats and calponin homology domain containing 1	Polymorphism in this gene may be associated with susceptibility to knee osteoarthritis.	0.00258	0.057 5	0.00867		

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cg053678 46	MICA L3	microtubule associated monooxygenase, calponin and LIM domain containing 3		0.00258		0.055 2	0.00116
cg266691 59	CAMT A1	calmodulin binding transcription activator 1	The encoded protein is thought to be a transcription factor and may be a tumor suppressor.	0.00260		- 0.110	0.00105
cg094525 68	ESM1	endothelial cell specific molecule 1	The expression of this gene is regulated by cytokines, suggesting that it may play a role in endothelium-dependent pathological disorders	0.00260		0.029 1	0.00176
cg053795 97	CAM K2G	calcium/calmodulin dependent protein kinase II gamma	The encoded protein is involved in calcium signaling, which is crucial for several aspects of plasticity at glutamatergic synapses.	0.00260		- 0.024 4	0.00541

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA Q-value	AN-Active vs. NED		AN-Active vs. AN-Remitted	
					Effec t	Q value	Effec t	Q value
cg196793 97	FADD	Fas associated via death domain	The protein encoded by this gene is an adaptor molecule that interacts with various cell surface receptors and mediates cell apoptotic signals. It participates in the death signaling initiated by these receptors.	0.00263			0.049 8	0.00374
cg027618 66	ASB8	ankyrin repeat and SOCS box containing 8		0.00265	0.038 2	0.00632		

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cg252219 75	FBLN 2	fibulin 2	The encoded protein may play a role during organ development, in particular, during the differentiation of heart, skeletal and neuronal structures.	0.00271	0.050 6	0.00316
cg082716 22	LOC3 88796	small nucleolar RNA host gene 17		0.00272	0.045 3	0.00172
cg024299 05	PRRT 1	proline rich transmembrane protein 1		0.00273	- 0.032 4	0.00166
cg091786 51	ITGA2 B	integrin subunit alpha 2b	The encoded receptor plays a crucial role in the blood coagulation system, by mediating platelet aggregation.	0.00273	- 0.033 7	0.000733
cg178166 37	SLC7 A4	solute carrier family 7 member 4		0.00279	0.050 5	0.00286
cg185444 50	LPHN 1	adhesion G protein-coupled receptor L1	The encoded protein may function in both cell adhesion and signal transduction.	0.00280	- 0.088 6	0.000358

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA	AN-Active vs. NED		AN-Active vs. AN-Remitted	
				Q-value	Effec t	Q value	Effec t	Q value
cg102401 50	CD28	CD28 molecule	The protein encoded by this gene is essential for T-cell proliferation and survival, cytokine production, and T-helper type-2 development.	0.00282	-	-	0.021 9	0.00962
cg260033 88	TMC8	transmembrane channel like 8	This gene encodes a transmembrane channel-like protein with 8 predicted transmembrane domains and 3 leucine zipper motifs	0.00282			0.027 2	0.00236

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cg272684 36	KIF4A	kinesin family member 4A	The encoded protein is an ATP dependent microtubule-based motor protein that is involved in the intracellular transport of membranous organelles. This protein also associates with condensed chromosome arms and may be involved in maintaining chromosome integrity during mitosis.	0.00289			0.051 3	0.00222
cg124854 28	SCAR F1	scavenger receptor class F member 1	The encoded protein regulates the uptake of chemically modified low density lipoproteins, including acetylated low density lipoprotein (Ac-LDL), and it may be involved in atherogenesis.	0.00301	0.029 5	0.00760		
cg012123 26	POU2 AF1	POU class 2 associating factor 1		0.00303			- 0.034 2	0.00521

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA Q-value	AN-Active vs. NED		AN-Active vs. AN-Remitted	
					Effec t	Q value	Effec t	Q value
cg002885 98	EIF2C 2	argonaute 2, RISC catalytic component	This gene encodes a member of the Argonaute family of proteins which play a role in RNA interference. It may interact with dicer1 and play a role in short-interfering-RNA-mediated gene silencing.	0.00314			0.057 9	0.00734

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cg061065 99	FADD	Fas associated via death domain	The protein encoded by this gene is an adaptor molecule that interacts with various cell surface receptors and mediates cell apoptotic signals. It participates in the death signaling initiated by these receptors.	0.00319	0.057 8	0.00224
cg059011 96	CCDC 6	coiled-coil domain containing 6	The encoded protein may function as a tumor suppressor.	0.00325	0.031 4	0.00627
cg216978 12	C11orf 91	chromosome 11 open reading frame 91		0.00329	- 0.045 4	0.00193
cg009558 08	FLJ22 536	cancer susceptibility 15 (non-protein coding)	This gene produces a long non-coding RNA that may regulate cell proliferation.	0.00338	- 0.059 1	0.00193
cg238957 22	C11orf 45	chromosome 11 open reading frame 45		0.00338	- 0.034 5	0.00142

Table S2 *continued*

CpG	Gene	Name	Function	<u>ANOVA</u>	<u>AN-Active vs.</u>	<u>AN-Active vs.</u>
				Q-value	Effec t	Q value
cg268713 47	MSI2	musashi RNA binding protein 2	The encoded protein is a transcriptional regulator that targets genes involved in development and cell cycle regulation.	0.00342	- 0.044 3	0.00417
cg265670 12	GLRA 1	glycine receptor alpha 1	The protein encoded by this gene is a subunit of a pentameric inhibitory glycine receptor, which mediates postsynaptic inhibition in the central nervous system.	0.00343	- 0.053 5	0.00158

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cg199350 65	DNTT	DNA nucleotidylexot ransferase	This gene encodes a template-independent DNA polymerase that catalyzes the addition of deoxynucleotides to the 3'- hydroxyl terminus of oligonucleotide primers.	0.00343	0.046 5	0.00933		
cg000138 99	CACH D1	cache domain containing 1		0.00368			- 0.051 5	0.00138
cg104038 49	TET1	tet methylcytosine dioxygenase 1	The protein encoded by this gene is a demethylase that belongs to the TET family. Members of the TET protein family play a role in the DNA methylation process and gene activation.	0.00368	0.071 3	0.00971		
cg126557 68	IQGA P2	IQ motif containing GTPase activating protein 2	The encoded protein helps to regulate cell morphology and motility. It also acts as a tumor suppressor and has been found to play a role in regulating innate antiviral responses.	0.00375	0.062 9	0.00954		

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA	AN-Active vs. NED		AN-Active vs. AN-Remitted	
				Q-value	Effec t	Q value	Effec t	Q value
cg183847 12	FAM5 5D	neurexophilin and PC-esterase domain family member 4		0.00375			0.049 7	0.00272
cg028128 91	ECEL 1P2	endothelin converting enzyme like 1 pseudogene 2		0.00376			0.042 1	0.00520

**Appendix 1** to Steiger H, Booij L, Kahan E, et al. A longitudinal, epigenome-wide study of DNA methylation in anorexia nervosa: results in actively ill, partially weight-restored, long-term remitted and non-eating-disordered women. *J Psychiatry Neurosci* 2019.

