

Summary-based methylome-wide association analyses suggest potential genetically driven epigenetic heterogeneity of Alzheimer's disease

Alireza Nazarian*, Anatoliy I. Yashin, and Alexander M. Kulminski*

Biodemography of Aging Research Unit, Social Science Research Institute, Duke University, Durham, NC, USA

*Corresponding Authors:

Alireza Nazarian and Alexander M. Kulminski

Duke University

Social Science Research Institute

Biodemography of Aging Research Unit

Erwin Mill Building, 2024 W. Main St.

Durham, NC 27705

Emails: alireza.nazarian@duke.edu and kulminsk@duke.edu

Supporting Acknowledgment

This research was supported by Grants No. P01AG043352, R01AG047310, and R01AG065477 from the National Institute on Aging. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

This manuscript was prepared using limited access datasets obtained through dbGaP (accession numbers: phs000287.v5.p1 (CHS), phs000007.v28.p10 (FHS), phs000428.v2.p2 (HRS), and phs000168.v2.p2 (LOADFS) at <https://www.ncbi.nlm.nih.gov/gap>) and the University of Michigan. Phenotypic HRS data are available publicly and through restricted access from <http://hrsonline.isr.umich.edu/index.php?p=data>.

The Cardiovascular Health Study (CHS) was supported by contracts HHSN268201200036C, HHSN268200800007C, N01-HC-85079, N01-HC-85080, N01-HC-85081, N01-HC-85082, N01-HC-85083, N01-HC-85084, N01-HC-85085, N01-HC-85086, N01-HC-35129, N01 HC-15103, N01 HC-55222, N01-HC-75150, N01-HC-45133, and N01-HC-85239; grant numbers U01 HL080295 and U01 HL130014 from the National Heart, Lung, and Blood Institute (NHLBI), and R01 AG-023629 from the National Institute on Aging, with additional contribution from the National Institute of Neurological Disorders and Stroke. A full list of principal CHS investigators and institutions can be found at <https://chs-nhlbi.org/pi>. This manuscript was not prepared in collaboration with CHS investigators and does not necessarily reflect the opinions or views of CHS, or the NHLBI. Support for the genotyping through the CARE Study was provided by NHLBI Contract N01-HC-65226. Additional support for infrastructure was provided by HL105756 and additional genotyping among the African-American cohort was supported in part by HL085251. DNA handling and genotyping at Cedars-Sinai Medical Center was supported in part by National Center for Research Resources grant UL1RR033176, now at the National Center for Advancing Translational Technologies CTSI grant UL1TR000124; in addition to the National Institute of Diabetes and Digestive and Kidney Diseases grant DK063491 to the Southern California Diabetes Endocrinology Research Center.

The Framingham Heart Study (FHS) is conducted and supported by the National Heart, Lung, and Blood Institute (NHLBI) in collaboration with Boston University (Contract No. N01-HC-25195 and HHSN268201500001I). This manuscript was not prepared in collaboration with investigators of the FHS and does not necessarily reflect the opinions or views of the FHS, Boston University, or NHLBI. Funding for SHARe Affymetrix genotyping was provided by NHLBI Contract N02-HL-64278. SHARe Illumina genotyping was provided under an agreement between Illumina and Boston University. Funding for CARE genotyping was provided by NHLBI Contract N01-HC-65226. Funding support for the Framingham Dementia dataset was provided by NIH/NIA grant R01 AG08122. Funding support for the Framingham Inflammatory Markers was provided by NIH grants R01 HL064753, R01 HL076784 and R01 AG028321. Funding support for the Framingham C-reactive Protein dataset was provided by NIH grants R01 HL064753, R01 HL076784 and R01 AG028321. Funding support for the Framingham Adiponectin dataset was provided by NIH/NHLBI grant R01-DK-080739. Funding support for the Framingham Interleukin-6 dataset was provided by NIH grants R01 HL064753, R01 HL076784 and R01 AG028321.

The Health and Retirement Study (HRS) genetic data is sponsored by the Genetics Resource with HRS April 21, 2010, version G Page 5 of 7 National Institute on Aging (grant numbers U01AG009740, RC2AG036495, and RC4AG039029) and was conducted by the University of Michigan. This manuscript

was not prepared in collaboration with HRS investigators and does not necessarily reflect the opinions or views of HRS.

Funding support for the Late Onset Alzheimer's Disease Family Study (LOADFS) was provided through the Division of Neuroscience, NIA. The LOADFS includes a genome-wide association study funded as part of the Division of Neuroscience, NIA. Assistance with phenotype harmonization and genotype cleaning, as well as with general study coordination, was provided by Genetic Consortium for Late Onset Alzheimer's Disease. This manuscript was not prepared in collaboration with LOADFS investigators and does not necessarily reflect the opinions or views of LOADFS.