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cg201040 18	C19orf 61	SMG9, nonsense mediated mRNA decay factor	This gene encodes a regulatory subunit of the SMG1 complex, which plays a critical role in nonsense-mediated mRNA decay (NMD).	0.00376			-	0.000504
							0.051 2	
cg045335 91	RPL39	ribosomal protein L39	Ribosomes, the organelles that catalyze protein synthesis, consist of a small 40S subunit and a large 60S subunit. This gene encodes a ribosomal protein that is a component of the 60S subunit.	0.00397			-	0.00279
							0.059 1	
cg036113 07	MIR12 05	microRNA 1205	microRNAs are short non-coding RNAs that are involved in post-transcriptional regulation of gene expression in multicellular organisms by affecting both the stability and translation of mRNAs.	0.00400	0.021	0.00606	3	

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA Q-value	AN-Active vs. NED		AN-Active vs. AN-Remitted	
					Effec t	Q value	Effec t	Q value
cg051319 40	PRKG 1	protein kinase, cGMP- dependent, type I	The PRKG1 proteins play a central role in regulating cardiovascular and neuronal functions in addition to relaxing smooth muscle tone, preventing platelet aggregation, and modulating cell growth.	0.00402			-	0.00112
							0.075 6	



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cg001223 47	TME M180	major facilitator superfamily domain containing 13A		0.00404	- 0.024 8	0.00789
cg150406 16	MEP1 A	meprin A subunit alpha		0.00405	0.041 6	0.00807
cg181247 06	ATG4 A	autophagy related 4A cysteine peptidase	This gene encodes a member of the autophagin protein family, which participate in autophagy.	0.00405	- 0.029 8	0.00567
cg075729 49	NLRP 10	NLR family pyrin domain containing 10	The encoded protein likely plays a regulatory role in the innate immune system.	0.00409	0.048 2	0.00149
cg169698 72	RBM2 6	RNA binding motif protein 26		0.00419	- 0.037 4	0.00313
cg191746 34	COG1	component of oligomeric golgi complex 1	The protein encoded by this gene forms part of a Golgi-localized complex (COG) required for normal Golgi morphology and function.	0.00432	- 0.027 7	0.00154
cg208172 28	LOC7 28855	long intergenic non-protein coding RNA 623		0.00432	0.034 7	0.00138

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA	AN-Active vs. NED		AN-Active vs. AN-Remitted	
				Q-value	Effec t	Q value	Effec t	Q value

**Appendix 1** to Steiger H, Booij L, Kahan E, et al. A longitudinal, epigenome-wide study of DNA methylation in anorexia nervosa: results in actively ill, partially weight-restored, long-term remitted and non-eating-disordered women. *J Psychiatry Neurosci* 2019.

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cg236706 31	LPPR3	phospholipid phosphatase related 3	The proteins in the lipid phosphate phosphatase family are integral membrane proteins that modulate bioactive lipid phosphates including phosphatidate, lysophosphatidate, and sphingosine-1-phosphate in the context of cell migration, neurite retraction, and mitogenesis.	0.00434	- 0.041 3	0.00161
cg080278 10	GABBR1	gamma-aminobutyric acid type B receptor subunit 1	This gene encodes a receptor for gamma-aminobutyric acid (GABA), which is the main inhibitory neurotransmitter in the mammalian central nervous system.	0.00434	- 0.051 0	0.00730
cg256947 90	DSTN	destrin, actin depolymerizing factor	This gene encodes the actin depolymerizing protein that severs actin filaments (F-actin) and binds to actin monomers (G-actin).	0.00434	- 0.028 4	0.00801
cg074729 53	CSF3	colony stimulating factor 3	The protein encoded by this gene is a cytokine that controls the production, differentiation, and function of granulocytes.	0.00435	0.029 1	0.00669
cg047123 21	ENTPD4	ectonucleoside triphosphate diphosphohydrolase 4	The encoded protein is an endo-apyrase and may play a role in salvaging nucleotides from lysosomes.	0.00438	- 0.035 5	0.00496

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Table S2 *continued*

CpG	Gene	Name	Function	ANOVA	AN-Active vs.	AN-Active vs.
				Q-value	NED	AN-Remitted
				Effec	Q value	Effec
				t		t
cg054201 34	RAB3 2	RAB32, member RAS oncogene family	The protein encoded by this gene aids in mitochondrial fission. The encoded protein also appears to be involved in autophagy and melanosome secretion.	0.00440	-	0.00506
					0.031	7
cg142072 67	IQCD	IQ motif containing D		0.00440	-	0.00473
					0.028	7
cg026390 95	TTC39 B	tetratricopeptid e repeat domain 39B		0.00441	-	0.00709
					0.021	2
cg127891 73	AMIC A1	junction adhesion molecule like		0.00441	-	0.00239
					0.046	9
cg169179 96	NRK	Nik related kinase	The encoded protein may be involved in the induction of actin polymerization in late embryogenesis.	0.00444	0.042	0.00508
					9	
cg007542 53	HRAS LS5	HRAS like suppressor family member 5		0.00448	-	0.00794
					0.025	5
cg110522 59	ADA M32	ADAM metallopeptidas e domain 32	This gene encodes a protein that plays a role in diverse biological processes such as brain development, fertilization, tumor development and inflammation.	0.00452	-	0.00322
					0.062	6
cg002072 26	FLJ44 606	chromosome 5 open reading frame 63		0.00467	-	0.00250
					0.029	2

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cg121889 28	SEZ6	seizure related 6 homolog		0.00467		- 0.029 3	0.000657
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Table S2 *continued*

CpG	Gene	Name	Function	<u>ANOVA</u>	<u>AN-Active vs.</u> <u>NED</u>	<u>AN-Active vs.</u> <u>AN-Remitted</u>	
				Q-value	Effec t	Q value	Effec t
cg160472 79	CCR7	C-C motif chemokine receptor 7	The encoded receptor has been shown to control the migration of memory T cells to inflamed tissues, as well as stimulate dendritic cell maturation.	0.00468		0.039 7	0.00453
cg125973 25	STX2	syntaxin 2	The product of this gene regulates epithelial-mesenchymal interactions and epithelial cell morphogenesis and activation.	0.00474		- 0.043 6	0.00241
cg104999 74	CCR1	C-C motif chemokine receptor 1	The encoded protein is a chemokine receptor. Chemokines and their receptors mediated signal transduction are critical for the recruitment of effector immune cells to the site of inflammation.	0.00485		- 0.028 0	0.00430
cg241148 99	MGC1 2982	FOXD2 adjacent opposite strand RNA 1		0.00489		- 0.063 2	0.00165
cg177178 66	HIVE P2	human immunodeficie ncy virus type I enhancer binding protein 2	The encoded protein regulates transcription by binding to regulatory regions of various cellular and viral genes that maybe involved in growth, development and metastasis.	0.00489		0.030 1	0.00240

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cg236918 73	HABP 2	hyaluronan binding protein 2	This extracellular protease binds hyaluronic acid and may play a role in the coagulation and fibrinolysis systems.	0.00496		0.043 1	0.00313
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Table S2 *continued*

CpG	Gene	Name	Function	ANOVA	AN-Active vs. NED		AN-Active vs. AN-Remitted	
				Q-value	Effec t	Q value	Effec t	Q value
cg057259 40	GSDM B	gasdermin B	This gene encodes a member of the gasdermin-domain containing protein family, which are implicated in the regulation of apoptosis in epithelial cells, and are linked to cancer.	0.00507		-	0.00795	
						0.052 4		
cg271389 01	CLEC 2D	C-type lectin domain family 2 member D	The encoded protein inhibits osteoclast formation.	0.00508		-	0.00807	
						0.039 9		
cg041983 60	PEG10	paternally expressed 10	The encoded protein is reported to have a role in cell proliferation, differentiation and apoptosis.	0.00509		-	0.00609	
						0.021 7		
cg212243 80	SSH1	slingshot protein phosphatase 1	The SSH family thus appears to play a role in actin dynamics.	0.00509		-	0.00326	
						0.028 3		
cg165240 49	LMX1 A	LIM homeobox transcription factor 1 alpha	The encoded protein is a transcription factor that acts as a positive regulator of insulin gene transcription. This gene also plays a role in the development of dopamine producing neurons during embryogenesis.	0.00511		-	0.00240	
						0.075 8		

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cg10882304	TACC2	transforming acidic coiled-coil containing protein 2	This gene lies within a chromosomal region associated with tumorigenesis.	0.00514	-	0.00367
					0.0457	
cg14306330	L3MBTL	L3MBTL1, histone methyl-lysine binding protein	The encoded protein functions to regulate gene activity. The encoded protein may also be necessary for mitosis.	0.00537	-	0.00355
					0.0439	

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA Q-value	AN-Active vs. NED		AN-Active vs. AN-Remitted	
					Effec t	Q value	Effec t	Q value
cg04348201	DTX1	deltex E3 ubiquitin ligase 1	The human gene encodes a protein that may play a role in basic helix-loop-helix transcription factor activity.	0.00542	-	0.00171		
					0.0583			
cg03888033	NTRK1	neurotrophic receptor tyrosine kinase 1	The encoded protein may play a role in specifying sensory neuron subtypes.	0.00549	-	0.00321		
					0.0527			
cg18418586	LASS6	ceramide synthase 6		0.00561	0.0478	0.000259		
cg16015113	KIAA0319L	KIAA0319 like	This gene is a candidate gene for dyslexia susceptibility.	0.00564	0.0724	0.00278		
cg25718604	TUBB1	tubulin beta 1 class VI	The encoded protein may be involved in proplatelet production and platelet release.	0.00564	-	0.00905		
					0.0332			
cg14027204	PTGFRN	prostaglandin F2 receptor inhibitor		0.00567	-	0.00296		
					0.0325			
cg24215973	HDAC4	histone deacetylase 4	The protein encoded by this gene possesses histone deacetylase activity and represses transcription when tethered to a promoter.	0.00574	0.0568	0.00241		

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cg006644 54	CPNE 2	copine 2	Calcium-dependent membrane-binding proteins may regulate molecular events at the interface of the cell membrane and cytoplasm.	0.00574	-	0.00109
					0.041	4
cg229566 35	HSF5	heat shock transcription factor 5		0.00575	-	0.00485
					0.072	8

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA	AN-Active vs. NED	AN-Active vs. AN-Remitted
				Q-value	Effec t	Q value t
cg037515 27	GHRL	ghrelin and obestatin prepropeptide	This gene encodes the ghrelin-obestatin preproprotein that yields two peptides, ghrelin and obestatin. Ghrelin is a powerful appetite stimulant. Ghrelin is thought to regulate multiple activities, including hunger, reward perception via the mesolimbic pathway, gastric acid secretion, gastrointestinal motility, and pancreatic glucose-stimulated insulin secretion.	0.00586	-	0.00542
					0.038	5
cg039587 44	RASA	RAS p21 protein activator 3	The encoded protein functions as a negative regulator of the Ras signalling pathway.	0.00586	0.053	0.00377
					1	
cg064668 39	RICS	Rho GTPase activating protein 32	RICS may regulate dendritic spine morphology and strength by modulating Rho GTPase activity.	0.00586	-	0.00172
					0.028	0

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cg128958 10	DENN D3	DENN domain containing 3		0.00589	- 0.053 1	0.00422
cg143813 50	STX2	syntaxin 2	The product of this gene regulates epithelial-mesenchymal interactions and epithelial cell morphogenesis and activation.	0.00617	0.069 1	0.00600
cg053045 31	DHDD S	dehydrodolichyl diphosphate synthase subunit	The protein encoded by this gene is involved in the biosynthesis of several classes of glycoproteins.	0.00642	0.056 8	0.00373

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA	AN-Active vs. NED	AN-Active vs. AN-Remitted
				Q-value	Effec t	Q value
cg093429 97	NRF1	nuclear respiratory factor 1 provided	This gene encodes a protein that functions as a transcription factor which activates the expression of some key metabolic genes regulating cellular growth and nuclear genes required for respiration, heme biosynthesis, and mitochondrial DNA transcription and replication. The protein has also been associated with the regulation of neurite outgrowth.	0.00642	-	0.00138
cg043440 00	DCBL D1	discoidin, CUB and LCCL domain containing 1		0.00646	-	0.00675
cg216108 39	UBE2 E1	ubiquitin conjugating enzyme E2 E1	This gene encodes a member of the E2 ubiquitin-conjugating enzyme family.	0.00657	0.044 7	0.000885



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cg017729 45	ZNF10 7	zinc finger protein 107	Proteins containing zinc fingers may act as transcriptional regulators, but may also have other cellular functions.	0.00657	- 0.045 8	0.00243
cg173361 39	PRAM E	preferentially expressed antigen in melanoma	The encoded protein acts as a repressor of retinoic acid receptor, and likely confers a growth advantage to cancer cells via this function.	0.00657	0.053 0	0.00291
cg070679 93	TME M132 D	transmembrane protein 132D		0.00665	- 0.042 6	0.00340

Table S2 *continued*

CpG	Gene	Name	Function	<u>ANOVA</u>	<u>AN-Active vs.</u>	<u>AN-Active vs.</u>
				Q-value	<u>NED</u>	<u>AN-Remitted</u>
				Effec t	Q value	Effec t
cg157011 49	RERE	arginine- glutamic acid dipeptide repeats	The encoded protein co- localizes with a transcription factor in the nucleus, and its overexpression triggers apoptosis.	0.00669	- 0.032 6	0.00154
cg072482 23	CCR7	C-C motif chemokine receptor 7	The encoded receptor has been shown to control the migration of memory T cells to inflamed tissues, as well as stimulate dendritic cell maturation.	0.00669	0.042 1	0.00686
cg028831 00	HSD1 7B10	hydroxysteroid 17-beta dehydrogenase 10	The gene product is a mitochondrial protein that catalyzes the oxidation of a wide variety of fatty acids and steroids.	0.00671	0.039 5	0.00627
cg082084 80	BRSK 2	BR serine/threonin e kinase 2		0.00673	0.186	0.00971

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cg074277 72	ATP8 B4	ATPase phospholipid transporting 8B4 (putative)	The encoded protein is involved in phospholipid transport in the cell membrane.	0.00673			- 0.033 7	0.00262
cg141539 19	CRAB P1	cellular retinoic acid binding protein 1	This gene encodes a specific binding protein for a vitamin A family member and is thought to play an important role in retinoic acid-mediated differentiation and proliferation processes.	0.00675	0.042	0.00990	8	
cg090960 31	RFTN 2	raftlin family member 2		0.00680			- 0.042 3	0.00499

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA	AN-Active vs.		AN-Active vs.	
				Q-value	AN-Active vs. NED	AN-Active vs. AN-Remitted	Effec t	Q value
cg058045 98	HERC 2P2	hect domain and RLD 2 pseudogene 2		0.00681			0.047 3	0.00222
cg219324 52	NOS3	nitric oxide synthase 3	Nitric oxide is a reactive free radical which acts as a biologic mediator in several processes, including neurotransmission and antimicrobial and antitumoral activities.	0.00691			- 0.031 6	0.00169
cg233161 61	ZNF60 5	zinc finger protein 605		0.00692			0.058 3	0.00213
cg241413 82	CTPS	CTP synthase 1	The encoded protein is involved in an important step in the biosynthesis of phospholipids and nucleic acids. Activity of this proten is important in the immune system.	0.00699			0.028 4	0.00341

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cg041735 86	DOT1 L	DOT1 like histone lysine methyltransferase	The protein encoded by this gene is a histone methyltransferase that methylates lysine-79 of histone H3.	0.00699	- 0.068 3	0.00696
cg196078 45	FBXO 9	F-box protein 9	The F-box proteins constitute one of the four subunits of the ubiquitin protein ligase complex called SCFs, which function in phosphorylation-dependent ubiquitination.	0.00714	- 0.029 8	0.00189
cg034792 89	C11orf 41	KIAA1549 like		0.00724	- 0.020 2	0.00331

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA	AN-Active vs. NED	AN-Active vs. AN-Remitted
				Q-value	Effec t	Q value
cg000142 03	KDM6 B	lysine demethylase 6B	This protein can demethylate non-histone proteins such as retinoblastoma protein. Through its demethylation activity this gene influences cellular differentiation and development, tumorigenesis, inflammatory diseases, and neurodegenerative diseases.	0.00732	- 0.060 6	0.00580
cg205139 76	LIME 1	Lck interacting transmembrane adaptor 1	This gene encodes a protein that links the T and B-cell receptor stimulation to downstream signaling pathways.	0.00733	0.029 0	0.00619

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cg084625 01	TBC1 D1	TBC1 domain family member 1	TBC1D1 is presumed to have a role in regulating cell growth and differentiation.	0.00759	- 0.031 1	0.00924
cg161119 24	SVOP L	SVOP like	The protein encoded by this gene is thought to transport toxins and drugs from the body.	0.00761	- 0.045 9	0.00685
cg006765 06	RPS4 Y2	ribosomal protein S4 Y- linked 2		0.00761	- 0.049 2	0.00223
cg195539 61	06- mars	retrotransposon Gag like 6		0.00767	- 0.038 5	0.00242
cg078797 85	CRYL 1	crystallin lambda 1	The product of this gene catalyzes the dehydrogenation of L- gulonate into dehydro-L- gulonate in the uronate cycle, which functions as an alternative glucose metabolic pathway, accounting for about 5% of daily glucose catabolism.	0.00773	- 0.025 9	0.00796