Tables

Table S1: Blood-based methylome-wide association results

ProbeID	Chr	ProbePos	Gene	SNP	Pos	A1	Freq	P _{GWAS}	P _{mQTL}	b _{SMR}	SE _{SMR}	P _{SMR}	P _{HEIDI}	N _{HEIDI}	Current?	Previous?	Region?
Plan 1: All Subjects																	
cg20486877	6p22.1	29626704	GABBR1	rs12530421	29581666	C	0.072	2.11E-04	3.47E-66	-0.284	0.057	5.17E-07	5.21E-02	20	N	N	N
cg12893697	11p15.5	970389	AP2A2	rs7395773	970503	C	0.481	1.34E-05	0	-0.168	0.031	6.64E-08	4.36E-01	20	S	S	S
cg06064525	11p15.5	970664	AP2A2	rs7395773	970503	C	0.481	1.34E-05	0	-0.158	0.029	6.30E-08	5.10E-01	20	S	S	S
cg05626073	11p15.5	971527	AP2A2	rs7395773	970503	C	0.481	1.34E-05	1.75E-305	-0.188	0.035	7.49E-08	1.25E-01	20	S	S	S
cg09162537	11p15.5	976950	AP2A2	rs7395402	950293	C	0.447	1.54E-05	4.81E-59	-0.352	0.069	3.04E-07	2.03E-01	20	S	S	S
cg21806090	12p13.33	2088868	CACNA1C	rs56401832	2074725	C	0.030	2.28E-03	5.18E-165	-0.141	0.028	3.43E-07	3.63E-01	6	N	N	N
cg00222015	12q24.31	121795469	LINC01089	rs7964357	121893222	C	0.025	3.21E-04	0	-0.130	0.021	1.54E-09	2.50E-01	20	N	N	N
cg06750524	19q13.32	44906698	APOE	rs769449	44906745	A	0.112	2.15E-83	9.38E-15	3.617	0.469	1.24E-14	9.03E-02	10	G	G	G
Plan 2: Only Males																	
cg20011360	4p14	37584038	C4orf19	rs2276944	37584048	A	0.106	5.94E-04	3.40E-180	0.366	0.058	2.62E-10	3.04E-01	17	N	N	N
cg23395749	5q35.3	177557245	IGR (FAM193B)	rs1001530	177558514	G	0.046	4.38E-03	2.55E-26	-0.559	0.109	2.95E-07	2.48E-01	5	N	S	S
cg04627871	6p21.33	31736144	CLIC1	rs34585796	31778065	T	0.013	2.46E-02	2.57E-54	0.339	0.059	1.09E-08	1.24E-01	10	N	G	S
cg15598276	6p21.32	32980566	BRD2	rs115417321	32973918	C	0.016	6.96E-03	9.03E-38	-0.484	0.073	2.68E-11	2.61E-01	14	N	G	G
cg01991743	6p21.32	33085831	HLA-DPB1	rs11551421	33085832	A	0.039	1.59E-03	0	-0.140	0.025	2.79E-08	2.29E-01	20	N	G	G
cg06527438	6q27	170236746	IGR (LOC154449)	rs58691983	170238096	A	0.013	2.95E-02	1.44E-25	-0.548	0.098	2.10E-08	4.10E-01	5	N	N	S
cg21205282	6q27	170244045	IGR (LOC154449)	rs58691983	170238096	A	0.013	2.95E-02	2.90E-16	-0.693	0.134	2.55E-07	8.05E-02	5	N	N	S
cg22883453	6q27	170244276	IGR (LOC154449)	rs58691983	170238096	A	0.013	2.95E-02	1.09E-19	-0.628	0.117	8.38E-08	5.52E-02	4	N	N	S
cg04505845	6q27	170244461	IGR (LOC154449)	rs58691983	170238096	A	0.013	2.95E-02	7.99E-22	-0.592	0.108	4.76E-08	2.03E-01	4	N	N	S
cg05526015	6q27	170244757	IGR (LOC154449)	rs58691983	170238096	A	0.013	2.95E-02	1.13E-35	-0.463	0.079	4.65E-09	2.18E-01	6	N	N	S
cg24651908	6q27	170245433	IGR (LOC154449)	rs58691983	170238096	A	0.013	2.95E-02	1.52E-18	-0.650	0.123	1.18E-07	5.85E-02	4	N	N	S
cg04386759	6q27	170245707	IGR (LOC154449)	rs58691983	170238096	A	0.013	2.95E-02	1.36E-25	-0.542	0.097	2.09E-08	5.91E-02	5	N	N	S
cg26180843	6q27	170248014	IGR (LOC154449)	rs58691983	170238096	A	0.013	2.95E-02	1.75E-21	-0.584	0.107	5.18E-08	1.14E-01	5	N	N	S
cg12035402	6q27	170250189	IGR (LOC154449)	rs58691983	170238096	A	0.013	2.95E-02	1.02E-16	-0.692	0.133	2.16E-07	7.79E-02	5	N	N	S
cg05438220	7q21.13	90643046	CDK14	rs17864073	90601202	A	0.022	6.89E-03	0	-0.125	0.023	3.54E-08	2.11E-01	15	N	N	S
cg11399834	8p22	14566901	SGCZ	rs7013654	14587192	T	0.047	1.75E-03	6.43E-156	-0.348	0.054	1.20E-10	2.06E-01	20	N	N	G
cg12185975	8q24.22	130761450	IGR (ADCY8)	rs79599781	130735526	A	0.057	5.42E-04	2.13E-165	-0.239	0.040	1.73E-09	6.17E-01	20	S	S	S
cg23402755	10p14	7702004	ITIH2	rs76129783	7716283	C	0.027	2.98E-03	1.29E-26	-0.453	0.089	3.85E-07	6.42E-01	12	N	G	G
cg14381908	10q11.21	43202369	RASGEF1A	rs35718664	43158746	G	0.056	2.03E-03	1.22E-195	0.204	0.040	4.90E-07	2.63E-01	18	N	N	N
cg25422051	11q13.1	65916842	C11orf68	rs7940700	65903526	T	0.015	2.87E-02	5.91E-26	-0.658	0.094	2.43E-12	3.54E-01	7	N	N	N
cg15007809	12q21.2	75883289	IGR (PHLDA1)	rs11180729	75883290	A	0.014	1.08E-02	1.65E-298	-0.190	0.021	8.73E-20	4.99E-01	10	N	G	G
cg19755435	14q31.3	88006657	GPR65	rs1372363	88006834	T	0.076	8.12E-04	2.90E-45	-0.462	0.087	1.04E-07	3.79E-01	20	N	N	S
cg20239174	15q24.1	73780023	IGR (C15orf59)	rs1869176	73789242	T	0.010	4.71E-02	3.59E-224	-0.160	0.025	2.42E-10	5.18E-01	7	N	N	N
cg24801087	17q25.3	78485647	DNAH17,DNAH17-AS1	rs654154	78485428	C	0.061	3.39E-03	2.53E-45	-0.573	0.106	6.81E-08	2.09E-01	13	N	S	S
cg08778119	17q25.3	78496484	DNAH17,DNAH17-AS1	rs12944401	78611646	T	0.028	3.54E-03	5.02E-40	-0.483	0.087	3.23E-08	3.68E-01	4	N	S	S
cg06750524	19q13.32	44906698	APOE	rs769449	44906745	A	0.112	7.08E-30	9.38E-15	3.651	0.477	1.92E-14	1.39E-01	10	G	G	G
cg05206559	19q13.32	45913997	NANOS2	rs66529687	45914171	A	0.133	1.83E-04	2.84E-41	0.723	0.125	7.67E-09	3.28E-01	20	G	G	G
cg25673584	19q13.32	45914293	NANOS2	rs66529687	45914171	A	0.133	1.83E-04	4.40E-30	0.849	0.152	2.45E-08	1.23E-01	20	G	G	G
cg14192299	19q13.32	45914381	NANOS2	rs66529687	45914171	A	0.133	1.83E-04	6.71E-42	0.718	0.124	7.30E-09	1.08E-01	20	G	G	G
cg19702802	19q13.32	45914471	NANOS2	rs66529687	45914171	A	0.133	1.83E-04	3.22E-39	0.743	0.129	9.10E-09	1.03E-01	20	G	G	G
cg02345758	19q13.43	55837753	NLRP4,NLRP11	rs7258704	55849297	T	0.031	5.98E-03	5.63E-73	-0.443	0.067	3.06E-11	5.82E-02	5	N	N	N
Plan 3: Only Females																	
cg25325322	2p11.2	84846591	TRABD2A	rs116716092	84837385	G	0.034	2.14E-04	1.11E-134	0.244	0.036	1.19E-11	2.20E-01	20	N	N	S
cg18572898	6p21.32	32744326	HLA-DQA2	rs7768538	32762044	C	0.426	6.15E-05	0	-0.167	0.032	1.80E-07	1.60E-01	20	S	G	G