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA	AN-Active vs. NED		AN-Active vs. AN-Remitted	
				Q-value	Effec t	Q value	Effec t	Q value
cg111731 31	C20orf 123	osteoclast stimulatory transmembrane protein		0.00783	0.025 3	0.00828		
cg040915 55	FRAS 1	Fraser extracellular matrix complex subunit 1	This gene encodes an extracellular matrix protein that appears to function in the regulation of epidermal-basement membrane adhesion and organogenesis during development.	0.00796			- 0.025 2	0.00674

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cg029406 61	KIAA 0125	family with sequence similarity 30 member A		0.00799	- 0.045 3	0.00801
cg005696 73	GPSM 3	G protein signaling modulator 3		0.00804	0.048 0	0.00297
cg093056 80	UTP23	UTP23, small subunit processome component		0.00804	- 0.041 4	0.00283
cg203902 53	C18orf 22	ribosome binding factor A		0.00806	- 0.059 0	0.00194
cg138803 03	APOC 1	apolipoprotein C1	The encoded protein plays a central role in high density lipoprotein (HDL) and very low density lipoprotein (VLDL) metabolism.	0.00832	- 0.061 7	0.00356

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA	AN-Active vs. NED	AN-Active vs. AN-Remitted
				Q-value	Effec t	Q value
cg229851 72	MTHF D1L	methylenetetra hydrofolate dehydrogenase (NADP+ dependent) 1 like	The protein encoded by this gene is involved in the synthesis of tetrahydrofolate (THF) in the mitochondrion. THF is important in the regeneration of methionine from homocysteine.	0.00837	- 0.044 7	0.00224
cg220948 45	ALPI	alkaline phosphatase, intestinal	The encoded enzyme is thought to function in the detoxification of lipopolysaccharide, and in the prevention of bacterial translocation in the gut.	0.00847	- 0.042 8	0.00957

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cg136366 40	DNM T3B	DNA methyltransferase 3 beta	This gene encodes a DNA methyltransferase which is thought to function in de novo methylation, rather than maintenance methylation.	0.00859	0.063 2	0.00471
cg263329 26	PRKG 1	protein kinase, cGMP-dependent, type I	The PRKG1 proteins play a central role in regulating cardiovascular and neuronal functions in addition to relaxing smooth muscle tone, preventing platelet aggregation, and modulating cell growth.	0.00866	- 0.073 3	0.00439
cg152851 12	C17orf 108	LYR motif containing 9		0.00866	- 0.044 8	0.00520
cg035794 46	NSMC E2	NSE2 (MMS21) homolog, SMC5-SMC6 complex SUMO ligase	The encoded protein is part of the complex which plays a key role genome maintenance, facilitating chromosome segregation and suppressing mitotic recombination.	0.00866	- 0.032 1	0.00254

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA Q-value	AN-Active vs. NED		AN-Active vs. AN-Remitted	
					Effec t	Q value	Effec t	Q value
cg061394 31	CACN A1H	calcium voltage-gated channel subunit alpha1 H	This gene encodes a T-type member of the alpha-1 subunit family, a protein in the voltage-dependent calcium channel complex.	0.00866	-	0.00457	0.063 5	
cg136728 00	C20orf 141	chromosome 20 open reading frame 141		0.00866	-	0.00794	0.025 1	

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cg157822 28	LAM A5	laminin subunit alpha 5	This gene encodes one of the vertebrate laminin alpha chains, which have been implicated in a wide variety of biological processes including cell adhesion, differentiation, migration, signaling, neurite outgrowth and metastasis.	0.00866	0.079 2	0.00416
cg218469 03	VTN	vitronectin	The protein encoded by this gene promotes cell adhesion and spreading, inhibits the membrane-damaging effect of the terminal cytolytic complement pathway, and binds to several serpin serine protease inhibitors.	0.00869	- 0.020 8	0.00383
cg154572 17	WDF Y1	WD repeat and FYVE domain containing 1	The protein encoded by this gene is a phosphatidylinositol 3-phosphate binding protein, which contains a FYVE zinc finger domain and multiple WD-40 repeat domains	0.00870	- 0.019 5	0.00313

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA Q-value	<u>AN-Active vs. NED</u>		<u>AN-Active vs. AN-Remitted</u>	
					Effec t	Q value	Effec t	Q value
cg000332 09	NAT1 5	N(alpha)- acetyltransferas e 60, NatF catalytic subunit	This gene encodes an enzyme that transfers an acetyl group to the N-terminus of free proteins. This enzyme acts on histones, and its activity is important for chromatin assembly and chromosome integrity.	0.00892	0.066 6	0.00933		

**Appendix 1** to Steiger H, Booij L, Kahan E, et al. A longitudinal, epigenome-wide study of DNA methylation in anorexia nervosa: results in actively ill, partially weight-restored, long-term remitted and non-eating-disordered women. *J Psychiatry Neurosci* 2019.

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cg169655 52	SPAT A6	spermatogenesis associated 6		0.00894	-	0.00520
					0.0381	
cg228074 49	HOXB 2	homeobox B2	The encoded protein functions as a sequence-specific transcription factor that is involved in development.	0.00905	-	0.00239
					0.0525	
cg254375 31	LMO2	LIM domain only 2	The LMO2 protein has a central and crucial role in hematopoietic development.	0.00915	-	0.00295
					0.0430	
cg034323 38	FAM8 9A	family with sequence similarity 89 member A		0.00923	0.0425	0.00287
cg227300 04	SPTA 1	spectrin alpha, erythrocytic 1	This gene encodes a protein that functions in the determination of cell shape, arrangement of transmembrane proteins, and organization of organelles.	0.00942	-	0.00416
					0.0490	
cg233331 46	EIF4E 3	eukaryotic translation initiation factor 4E family member 3	EIF4E3 belongs to the EIF4E family of translational initiation factors.	0.00944	-	0.00286
					0.0342	

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA	AN-Active vs. NED	AN-Active vs. AN-Remitted
				Q-value	Effec t Q value	Effec t Q value
cg134489 78	FGR	FGR proto-oncogene, Src family tyrosine kinase	The encoded protein functions as a negative regulator of cell migration and adhesion triggered by the beta-2 integrin signal transduction pathway.	0.00955		0.0316 0.00444



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cg268912 10	CTSS	cathepsin S	The encoded protein can function as an elastase over a broad pH range in alveolar macrophages.	0.00955	-	0.00292
					0.0598	
cg161530 42	SLC22 A23	solute carrier family 22 member 23	SLC22A23 functions as a uniporter, symporter, and an antiporter that transports organic ions across cell membranes	0.00955	-	0.00256
					0.0321	
cg069928 46	TRIB1	tribbles pseudokinase 1		0.00955	-	0.00567
					0.0418	
cg167689 66	GAS7	growth arrest specific 7	GAS7 plays a putative role in neuronal development.	0.00955	-	0.00498
					0.0225	
cg177184 01	SNOR A24	small nucleolar RNA, H/ACA box 24		0.00955	0.0452	0.00272
cg059141 50	PIK3R 1	phosphoinositid e-3-kinase regulatory subunit 1	Phosphatidylinositol 3-kinase plays an important role in the metabolic actions of insulin.	0.00964	-	0.00608
					0.0284	
cg263470 89	VWA3 B	von Willebrand factor A domain containing 3B	Intracellular proteins with VWA domains are thought to function in transcription, DNA repair, ribosomal and membrane transport and the proteasome.	0.00969	-	0.00188
					0.0650	
cg206841 10	ADO	2-aminoethanethiol dioxygenase		0.00973	0.0392	0.00377

Table S2 *continued*

CpG	Gene	Name	Function	ANOVA	AN-Active vs. NED		AN-Active vs. AN-Remitted	
				Q-value	Effec t	Q value	Effec t	Q value
cg032240 13	KIAA 0125	family with sequence similarity 30 member A		0.00981	-	0.00380		
					0.0537			

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cg040166 60	KIAA 0513	KIAA0513	0.00981	-	0.00285
				0.029 9	
cg021608 72	CCDC 127	coiled-coil domain containing 127	0.00991	0.044 6	0.00239
cg089491 92	RUSC 1	RUN and SH3 domain containing 1	0.00998	-	0.00145
				0.038 8	

<sup>1</sup>The table shows 295 probes with *Q* values < 0.01. Genes and gene functions are taken from the NCBI gene database <https://www.ncbi.nlm.nih.gov/gene>. (Empty cells imply that clearly established functions are lacking as per the NCBI gene database).

Table S3. Probes (and corresponding genes) on which methylation levels differ significantly in ANOVA and pairwise comparisons among AN-R vs. AN-B/P vs. NED. (See footnotes at the bottom of the table)

Gene	Name	Function	<u>Overall ANOVA</u> Q-value	<u>AN-R vs. NED</u> Effect	<u>AN-B/P vs. NED</u> Q value	<u>AN-B/P vs. NED</u> Effect	<u>AN-B/P vs. NED</u> Q Value
cg17272549	EML6	echinoderm microtubule associated protein like 6	0.000126	0.0533	0.0168 <sup>a</sup>	0.0632	0.000301 <sup>a</sup>
cg00323842	ZNF608	zinc finger protein 608	0.000173	0.0577	0.000821	0.0373	0.0196
cg06983052	LRRC8D	leucine rich repeat containing 8 VRAC subunit D	0.000949	0.0430	0.00530	0.0427	0.00569 <sup>a</sup>

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cg14422240	FTSJD2	cap methyltransferase 1		0.000949	0.0591	0.00530	0.0551	0.00569 <sup>a</sup>
cg18734095	NOSIP	nitric oxide synthase interacting protein	The protein encoded by this gene may modulate the activity and localization of nitric oxide synthase and thus nitric oxide production,	0.00258	0.0221	0.0424 <sup>a</sup>	0.0327	0.00577 <sup>a</sup>
cg02183564	CCDC146	coiled-coil domain containing 146		0.00328	0.0530	0.0214 <sup>a</sup>	0.0472	0.0116 <sup>a</sup>
cg26701785	SYNJ2	synaptojanin 2	The encoded protein can inhibit clathrin-mediated endocytosis.	0.00332	-0.0564	0.00530		
cg00669330	C2orf85	receptor transporter protein 5 (putative)		0.00447	0.0257	0.0173 <sup>a</sup>	0.0289	0.0196 <sup>b</sup>

Table S3 *continued*

Gene	Name	Function		Overall ANOVA	AN-R vs. NED		AN-B/P vs. NED	
				Q-value	Effect	Q value	Effect	Q Value
cg03233624	MSI2	musashi RNA binding protein 2	This gene encodes an RNA-binding protein that is a member of the Musashi protein family. The encoded protein is transcriptional regulator that targets genes involved in	0.00517	0.0475	0.0309 <sup>a</sup>	0.0498	0.0272 <sup>b</sup>

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development and  
cell cycle  
regulation.  
Mutations in this  
gene are  
associated with  
poor prognosis in  
certain types of  
cancers. This  
gene has also  
been shown to be  
rearranged in  
certain cancer  
cells.

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<sup>1</sup>The table shows 9 probes with *Q* values < 0.01 on the ANOVA. Genes and gene functions are taken from the NCBI gene database <https://www.ncbi.nlm.nih.gov/gene>. (Empty cells correspond to genes lacking clearly established functions as per the NCBI gene database).

<sup>a</sup>  $p < .05$  after adjustments for age and smoking

<sup>b</sup> non-significant ( $p > .05$ ) after adjustments for age and smoking

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Table S4

*Probes (and corresponding genes) on which methylation levels are significantly correlated ( $Q < .01$ ) with illness chronicity. Negative effects associate greater chronicity with lower methylation.*

Cg site	Gene	Name	Function	Effect	P-value	Q-value
cg16867657	ELOVL2	ELOVL fatty acid elongase 2		0.000561	2.70E-15	8.20E-11
cg22454769	FHL2	four and a half LIM domains 2	This gene encodes a protein that is thought to have a role in the assembly of extracellular membranes.	0.000652	1.80E-10	1.82E-06
cg12934382	GRM2	glutamate metabotropic receptor 2	L-glutamate is the major excitatory neurotransmitter in the central nervous system and activates both ionotropic and metabotropic glutamate receptors.	0.000855	1.34E-10	1.82E-06
cg05404236	IRS2	insulin receptor substrate 2	This gene encodes the insulin receptor substrate 2 that mediates effects of insulin, insulin-like growth factor 1, and other cytokines by acting as a molecular adaptor between diverse receptor tyrosine kinases and downstream effectors.	0.000546	2.98E-10	2.26E-06

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cg00664406	GRM2	glutamate metabotropic receptor 2	L-glutamate is the major excitatory neurotransmitter in the central nervous system and activates both ionotropic and metabotropic glutamate receptors.	0.000546	1.79E-09	1.09E-05
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Table S4 *continued*

Cg site	Gene	Name	Function	Effect	P-value	Q-value
cg00329615	IGSF11	Immuno-globulin superfamily member 11	IGSF11 is an immunoglobulin (Ig) superfamily member that is preferentially expressed in brain and testis.	-0.000740	2.71E-09	1.37E-05
cg00602811	ZEB2	zinc finger E-box binding homeobox 2	The protein encoded by this gene functions as a DNA-binding transcriptional repressor that interacts with activated SMADs.	-0.000450	5.14E-09	1.99E-05
cg00573770	ZEB2	zinc finger E-box binding homeobox 2	The protein encoded by this gene functions as a DNA-binding transcriptional repressor that interacts with activated SMADs.	-0.000897	6.83E-09	2.30E-05

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cg16590012	TAS1R3	taste 1 receptor member 3	The protein encoded by this gene is a G-protein coupled receptor involved in taste responses. The encoded protein can elicit the umami taste response, or it can form a receptor for the sweet taste response.	-0.000438	1.37E-08	3.67E-05
cg05227556	TNXB	tenascin XB	This gene encodes a member of the tenascin family of extracellular matrix glycoproteins. This protein is thought to function in matrix maturation during wound healing.	-0.000863	1.45E-08	3.67E-05
cg26505300	DOPEY2	dopey family member 2		-0.000632	1.60E-08	3.74E-05

Table S4 *continued*

Cg site	Gene	Name	Function	Effect	P-value	Q-value
cg14255824	TJP2	tight junction protein 2	The encoded protein functions as a component of the tight junction barrier in epithelial and endothelial cells and is necessary for proper assembly of tight junctions.	-0.000507	1.76E-08	3.80E-05

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cg17372101	CNTNAP2	contactin associated protein like 2	The encoded protein mediates interactions between neurons and glia during nervous system development and is also involved in localization of potassium channels within differentiating axons.	-0.000368	3.72E-08	6.18E-05
cg12317815	ASPA	aspartoacylase	This gene encodes an enzyme that catalyzes the conversion of N-acetyl_L-aspartic acid (NAA) to aspartate and acetate. NAA is abundant in the brain where hydrolysis by aspartoacylase is thought to help maintain white matter.	-0.000469	3.87E-08	6.18E-05
cg19283806	CCDC102B	coiled-coil domain containing 102B		-0.000567	7.27E-08	0.000110

Table S4 *continued*

Cg site	Gene	Name	Function	Effect	P-value	Q-value
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cg18647570	DHX8	DEAH-box helicase 8	The encoded protein is thought to function as an ATP-dependent RNA helicase that regulates the release of spliced mRNAs from spliceosomes prior to their export from the nucleus.	-0.000415	1.00E-07	0.000145
cg11693709	PAK6	p21 (RAC1) activated kinase 6	The protein encoded by this gene interacts with androgen receptor (AR) and translocates to the nucleus, where it is involved in transcriptional regulation.	-0.000511	1.57E-07	0.000217
cg26877720	FAM107B	family with sequence similarity 107 member B		-0.000396	2.07E-07	0.000262

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cg26685941	ABCC4	ATP binding cassette subfamily C member 4	This protein is a member of the MRP subfamily which is involved in multi-drug resistance. This family member plays a role in cellular detoxification as a pump for its substrate, organic anions. It may also function in prostaglandin-mediated cAMP signaling in ciliogenesis.	-0.000425	2.24E-07	0.000271
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Table S4 *continued*