cg10218546	6p21.32	32762046	HLA-DQB2	rs7768538	32762044	C	0.426	6.15E-05	1.30E-126	-0.304	0.060	3.27E-07	6.43E-02	20	S	G	G
cg02786056	8q13.2	69589075	SULF1	rs76431927	69661855	A	0.012	2.19E-02	3.14E-44	-0.421	0.062	1.22E-11	8.98E-01	10	N	N	G
cg00222015	12q24.31	121795469	LINC01089	rs7964357	121893222	C	0.025	7.48E-04	0	-0.165	0.025	4.77E-11	1.93E-01	20	N	N	N
cg13328209	12q24.31	124738956	IGR (SCARB1)	rs79981325	124732494	T	0.066	9.49E-04	4.32E-34	-0.515	0.102	4.89E-07	9.19E-02	10	N	N	N
cg17632299	13q14.3	52738831	LECT1	rs4885947	52735009	C	0.037	2.28E-03	7.51E-54	0.395	0.075	1.67E-07	6.33E-02	20	N	G	G
cg18379295	14q22.1	51859437	GNG2	rs17124656	51859367	C	0.217	1.81E-05	7.51E-28	-0.597	0.116	2.79E-07	3.75E-01	20	N	S	G
cg06750524	19q13.32	44906698	APOE	rs769449	44906745	A	0.112	6.07E-47	9.38E-15	3.521	0.458	1.58E-14	8.74E-02	10	G	G	G
Plan 4: Hypertensive Subjects																	
cg22472863	4q31.22	147096252	IGR (TTC29)	rs1507499	147072520	A	0.016	6.68E-04	9.88E-46	-0.314	0.048	7.53E-11	1.78E-01	17	N	N	N
cg23395749	5q35.3	177557245	IGR (FAM193B)	rs1001530	177558514	G	0.046	3.36E-04	2.55E-26	-0.484	0.088	3.08E-08	8.77E-02	5	N	S	S
cg06527438	6q27	170236746	IGR (LOC154449)	rs58691983	170238096	A	0.013	2.37E-02	1.44E-25	-0.470	0.092	3.40E-07	6.30E-01	5	N	N	S
cg05526015	6q27	170244757	IGR (LOC154449)	rs58691983	170238096	A	0.013	2.37E-02	1.13E-35	-0.397	0.075	1.22E-07	1.20E-01	6	N	N	S
cg00222015	12q24.31	121795469	LINC01089	rs7964357	121893222	C	0.025	3.54E-03	0	-0.139	0.027	1.58E-07	1.84E-01	20	N	N	N
cg06750524	19q13.32	44906698	APOE	rs769449	44906745	A	0.112	4.22E-39	9.38E-15	3.090	0.405	2.23E-14	1.01E-01	10	G	G	G
Plan 5: Non-hypertensive Subjects																	
cg15076811	1p36.22	10940981	IGR (C1orf127)	rs744921	10938452	A	0.079	3.93E-03	2.26E-43	-0.567	0.112	4.46E-07	7.68E-01	4	N	S	S
cg27535302	1p34.2	42165766	GUCA2A	rs116679095	42165766	T	0.013	6.49E-03	3.65E-179	-0.193	0.023	1.38E-16	3.99E-01	13	N	N	G
cg04510459	1p22.1	91582730	IGR (CDC7)	rs75735322	91587247	T	0.019	2.71E-03	9.42E-25	0.801	0.115	2.89E-12	3.22E-01	12	N	N	N
cg20306265	1p12	117615002	FAM46C	rs2884587	117623474	T	0.170	7.60E-04	3.24E-69	-0.484	0.094	2.81E-07	6.42E-02	20	N	N	N
cg18342183	1q31.1	186763783	IGR (PLA2G4A)	rs75463571	186219083	A	0.026	6.25E-03	3.30E-126	-0.402	0.049	2.95E-16	1.40E-01	18	N	S	N
cg23924526	2p21	45771409	PRKCE	rs4952770	45771583	A	0.012	4.24E-02	1.41E-27	-0.431	0.078	3.34E-08	9.57E-02	4	N	S	S
cg03063511	2p13.1	73930386	DGUOK	rs6737156	73932607	C	0.036	5.62E-03	2.71E-227	-0.247	0.041	2.74E-09	1.09E-01	11	N	N	N
cg25325322	2p11.2	84846591	TRABD2A	rs116716092	84837385	G	0.034	1.34E-02	1.11E-134	0.265	0.051	1.86E-07	1.39E-01	20	N	N	S
cg27608154	2q13	111124233	BCL2L1	rs3789067	111152506	T	0.061	2.21E-03	4.75E-135	-0.310	0.056	3.03E-08	2.81E-01	11	N	N	G
cg25679431	3p22.3	32147516	GPD1L	rs11922351	32130428	G	0.020	3.24E-02	2.00E-182	-0.221	0.043	3.06E-07	1.62E-01	9	N	N	S
cg01317029	3q27.1	184345709	FAM131A	rs1049448	184308935	A	0.024	1.91E-02	7.88E-24	0.616	0.122	4.98E-07	1.62E-01	11	N	N	N
cg02951719	4p16.3	1518424	IGR (NKX1-1)	rs111388896	1166078	T	0.043	5.15E-03	3.55E-48	-0.490	0.090	5.71E-08	1.46E-01	20	N	N	S
cg05638493	5q31.3	141303800	SLC25A2	rs7706206	141322835	A	0.046	2.89E-03	5.84E-34	-0.611	0.105	6.00E-09	2.78E-01	18	N	G	G
cg08631357	5q32	150209647	SLC6A7	rs10076748	150209303	A	0.107	1.77E-03	1.54E-193	0.288	0.056	3.18E-07	2.02E-01	20	N	N	G
cg17781669	5q33.1	150488796	IGR (NDST1)	rs12519820	150488714	A	0.073	2.10E-03	5.39E-203	0.274	0.050	5.00E-08	1.30E-01	14	N	N	S
cg15538767	5q33.1	150490833	IGR (NDST1)	rs12519820	150488714	A	0.073	2.10E-03	1.41E-39	0.552	0.108	3.27E-07	6.20E-01	7	N	N	S
cg19810457	5q35.3	180247356	MAPK9	rs77155114	180300706	G	0.016	3.05E-02	4.20E-85	-0.346	0.061	1.16E-08	1.18E-01	6	N	S	S
cg09198601	6p24.3	10318947	IGR (TFAP2A)	rs6921983	10318317	T	0.027	1.97E-03	5.34E-22	-0.742	0.117	2.37E-10	3.87E-01	9	N	N	N
cg14466923	6p21.32	33182959	COL11A2	rs114068468	33086686	T	0.013	3.09E-02	2.47E-51	-0.226	0.045	4.59E-07	6.83E-02	10	N	G	G
cg17430214	6p21.1	41279166	TREM1	rs16894069	40823401	G	0.035	3.43E-03	1.71E-22	0.672	0.123	4.60E-08	7.38E-02	10	N	G	G
cg00531924	6q21	110958687	GTF3C6	rs59393044	110958643	C	0.041	6.48E-04	1.54E-16	-1.087	0.188	7.54E-09	1.38E-01	12	N	N	S
cg24039042	6q27	170271859	IGR (LOC154449)	rs79920678	170266664	C	0.019	8.48E-03	5.14E-140	0.310	0.044	3.10E-12	1.63E-01	4	N	N	S
cg01766850	6q27	170271878	IGR (LOC154449)	rs79920678	170266664	C	0.019	8.48E-03	1.42E-211	0.265	0.038	1.59E-12	2.13E-01	4	N	N	S
cg05973084	6q27	170271951	IGR (LOC154449)	rs79920678	170266664	C	0.019	8.48E-03	0	0.193	0.027	6.15E-13	4.25E-01	4	N	N	S
cg09344348	6q27	170271997	IGR (LOC154449)	rs79920678	170266664	C	0.019	8.48E-03	0	0.208	0.029	7.58E-13	4.10E-01	4	N	N	S
cg18555277	6q27	170272160	IGR (LOC154449)	rs79920678	170266664	C	0.019	8.48E-03	0	0.201	0.028	6.84E-13	3.90E-01	4	N	N	S
cg01209642	6q27	170272267	IGR (LOC154449)	rs79920678	170266664	C	0.019	8.48E-03	0	0.200	0.028	6.67E-13	3.49E-01	4	N	N	S
cg21138542	6q27	170272414	IGR (DLL1)	rs79920678	170266664	C	0.019	8.48E-03	2.18E-197	0.271	0.038	1.75E-12	1.97E-01	4	N	N	S
cg03899510	6q27	170272602	IGR (DLL1)	rs79920678	170266664	C	0.019	8.48E-03	2.06E-45	0.510	0.079	1.07E-10	9.71E-02	4	N	N	S
cg23988375	6q27	170275018	IGR (DLL1)	rs79920678	170266664	C	0.019	8.48E-03	1.42E-26	-0.665	0.111	1.97E-09	2.44E-01	4	N	N	S
cg16108844	6q27	170275085	IGR (DLL1)	rs79920678	170266664	C	0.019	8.48E-03	1.40E-20	-0.760	0.133	1.06E-08	1.74E-01	3	N	N	S
cg23534345	7p22.1	5639075	RNF216	rs852474	5639183	T	0.044	4.34E-04	9.48E-12	1.189	0.234	3.94E-07	5.89E-01	17	N	N	G
cg27103343	7p21.3	10779424	IGR (NDUFA4)	rs117926694	10801559	T	0.024	1.18E-02	0	-0.184	0.031	2.96E-09	6.12E-01	20	N	G	G
cg07227187	7q11.21	64192342	IGR (ZNF735P)	rs2099421	64206949	G	0.031	6.33E-03	0	-0.149	0.027	3.66E-08	5.84E-01	20	N	S	S

cg01391867	7q22.1	99500248	ZNF394	rs117700582	100248819	T	0.026	4.21E-03	2.36E-18	0.787	0.136	7.78E-09	4.44E-01	8	N	G	G
cg23891049	7q33	134679117	BPGM	rs73441994	134679118	A	0.021	4.26E-02	1.18E-229	-0.156	0.030	1.70E-07	6.07E-01	4	N	S	S
cg27057461	7q36.3	158343687	PTPRN2	rs11975566	158366864	A	0.020	4.60E-03	1.83E-17	-0.750	0.129	6.02E-09	4.46E-01	5	N	N	S
cg04035728	8p21.2	27465950	CHRNA2	rs919493	27434040	T	0.139	1.31E-03	1.83E-194	-0.335	0.062	8.00E-08	5.36E-01	20	N	G	G
cg23277389	8q11.21	48921984	SNAI2	rs117931199	48936117	T	0.027	1.49E-02	1.33E-26	-0.601	0.118	3.71E-07	3.16E-01	7	N	N	N
cg26687619	8q24.22	133904113	IGR (ST3GAL1)	rs55923676	133886617	C	0.020	8.88E-03	5.14E-18	-0.716	0.124	8.59E-09	5.88E-01	3	N	N	S
cg23402755	10p14	7702004	ITIH2	rs76129783	7716283	C	0.027	2.75E-04	1.29E-26	-0.726	0.099	2.53E-13	5.25E-01	12	N	G	G
cg23809813	10q23.31	88457915	RNLS	rs4933483	88458165	A	0.158	5.70E-04	5.71E-131	0.388	0.071	4.57E-08	5.26E-01	20	N	S	S
cg05399434	10q26.13	121609167	IGR (FGFR2)	rs59251821	121607733	T	0.029	7.67E-04	4.58E-26	-0.897	0.119	5.54E-14	5.26E-02	20	N	S	N
cg01628053	10q26.13	121609218	IGR (FGFR2)	rs59251821	121607733	T	0.029	7.67E-04	3.77E-23	-0.949	0.131	3.52E-13	1.40E-01	20	N	S	N
cg24635736	10q26.13	122979534	PSTK	rs2421140	123027854	A	0.029	8.09E-03	2.67E-77	-0.346	0.060	6.12E-09	7.16E-01	8	N	N	N
cg16255663	10q26.3	129552735	MGMT	rs76299173	129527894	T	0.083	1.19E-03	0	-0.204	0.036	8.69E-09	1.05E-01	20	N	S	N
cg17686260	10q26.3	129614500	MGMT	rs7893831	129618819	A	0.088	8.70E-04	0	-0.213	0.036	4.05E-09	3.03E-01	20	N	S	N
cg05741225	10q26.3	132103799	JAKMIP3	rs78086323	132098502	A	0.022	2.94E-02	3.73E-143	-0.218	0.039	2.91E-08	2.21E-01	6	N	N	N
cg10427719	10q26.3	133334898	CALY	rs78775728	133362250	C	0.046	8.30E-03	2.79E-164	-0.262	0.050	1.77E-07	1.21E-01	20	N	N	N
cg02114346	10q26.3	133378038	PAOX	rs11101724	133378649	A	0.049	4.14E-03	7.40E-24	0.688	0.137	5.26E-07	1.26E-01	11	N	N	N
cg11435872	11p11.2	45805924	SLC35C1	rs2666890	45771472	G	0.066	6.45E-06	1.05E-09	1.519	0.291	1.88E-07	2.73E-01	20	S	N	G
cg05360847	11q13.4	71576873	IGR (KRTAP5-11)	rs11827208	71578103	T	0.020	1.70E-03	3.47E-13	-0.942	0.159	3.50E-09	2.02E-01	4	N	N	S
cg02850715	11q24.3	130159317	ST14	rs34008994	130165703	T	0.096	1.55E-04	1.21E-26	-0.812	0.138	4.14E-09	7.87E-01	20	N	N	G
cg21029769	11q24.3	130159620	ST14	rs34008994	130165703	T	0.096	1.55E-04	4.09E-18	-1.006	0.184	4.58E-08	9.16E-01	20	N	N	G
cg19153300	11q25	134925086	IGR (LOC283177)	rs79428444	134915582	T	0.039	5.22E-03	0	-0.201	0.033	1.18E-09	1.89E-01	20	N	N	N
cg21806090	12p13.33	2088868	CACNA1C	rs56401832	2074725	C	0.030	2.14E-02	5.18E-165	-0.208	0.040	1.66E-07	5.05E-01	6	N	N	N
cg11915525	12p11.23	27469767	SMC2O	rs67786386	27463248	A	0.058	1.30E-03	2.98E-47	-0.502	0.085	3.10E-09	5.37E-01	20	N	N	N
cg21922731	12q13.3	56763346	HSD17B6	rs57682836	56774236	T	0.028	1.34E-03	1.86E-14	-0.920	0.167	3.47E-08	8.65E-01	9	N	S	S