Cg site	Gene	Name	Function	Effect	P-value	Q-value
cg19991948	TIAL1	TIA1 cytotoxic granule associated RNA binding protein like 1	The protein encoded by this gene regulates various activities including translational control, splicing and apoptosis.	-0.0005494	2.62E-07	0.000306
cg18738190	CHST3	carbohydrate sulfotransferase 3	This gene encodes an enzyme which catalyzes the sulfation of chondroitin, a proteoglycan found in the extracellular matrix and most cells which is	-0.000523	3.29E-07	0.000344

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			involved in cell migration and differentiation.			
cg07091478	ZBTB46	zinc finger and BTB domain containing 46		-0.000558	3.20E-07	0.000344
cg13246235	PHACTR1	phosphatase and actin regulator 1	The protein encoded by this gene is a member of the phosphatase and actin regulator family of proteins.	0,000284	3.91E-07	0.000396
cg04265051	LRP5	LDL receptor related protein 5	The encoded protein plays a key role in skeletal homeostasis and many bone density related diseases are caused by mutations in this gene.	0.000414	4.70E-07	0.000460
cg22078805	FAM171A2	family with sequence similarity 171 member A2		0.000678	5.08E-07	0.000481
cg11842367	MGC27382	uncharacterized MGC27382		0.000591	5.24E-07	0.000482

Table S4 *continued*

Cg site	Gene	Name	Function	Effect	P-value	Q-value
cg19601530	AFAP1	actin filament associated protein 1		-0.00123	5.56E-07	0.000496

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cg26008509	EXOC3L2	exocyst complex component 3 like 2	The encoded protein may be part of an exocyst complex that plays a role in cell membrane dynamics.	-0.000587	5.90E-07	0.000511
cg22730004	SPTA1	spectrin alpha, erythrocytic 1	Spectrin functions in the determination of cell shape, arrangement of transmembrane proteins, and organization of organelles.	-0.000447	6.62E-07	0.000557
cg14517133	PRPH2	peripherin 2	The protein encoded by this gene mediates signal transduction events that play a role in the regulation of cell development, activation, growth and motility.	-0.000400	7.92E-07	0.000635
cg23766254	FAM171A2	family with sequence similarity 171 member A2		0.000650	1.02E-06	0.000772
cg20102280	HTR2A	5-hydroxy-tryptamine receptor 2A	This gene encodes one of the receptors for serotonin, a neurotransmitter with many roles.	-0.000460	1.07E-06	0.000791

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cg26237066	FRS3	fibroblast growth factor receptor substrate 3	The encoded protein links fibroblast growth factor receptor stimulation to activators of Ras. The encoded protein down-regulates extracellular regulated kinase 2 through direct binding.	-0.000402	1.11E-06	0.000803
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Table S4 *continued*

Cg site	Gene	Name	Function	Effect	P-value	Q-value
cg23186333	CD44	CD44 molecule (Indian blood group)	The protein encoded by this gene is a cell-surface glycoprotein involved in cell-cell interactions, cell adhesion and migration. This protein participates in a wide variety of cellular functions including lymphocyte activation, recirculation and homing, hematopoiesis, and tumor metastasis.	-0.000571	1.47E-06	0.00104
cg27209729	NRXN2	neurexin 2	This gene encodes a member of the neurexin gene family. The products of these genes function as cell adhesion molecules and receptors in the vertebrate nervous system.	-0.000363	1.52E-06	0.00105

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cg20592391	AP3B2	adaptor related protein complex 3 beta 2 subunit	The encoded subunit binds clathrin and is phosphorylated by a casein kinase-like protein, which mediates synaptic vesicle coat assembly.	0.000290	1.98E-06	0.00129
cg03650189	ICAM5	inter-cellular adhesion molecule 5	The encoded protein displays two types of adhesion activity, homophilic binding between neurons and heterophilic binding between neurons and leukocytes.	0.000524	1.99E-06	0.00129

Table S4 *continued*

Cg site	Gene	Name	Function	Effect	P-value	Q-value
cg21184711	CADPS2	calcium dependent secretion activator 2	This gene encodes a member of the calcium-dependent activator of secretion (CAPS) protein family, which are calcium binding proteins that regulate the exocytosis of synaptic and dense-core vesicles in neurons and neuroendocrine cells.	0.000517	2.29E-06	0.00141

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cg22910295	ICAM5	inter-cellular adhesion molecule 5	The encoded protein displays two types of adhesion activity, homophilic binding between neurons and heterophilic binding between neurons and leukocytes.	0.000457	2.32E-06	0.00141
cg15011409	ICAM5	inter-cellular adhesion molecule 5	The encoded protein displays two types of adhesion activity, homophilic binding between neurons and heterophilic binding between neurons and leukocytes.	0.000522	3.93E-06	0.00234
cg02220481	MYH11	myosin heavy chain 11	The encoded protein functions as a major contractile protein, converting chemical energy into mechanical energy through the hydrolysis of ATP.	-0.000172	4.41E-06	0.00253

Table S4 *continued*

Cg site	Gene	Name	Function	Effect	P-value	Q-value
cg04295144	ICAM5	intercellular adhesion molecule 5	The encoded protein displays two types of adhesion activity, homophilic binding between neurons and heterophilic binding between	0.000746	4.73E-06	0.00266

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			neurons and leukocytes.			
cg27133711	NRG1	neuregulin 1	The protein encoded by this gene is a membrane glycoprotein that mediates cell-cell signaling and plays a critical role in the growth and development of multiple organ systems.	-0.00101	5.42E-06	0.00294
cg16053580	KLK13	kallikrein related peptidase 13	Kallikreins are a subgroup of serine proteases having diverse physiological functions. Growing evidence suggests that many kallikreins are implicated in carcinogenesis and some have potential as novel cancer and other disease biomarkers.	0.000348	6.07E-06	0.00317
cg17190891	SH2B2	SH2B adaptor protein 2	The protein encoded by this gene appears to play a role in signal transduction from the receptor to the Shc/Grb2 pathway.	0.000390	6.20E-06	0.00319



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cg23256579	PRR4	proline rich 4 (lacrima)	This protein may play a role in protective functions in the eye.	-0.000358	6.96E-06	0.00352
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Table S4 *continued*

Cg site	Gene	Name	Function	Effect	P-value	Q-value
cg19995459	TGFBR2	transforming growth factor beta receptor 2	The protein encoded by this gene is involved in the regulation of the transcription of genes related to cell proliferation, cell cycle arrest, wound healing, immuno- suppression, and tumorigenesis.	-0.000364	7.48E-06	0.00372
cg27057509	VAR2	valyl-tRNA synthetase 2, mitochon- drial	This gene encodes a mitochondrial aminoacyl-tRNA synthetase, which catalyzes the attachment of valine to tRNA(Val) for mitochondrial translation.	-0.000372	8.51E-06	0.00410
cg22984380	RPTOR	regulatory associated protein of MTOR complex 1	This gene encodes a component of a signaling pathway that regulates cell growth in response to nutrient and insulin levels.	-0.000386	8.72E-06	0.00411
cg10604476	ICAM5	inter- cellular adhesion molecule 5	The encoded protein displays two types of adhesion activity, homophilic binding between neurons and heterophilic	0.000943	8.80E-06	0.00411

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			binding between neurons and leukocytes.			
cg00303541	GRM2	glutamate metabotropic receptor 2	This gene encodes a glutamate receptor. L-glutamate is the major excitatory neurotransmitter in the central nervous system and activates both ionotropic and metabotropic glutamate receptors.	0.000528	9.24E-06	0.00424

Table S4 *continued*

Cg site	Gene	Name	Function	Effect	P-value	Q-value
cg17344770	C19orf71	Chromosome 19 open reading frame 71		0.000251	9.80E-06	0.00444
cg22929506	PNKD	PNKD, MBL domain containing	This gene is thought to play a role in the regulation of myofibrillogenesis.	-0.000362	1.35E-05	0.00570
cg03025830	FGF17	fibroblast growth factor 17	Member of the FGF family are involved in a variety of biological processes including embryonic development, cell growth, morphogenesis, tissue repair, tumor growth and invasion.	0.000601	1.45E-05	0.00593