cg05979241	12q21.2	77326379	IGR (E2F7)	rs10219515	77332811	C	0.026	1.27E-02	8.22E-57	0.424	0.068	3.95E-10	3.58E-01	18	N	N	G
cg24420742	12q21.2	77328028	IGR (E2F7)	rs17043304	77308159	G	0.025	1.27E-02	2.67E-80	-0.369	0.057	1.24E-10	7.62E-01	16	N	N	G
cg20090301	12q21.2	77362321	IGR (E2F7)	rs10219515	77332811	C	0.026	1.27E-02	1.22E-26	0.624	0.109	9.45E-09	2.98E-01	9	N	N	G
cg20045970	12q24.11	109881214	GLTP	rs2287175	110037732	T	0.036	9.24E-03	2.60E-25	-0.704	0.135	1.84E-07	4.11E-01	17	N	N	S
cg17632299	13q14.3	52738831	LECT1	rs4885947	52735009	C	0.037	1.23E-03	7.51E-54	0.592	0.085	2.67E-12	1.34E-01	20	N	G	G
cg09557313	13q14.3	52739039	LECT1	rs4885947	52735009	C	0.037	1.23E-03	1.46E-40	0.675	0.100	1.37E-11	1.02E-01	20	N	G	G
cg13822911	13q33.2	106376925	LINC00460	rs1351059	106378937	A	0.163	4.74E-04	3.61E-38	-0.649	0.125	2.03E-07	5.71E-02	16	N	S	S
cg05099145	16p13.3	1746332	MAPK8IP3	rs114127401	1746293	A	0.011	9.72E-03	6.95E-17	-1.613	0.196	2.07E-16	8.07E-01	8	N	S	G
cg11220950	16p13.3	1992692	SYNGR3	rs11542302	1986934	C	0.181	7.26E-05	8.47E-17	-1.153	0.223	2.27E-07	5.53E-02	17	N	S	G
cg04519296	16p13.3	1993014	SYNGR3	rs11248905	1999727	T	0.181	4.88E-05	8.21E-26	-1.037	0.176	3.88E-09	9.73E-02	17	N	S	G
cg09397293	16p13.3	2005032	ZNF598	rs72766639	2005819	A	0.174	1.69E-04	5.78E-51	0.688	0.116	3.06E-09	2.85E-01	20	N	S	G
cg26804891	16p13.3	2005241	ZNF598	rs11248905	1999727	T	0.181	4.88E-05	3.56E-98	0.539	0.080	1.62E-11	7.60E-02	20	N	S	G
cg08576185	16p13.3	2005683	ZNF598	rs72766639	2005819	A	0.174	1.69E-04	4.06E-44	0.740	0.126	4.76E-09	3.59E-01	20	N	S	G
cg10470208	16p13.3	2008700	ZNF598	rs1058474	1998795	T	0.181	6.82E-05	6.56E-19	1.112	0.209	1.02E-07	7.58E-02	14	N	S	G
cg06998361	16q21	58110599	IGR (C16orf80)	rs10445026	58109349	G	0.069	5.00E-04	5.61E-97	-0.442	0.069	1.35E-10	2.53E-01	20	N	S	S
cg15638306	17q21.33	49506292	NGFR,LOC100288866	rs55759007	49506219	G	0.109	5.49E-04	7.80E-19	-1.047	0.206	3.96E-07	3.09E-01	15	N	G	G
cg25674938	19p13.3	1360982	MUM1	rs3760991	1402998	A	0.026	2.54E-02	1.78E-101	-0.315	0.053	2.97E-09	2.54E-01	8	N	G	G
cg06750524	19q13.32	44906698	APOE	rs769449	44906745	A	0.112	8.19E-30	9.38E-15	4.407	0.573	1.39E-14	6.84E-02	10	G	G	G
cg04698472	19q13.41	51497571	SIGLEC12	rs56102305	51498028	A	0.035	3.19E-03	0	-0.170	0.027	1.62E-10	8.24E-02	20	N	G	G
cg18795732	19q13.42	55549968	IGR (SBK3)	rs61747393	55500206	T	0.027	1.08E-02	2.08E-84	-0.310	0.051	1.12E-09	3.97E-01	8	N	N	S
cg02345758	19q13.43	55837753	NLRP4,NLRP11	rs7258704	55849297	T	0.031	9.01E-03	5.63E-73	-0.463	0.070	2.75E-11	7.09E-01	5	N	N	N
cg23062096	20p13	2747930	EBF4	rs16990611	2747924	G	0.121	2.50E-04	5.77E-20	0.912	0.180	3.89E-07	5.32E-01	6	N	G	G
cg18120111	21q22.3	42496937	RSPH1	rs73227543	42503966	G	0.192	7.00E-04	2.03E-108	-0.400	0.078	2.64E-07	2.44E-01	20	N	S	G
cg20460554	21q22.3	42497150	RSPH1	rs73227543	42503966	G	0.192	7.00E-04	0	-0.273	0.052	1.57E-07	1.21E-01	20	N	S	G
cg04903116	22q11.21	21443870	HIC2	rs78037651	21646689	G	0.023	8.82E-03	8.21E-82	-0.356	0.058	9.59E-10	3.16E-01	13	N	N	S

cg22846809	22q11.21	21646831	IGR (<i>SDF2L1</i>)	rs78037651	21646689	G	0.023	8.82E-03	4.16E-91	0.340	0.055	7.80E-10	3.66E-01	13	N	N	S
------------	----------	----------	-----------------------	------------	----------	---	-------	----------	----------	-------	-------	----------	----------	----	---	---	---

Genomic coordinates are based on Human Genome version 38 (hg38).

Chr: chromosomal region (i.e., cytogenetic band); ProbePos: probe position; Gene: the gene or closest gene corresponding to the probe; IGR: intergenic region; SNP: top methylation quantitative trait locus (mQTL); Pos: SNP position; A1/Freq: SNP's effect allele and its frequency; P_{GWAS} : p-value of the SNP in genome-wide association meta-analysis; P_{mQTL} : p-value of the SNP in mQTLs analysis; β_{SMR} , SE_{SMR} , and P_{SMR} : beta coefficient, its standard error, and p-value of the probe in summary data-based Mendelian randomization (SMR) test; P_{HEIDI} : p-value of the heterogeneity in dependent instruments (HEIDI) test; N_{HEIDI} : number of single-nucleotide polymorphisms used for HEIDI test; Current?: whether there is any AD-associated SNP within ± 1 Mb of the probe in the current genome-wide meta-analysis (N: None, G: SNP with $P_{\text{GWAS}} < 5E-08$, and S: SNP with $5E-08 \leq P_{\text{GWAS}} < 5E-06$); Previous?: whether there is any AD-associated SNP within ± 1 Mb of the probe in previous GWAS (N: None, G: SNP with $P_{\text{GWAS}} < 5E-08$, and S: SNP with $5E-08 \leq P_{\text{GWAS}} < 5E-06$); Region?: whether there is any AD-associated SNP within the chromosomal region (i.e., cytogenetic band) corresponding to the probe (N: None, G: SNP with $P_{\text{GWAS}} < 5E-08$, and S: SNP with $5E-08 \leq P_{\text{GWAS}} < 5E-06$).