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cg25773262	BCAN	brevican	The encoded protein may function in the formation of the brain extracellular matrix. This protein may promote the growth and cell motility of brain tumor cells.	0.000437	1.56E-05	0.00628
cg04503319	ANKRD11	ankyrin repeat domain 11	The encoded protein inhibits ligand-dependent activation of transcription.	-0.000347	1.57E-05	0.00628
cg07568841	ZNRF2	zinc and ring finger 2		-0.000314	1.89E-05	0.00725
cg08952306	SH2B2	SH2B adaptor protein 2	The protein encoded by this gene appears to play a role in signal transduction from the receptor to the Shc/Grb2 pathway.	0.000528	1.88E-05	0.00725

Table S4 *continued*

Cg site	Gene	Name	Function	Effect	P-value	Q-value
cg00342891	FAM19A3	family with sequence similarity 19 member A3, C-C motif chemokine like	This gene is a member of the TAFAs family which are postulated to function as brain-specific chemokines or neurokines, that act as regulators of immune and nervous cells.	- 0.0001955	2.22E-05	0.00830

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cg24125828	PRRT1	proline rich trans-membrane protein 1		0.000392	2.41E-05	0.00892
cg02001899	EPHB4	EPH receptor B4	The protein encoded by this gene binds to ephrin-B2 and plays an essential role in vascular development.	-0.000327	2.60E-05	0.00950
cg01561629	OSBPL9	oxysterol binding protein like 9	This gene encodes a member of the oxysterol-binding protein (OSBP) family, a group of intracellular lipid receptors. This family member functions as a cholesterol transfer protein that regulates Golgi structure and function.	-0.00112	2.67E-05	0.00964
cg27136847	CRISP3	cysteine rich secretory protein 3	This gene is expressed in the female reproductive tract where it plays a role in endometrial receptivity for embryo implantation.	-0.000346	2.79E-05	0.00973

Table S4 *continued*

Cg site	Gene	Name	Function	Effect	P-value	Q-value
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cg13221458	SOD2	superoxide dismutase 2, mitochondrial	This gene is a member of the iron/manganese superoxide dismutase family. This protein binds to the superoxide by-products of oxidative phosphorylation and converts them to hydrogen peroxide and diatomic oxygen.	-0.000410	2.77E-05	0.00973
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<sup>1</sup>The table shows 64 probes with *Q* values < 0.01. Genes and gene functions are taken from the NCBI gene database <https://www.ncbi.nlm.nih.gov/gene>. (Empty cells in the Function column imply absence of clearly established functions as per the NCBI gene database).

Table S5

*Probes (and corresponding genes) on which methylation levels are significantly correlated ( $Q < .05$ ) with median BMI change. Positive effects associate increased BMI with increased methylation levels. (See footnote 1 below)*

Cg site	Gene	Name	Function	Effect	P-value	Q-value
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cg00992687	ESM1	endothelial cell specific molecule 1	The encoded gene may play a role in endothelium-dependent pathological disorders.	0.0128	1.29E-09	2.03E-05
cg15393936	FAM171A1	family with sequence similarity 171 member A1		0.00612	6.50E-10	2.03E-05
cg07216976	FAM160B1	family with sequence similarity 160 member B1		0.00900	2.27E-08	0.000237
cg01745766	FAM117B	family with sequence similarity 117 member B		0.00917	4.44E-08	0.000348
cg16151538	TRPC4AP	transient receptor potential cation channel subfamily C member 4 associated protein		0.00851	9.73E-08	0.000609
cg08928871	SOLH	calpain 15	The encoded protein may function as a transcription factor, RNA-binding protein, or in protein-protein interactions during visual system development.	-0.00455	4.00E-07	0.00209

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Table S5 *continued*

Cg site	Gene	Name	Function	Effect	P-value	Q-value
cg01211283	PEBP4	phosphatidylethanolamine binding protein 4	The phosphatidylethanolamine binding proteins have different functions such as lipid binding and inhibition of serine proteases.	0.00886	1.51E-06	0.00648
cg22563815	CHRNA5	cholinergic receptor nicotinic alpha 5 subunit	The protein encoded by this gene is a nicotinic acetylcholine receptor subunit that mediates fast signal transmission at synapses.	0.0100	1.65E-06	0.00648
cg04559908	DPCR1	mucin like 3		0.00989	4.23E-06	0.0102
cg03029551	MIR604			0.0111	4.19E-06	0.0102
cg01550445	P2RY2			0.00783	3.70E-06	0.0102

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cg08401758	SLC7A5	solute carrier family 7 member 5		0.00677	3.44E-06	0.0102
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Table S5 *continued*

Cg site	Gene	Name	Function	Effect	P-value	Q-value
cg20875821	SERPINB2	serpin family B member 2		0.00574	3.94E-06	0.0102
cg03732020	NR1H3	nuclear receptor subfamily 1 group H member 3	The protein encoded by this gene is involved in regulating macrophage function, controlling transcriptional programs involved in lipid homeostasis and inflammation.	-0.00793	5.66E-06	0.0118
cg27615938	NCRNA00188	LRRC75A antisense RNA 1		0.0103	5.62E-06	0.0118



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cg18335247	SIK1	salt inducible kinase 1	The encoded protein is a member of a subfamily of kinases that play a role in conserved signal transduction pathways	-0.00664	6.80E-06	0.0133
cg26955845	GPR56	adhesion G protein-coupled receptor G1	This gene encodes a member of the G protein-coupled receptor family and regulates brain cortical patterning.	0.00709	7.93E-06	0.0138

Table S5 *continued*

Cg site	Gene	Name	Function	Effect	P-value	Q-value
cg17194270	SYNGR1	synaptogyrin 1	This gene encodes an integral membrane protein associated with presynaptic vesicles in neuronal cells.	0.00729	7.78E-06	0.0138
cg22472290	ZNF577	zinc finger protein 577		0.00402	9.84E-06	0.0162

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cg20070090	S100A8	S100 calcium binding protein A8	This protein may function in the inhibition of casein kinase and as a cytokine.	-0.00829	1.27E-05	0.0165
cg17870520	GTDC1	Glycosyl-transferase like domain containing 1		0.0113	1.11E-05	0.0165
cg20561938	RNF39	ring finger protein 39		0.0125	1.31E-05	0.0165
cg13912964	ZNHIT1	zinc finger HIT-type containing 1		-0.00679	1.15E-05	0.0165
cg07895132	SLFN12L	schlafen family member 12 like		-0.00891	1.22E-05	0.0165

Table S5 *continued*

Cg site	Gene	Name	Function	Effect	P-value	Q-value
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cg14585353	ZBP2	zona pellucida binding protein 2		0.00907	1.25E-05	0.0165
cg04703221	WWP2	WW domain containing E3 ubiquitin protein ligase 2	The encoded protein may play a role in multiple processes including chondrogenesis and the regulation of oncogenic signaling pathways.	0.00700	1.63E-05	0.0197
cg01687189	GNPTAB	N-acetylglucosamine-1-phosphate transferase subunits alpha and beta	The encoded protein is essential for appropriate trafficking of lysosomal enzymes.	0.00924	1.75E-05	0.0203
cg04173252	IMP4	IMP4, U3 small nucleolar ribonucleoprotein	The protein encoded by this gene is part of the 60-80S U3 small nucleolar ribonucleoprotein complex, which is necessary for the early cleavage steps of pre-18S ribosomal RNA processing.	-0.00548	2.04E-05	0.0220
cg03665229	CNOT1	CCR4-NOT transcription complex subunit 1		0.00985	2.02E-05	0.0220

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cg07241909	USH1C	USH1 protein network component harmonin	This gene encodes a scaffold protein that functions in the assembly of Usher protein complexes.	0.00896	2.18E-05	0.0228
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Table S5 continued

Cg site	Gene	Name	Function	Effect	P-value	Q-value
cg25919221	CA6	carbonic anhydrase 6	This protein may play a role in the reversible hydration of carbon dioxide.	0.0116	2.37E-05	0.0240
cg24109894	PSMB2	proteasome subunit beta 2	The encoded subunit cleaves peptides in an ATP/ubiquitin-dependent process in a non-lysosomal pathway.	0.00883	2.53E-05	0.0240
cg19492632	SLC7A9	solute carrier family 7 member 9	The encoded protein plays a role in the high-affinity and sodium-independent transport of cystine and neutral and dibasic amino acids, and appears to function in the reabsorption of cystine in the kidney tubule.	0.00733	2.48E-05	0.0240
cg23746239	LOC729668	GOLGA2 pseudogene 6		0.00552	2.70E-05	0.0242