Table S2: Brain-specific methylome-wide association results

ProbeID	Chr	ProbePos	Gene	SNP	Pos	A1	Freq	P _{GWAS}	P _{mQTL}	b _{SMR}	SE _{SMR}	P _{SMR}	P _{HEIDI}	N _{HEIDI}	Current?	Previous?	Region?
Plan 1: All Subjects																	
cg23395749	5q35.3	177557245	<i>IGR (FAM193B)</i>	rs1001530	177558514	A	0.954	4.88E-05	2.34E-15	-0.726	0.139	1.90E-07	7.31E-02	5	N	S	S
cg02613937	19q13.32	44892040	<i>TOMM40</i>	rs157582	44892962	C	0.789	3.73E-63	1.84E-08	-3.518	0.629	2.28E-08	7.24E-01	7	G	G	G
Plan 2: Only Males																	
cg17249452	2q37.3	239609813	<i>IGR (LOC150935)</i>	rs72998459	239625495	C	0.933	5.39E-04	1.00E-300	-0.192	0.031	9.13E-10	8.18E-01	13	N	S	S
cg23902610	2q37.3	239609910	<i>IGR (LOC150935)</i>	rs72998459	239625495	C	0.933	5.39E-04	3.45E-31	-0.355	0.065	4.35E-08	1.85E-01	15	N	S	S
cg23379309	9q22.33	99295046	<i>IGR (NAMA)</i>	rs431892	99293775	C	0.985	2.27E-02	2.67E-34	-0.755	0.126	2.18E-09	7.02E-02	5	N	N	S
cg03080043	16q24.2	88484856	<i>ZFPM1</i>	rs34353181	88481573	A	0.050	2.49E-03	7.88E-19	-0.567	0.106	9.96E-08	8.10E-01	4	N	S	S
cg02613937	19q13.32	44892040	<i>TOMM40</i>	rs157582	44892962	C	0.789	9.84E-24	1.84E-08	-3.636	0.656	3.06E-08	7.90E-01	7	G	G	G
cg05206559	19q13.32	45913997	<i>NANOS2</i>	rs66529687	45914171	G	0.867	1.83E-04	5.86E-298	0.272	0.043	2.96E-10	8.50E-01	19	G	G	G
Plan 3: Only Females																	
cg12833011	5q35.1	170503531	<i>KCNIP1</i>	rs57212455	170519236	T	0.905	5.78E-04	1.86E-266	0.200	0.038	2.10E-07	8.90E-02	5	N	N	N
cg04322111	6p21.32	32761987	<i>HLA-DQB2</i>	rs7768538	32762044	A	0.574	6.15E-05	0	-0.201	0.039	2.21E-07	8.61E-02	20	S	G	G
cg10218546	6p21.32	32762046	<i>HLA-DQB2</i>	rs7768538	32762044	A	0.574	6.15E-05	0	-0.198	0.038	2.18E-07	8.32E-02	20	S	G	G
cg02613937	19q13.32	44892040	<i>TOMM40</i>	rs157582	44892962	C	0.789	2.17E-35	1.84E-08	-3.371	0.607	2.77E-08	7.08E-01	7	G	G	G
Plan 4: Hypertensive Subjects																	
cg11750962	1p36.22	11134621	<i>MTOR</i>	rs2275528	11139092	T	0.979	3.00E-03	2.11E-41	-0.411	0.075	5.14E-08	9.76E-02	4	N	S	S
cg12833011	5q35.1	170503531	<i>KCNIP1</i>	rs57212455	170519236	T	0.905	2.77E-04	1.86E-266	0.215	0.038	1.91E-08	4.09E-01	5	N	N	N
cg23395749	5q35.3	177557245	<i>IGR (FAM193B)</i>	rs1001530	177558514	A	0.954	3.36E-04	2.34E-15	-0.791	0.157	5.17E-07	1.01E-01	5	N	S	S
cg02613937	19q13.32	44892040	<i>TOMM40</i>	rs157582	44892962	C	0.789	8.91E-29	1.84E-08	-2.933	0.532	3.51E-08	6.40E-01	7	G	G	G
Plan 5: Non-hypertensive Subjects																	
cg09127005	1p34.1	43950718	<i>IPO13</i>	rs3791118	43963230	G	0.962	8.98E-04	3.11E-13	-0.668	0.123	5.13E-08	5.72E-01	11	N	S	N
cg11003133	1q23.1	159076601	<i>AIM2</i>	rs16841642	159077008	G	0.952	5.30E-03	6.30E-82	-0.312	0.062	4.62E-07	3.40E-01	18	N	S	N
cg04198912	1q32.1	205567693	<i>MFSD4</i>	rs6674683	205532045	C	0.971	1.41E-03	3.99E-10	0.654	0.123	1.08E-07	7.41E-01	3	N	N	S
cg03706720	3q27.1	184513150	<i>IGR (EPHB3)</i>	rs28729155	184513380	A	0.174	5.48E-05	2.20E-291	-0.328	0.048	1.05E-11	2.27E-01	20	N	N	N
cg06691616	4q31.1	138609944	<i>IGR (LINC00499)</i>	rs17317347	138607917	C	0.960	1.59E-03	2.20E-17	0.522	0.094	2.84E-08	1.65E-01	8	N	S	G
cg08631357	5q32	150209647	<i>SLC6A7</i>	rs10076748	150209303	C	0.893	1.77E-03	2.82E-295	0.230	0.045	2.76E-07	2.24E-01	18	N	N	G
cg02769614	6p21.32	32167275	<i>PPT2-EGFL8,EGFL8</i>	rs17493811	32177622	C	0.970	6.41E-04	5.16E-18	0.535	0.089	1.58E-09	2.46E-01	3	N	G	G
cg08288383	7q21.3	98051318	<i>IGR (LMTK2)</i>	rs12538837	98055156	C	0.266	1.86E-04	4.49E-27	0.658	0.128	2.86E-07	8.87E-02	19	N	S	S
cg10308629	7q33	134670051	<i>BPGM</i>	rs73439998	134663724	C	0.979	3.01E-02	9.28E-48	-0.520	0.101	2.88E-07	2.57E-01	3	N	S	S
cg04388919	7q36.1	149422042	<i>IGR (ZNF777)</i>	rs10248356	149423091	G	0.837	2.01E-02	4.78E-15	1.421	0.229	4.97E-10	2.44E-01	10	N	S	S
cg07189157	7q36.1	149422316	<i>IGR (ZNF777)</i>	rs10248356	149423091	G	0.837	2.01E-02	1.30E-22	1.172	0.166	1.52E-12	4.69E-01	9	N	S	S
cg24635736	10q26.13	122979534	<i>PSTK</i>	rs13328826	122992107	A	0.970	6.26E-03	2.48E-20	-0.374	0.072	1.68E-07	8.24E-01	3	N	N	N
cg25214093	10q26.13	124447241	<i>IGR (NKX1-2)</i>	rs1399928	124446693	T	0.147	7.38E-04	1.89E-296	0.260	0.047	3.31E-08	5.00E-01	10	N	N	N
cg15567360	11q13.4	71611653	<i>IGR (KRTAP5-11)</i>	rs11827208	71578103	C	0.980	1.70E-03	9.66E-10	-0.679	0.130	1.67E-07	3.71E-01	3	N	N	S
cg03249590	12q13.3	56646415	<i>ATP5B,SNORD59A</i>	rs12321649	56621349	T	0.985	3.22E-02	4.91E-28	0.331	0.059	2.00E-08	5.50E-02	3	N	S	S
cg06679265	12q13.3	56646420	<i>ATP5B,SNORD59A</i>	rs12321649	56621349	T	0.985	3.22E-02	2.16E-23	0.359	0.066	4.72E-08	2.41E-01	3	N	S	S
cg09557313	13q14.3	52739039	<i>LECT1</i>	rs4885961	52755200	C	0.960	4.63E-03	6.93E-31	0.547	0.103	1.06E-07	5.67E-01	7	N	G	G
cg04870949	13q34	113455542	<i>IGR (DCUN1D2)</i>	rs9577553	113455830	C	0.870	1.83E-03	3.84E-282	-0.270	0.053	4.21E-07	1.29E-01	18	N	S	S
cg07011318	16p13.3	2004943	<i>ZNF598</i>	rs72766639	2005819	G	0.826	1.69E-04	0	0.291	0.046	1.96E-10	1.12E-01	17	N	S	G
cg09397293	16p13.3	2005032	<i>ZNF598</i>	rs72766639	2005819	G	0.826	1.69E-04	0	0.282	0.044	1.86E-10	1.13E-01	18	N	S	G
cg05211189	16p13.3	2005402	<i>ZNF598</i>	rs11542302	1986934	T	0.819	7.26E-05	0	0.283	0.043	7.47E-11	1.01E-01	18	N	S	G
cg08576185	16p13.3	2005683	<i>ZNF598</i>	rs72766639	2005819	G	0.826	1.69E-04	0	0.295	0.046	2.00E-10	9.02E-02	16	N	S	G
cg06998361	16q21	58110599	<i>IGR (C16orf80)</i>	rs74019790	58107923	T	0.931	5.00E-04	4.77E-20	-0.591	0.109	5.49E-08	6.81E-01	11	N	S	S
cg10191399	16q23.3	81693451	<i>CMIP</i>	rs72831117	81693634	G	0.914	1.04E-03	0	0.246	0.041	1.54E-09	8.86E-02	20	N	G	G