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cg03721887	CTDP1	CTD phosphatase subunit 1	This gene encodes a protein that functions as a phosphatase that processively dephosphorylates the C-terminus of POLR2A, making it available for initiation of gene expression.	0.00614	2.71E-05	0.0242
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Table S5 *continued*

Cg site	Gene	Name	Function	Effect	P-value	Q-value
cg21250433	CLEC7A	C-type lectin domain containing 7A	The encoded glycoprotein functions as a pattern-recognition receptor that plays a role in innate immune response.	0.0112	2.96E-05	0.0244
cg13667389	FLJ90757	BAIAP2 divergent transcript		-0.00825	2.95E-05	0.0244
cg12948621	HKR1	HKR1, GLI-Kruppel zinc finger family member		0.00640	2.89E-05	0.0244

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cg11400325	ANKRD36B L1	ankyrin repeat domain 36B pseudogene 1		0.0119	3.45E-05	0.0263
cg02483058	EML6	echinoderm microtubule associated protein like 6		-0.0178	3.38E-05	0.0263
cg22940798	TAP2	transporter 2, ATP binding cassette subfamily B member	The protein encoded by this gene is involved in antigen presentation.	0.00576	3.64E-05	0.0263
cg19566648	RPS6KA2	ribosomal protein S6 kinase A2	The activity of the encoded protein has been implicated in controlling cell growth and differentiation.	-0.0113	3.70E-05	0.0263

Table S5 *continued*

Cg site	Gene	Name	Function	Effect	P-value	Q-value
cg01675512	RPL23AP64	ribosomal protein L23a pseudogene 64		0.0154	3.65E-05	0.0263
cg14729980	SIGLEC15	sialic acid binding Ig like lectin 15		0.0132	3.31E-05	0.0263

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cg16936953	TMEM49	vacuole membrane protein 1	This gene encodes a transmembrane protein that plays a key regulatory role in the process of autophagy.	0.0158	3.82E-05	0.0266
cg09727210	CARD11	caspase recruitment domain family member 11	The protein encoded by this gene belongs to a class of proteins that functions as molecular scaffolds for the assembly of multiprotein complexes at specialized regions of the plasma membrane.	-0.00495	3.92E-05	0.0267
cg19894085	IRAK3	interleukin 1 receptor associated kinase 3	The encoded protein is primarily expressed in monocytes and macrophages and functions as a negative regulator of Toll-like receptor signaling.	0.0145	4.34E-05	0.0289

Table S5 *continued*

Cg site	Gene	Name	Function	Effect	P-value	Q-value
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cg22031873	INPP4B	inositol polyphosphate -4-phosphatase type II B	INPP4B encodes the inositol polyphosphate 4-phosphatase type II, one of the enzymes involved in phosphatidylinositol signaling pathways.	0.00803	4.88E-05	0.0315
cg13345299	HPS4	HPS4, biogenesis of lysosomal organelles complex 3 subunit 2	This gene encodes a protein component of biogenesis of lysosome-related organelles complexes.	0.00720	4.93E-05	0.0315
cg25801976	KIAA0146	scaffold protein involved in DNA repair		0.00772	5.27E-05	0.0330
cg01742680	RAP2B	RAP2B, member of RAS oncogene family	The encoded protein may be polyisoprenylated and palmitoylated	0.00579	5.92E-05	0.0357
cg16805553	MPZL3	myelin protein zero like 3		0.00997	5.82E-05	0.0357



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cg12317815	ASPA	aspartoacylase	This gene encodes an enzyme that catalyzes the conversion of N-acetyl_L-aspartic acid (NAA) to aspartate and acetate, which is thought to help maintain white matter.	0.0124	6.49E-05	0.0384
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Table S5 continued

Cg site	Gene	Name	Function	Effect	P-value	Q-value
cg03714676	KIAA0146	scaffold protein involved in DNA repair		0.0107	7.06E-05	0.0410
cg06636195	EDAR	ectodysplasin A receptor		-0.0109	7.79E-05	0.0414
cg14933468	ASRGL1	asparaginase like 1		0.00489	7.79E-05	0.0414

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cg00689225	NFKBIA	NFKB inhibitor alpha	The encoded protein interacts with REL dimers to inhibit NF-kappa-B/REL complexes which are involved in inflammatory responses.	0.0124	7.52E-05	0.0414
cg04057642	KPNB1	karyopherin subunit beta 1	The protein encoded by this gene is a member of the importin beta family, which play a role in nucleocytoplasmic transport.	0.0113	7.67E-05	0.0414
cg07285621	CLDN14	claudin 14	The protein encoded by this gene is an integral membrane protein and a component of tight junction strands.	-0.00959	7.45E-05	0.0414

Table S5 *continued*

Cg site	Gene	Name	Function	Effect	P-value	Q-value
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cg08817540	HHLA2	HERV-H LTR- associating 2	The encoded protein is thought to regulate cell-mediated immunity by binding to a receptor on T lymphocytes and inhibiting the proliferation of these cells.	0.0138	8.92E-05	0.0451
cg01538969	DHX16	DEAH-box helicase 16	The encoded protein is a DEAD box protein, which are implicated in a number of cellular processes involving alteration of RNA secondary structure such as translation initiation, nuclear and mitochondrial splicing, and ribosome and spliceosome assembly.	-0.00655	8.80E-05	0.0451
cg08119150	RADIL	Rap associating with DIL domain		0.00630	8.68E-05	0.0451
cg21610854	RETNLB	resistin like beta		0.0193	9.21E-05	0.0451

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cg14309283	ZBTB22	zinc finger and BTB domain containing 22		-0.0103	9.13E-05	0.0451
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Table S5 *continued*

Cg site	Gene	Name	Function	Effect	P-value	Q-value
cg01290568	IL1B	interleukin 1 beta	The encoded cytokine is an important mediator of the inflammatory response, and is involved in a variety of cellular activities, including cell proliferation, differentiation, and apoptosis.	0.00866	9.68E-05	0.0467
cg22871253	EZR	ezrin	The encoded protein plays a key role in cell surface structure adhesion, migration and organization, and it has been implicated in various human cancers.	0.0135	0.000101	0.0480

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cg12754982	IGF2R	insulin like growth factor 2 receptor	The encoded receptor has various functions, including in the intracellular trafficking of lysosomal enzymes, the activation of transforming growth factor beta, and the degradation of insulin-like growth factor 2.	0.0124	0.000104	0.0485
cg16100392	TAAR3	trace amine associated receptor 3, pseudogene		0.00817	0.000108	0.0485

Table S5 *continued*

Cg site	Gene	Name	Function	Effect	P-value	Q-value
cg05516061	OR4C45	olfactory receptor family 4 subfamily C member 45 (gene/pseudogene)	Olfactory receptors interact with odorant molecules in the nose, to initiate a neuronal response that triggers the perception of a smell.	0.0116	0.000106	0.0485

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cg10717149	SLC25A14	solute carrier family 25 member 14	The encoded protein is involved in facilitating the transfer of anions from the inner to the outer mitochondrial membrane and the return transfer of protons from the outer to the inner mitochondrial membrane.	-0.00783	0.000108	0.0485
cg23232773	HCP5	HLA complex P5		0.00887	0.000113	0.0485
cg27405731	CUX1	cut like homeobox 1	The protein encoded by this gene may regulate gene expression, morphogenesis, and differentiation.	-0.00828	0.000111	0.0485
cg04527429	PALM	paralemmin	The product of this gene is implicated in plasma membrane dynamics in neurons and other cell types.	0.00763	0.000112	0.0485

<sup>1</sup>The table shows 73 probes with *Q* values < 0.05. Genes and gene functions are taken from the NCBI gene database <https://www.ncbi.nlm.nih.gov/gene>. (Empty cells imply that clearly established functions are lacking as per the NCBI gene database).

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