cg02613937	19q13.32	44892040	<i>TOMM40</i>	rs157582	44892962	C	0.789	2.71E-24	1.84E-08	-4.421	0.793	2.50E-08	6.07E-01	7	G	G	G
cg20002045	21q22.3	42499561	<i>SLC37A1</i>	rs73227543	42503966	G	0.192	7.00E-04	5.50E-63	-0.456	0.090	4.49E-07	1.87E-01	20	N	S	G
cg01716252	21q22.3	45132690	<i>ADARB1</i>	rs439884	45114025	C	0.903	8.78E-04	3.49E-19	0.827	0.164	4.46E-07	1.32E-01	17	N	S	G

Please see the description provided below Table S1.

Table S3: Wald chi-square test to compare probes effects between males and females for probes that were significant in blood-based analyses of only one of the two groups

Significant Probes				Males					Females					Comparison		
ProbeID	Chr	ProbePos	Gene	b _{SMR}	SE _{SMR}	P _{SMR}	P _{HEIDI}	N _{HEIDI}	b _{SMR}	SE _{SMR}	P _{SMR}	P _{HEIDI}	N _{HEIDI}	Chisq	P	Sig?
Plan 2: Only Males																
cg20011360	4p14	37584038	<i>C4orf19</i>	0.366	0.058	2.62E-10	3.04E-01	17	0.075	0.059	2.03E-01	1.72E-02	17	12.518	4.03E-04	Y
cg23395749	5q35.3	177557245	<i>IGR (FAM193B)</i>	-0.559	0.109	2.95E-07	2.48E-01	5	-0.396	0.087	4.89E-06	3.05E-02	5	1.385	2.39E-01	N
cg04627871	6p21.33	31736144	<i>CLIC1</i>	0.339	0.059	1.09E-08	1.24E-01	10	-0.157	0.200	4.32E-01	1.44E-01	10	5.670	1.73E-02	N
cg15598276	6p21.32	32980566	<i>BRD2</i>	-0.484	0.073	2.68E-11	2.61E-01	14	-0.078	0.115	4.97E-01	7.35E-01	14	8.931	2.80E-03	N
cg01991743	6p21.32	33085831	<i>HLA-DPB1</i>	-0.140	0.025	2.79E-08	2.29E-01	20	-0.017	0.033	6.04E-01	6.31E-01	20	8.742	3.11E-03	N
cg06527438	6q27	170236746	<i>IGR (LOC154449)</i>	-0.548	0.098	2.10E-08	4.10E-01	5	-0.188	0.117	1.08E-01	3.73E-01	5	5.579	1.82E-02	N
cg21205282	6q27	170244045	<i>IGR (LOC154449)</i>	-0.693	0.134	2.55E-07	8.05E-02	5	-0.237	0.149	1.11E-01	1.68E-01	5	5.148	2.33E-02	N
cg22883453	6q27	170244276	<i>IGR (LOC154449)</i>	-0.628	0.117	8.38E-08	5.52E-02	4	-0.215	0.135	1.10E-01	1.81E-01	4	5.349	2.07E-02	N
cg04505845	6q27	170244461	<i>IGR (LOC154449)</i>	-0.592	0.108	4.76E-08	2.03E-01	4	-0.203	0.127	1.09E-01	2.38E-01	4	5.446	1.96E-02	N
cg05526015	6q27	170244757	<i>IGR (LOC154449)</i>	-0.463	0.079	4.65E-09	2.18E-01	6	-0.159	0.098	1.07E-01	2.65E-01	6	5.807	1.60E-02	N
cg24651908	6q27	170245433	<i>IGR (LOC154449)</i>	-0.650	0.123	1.18E-07	5.85E-02	4	-0.223	0.140	1.10E-01	1.32E-01	4	5.290	2.15E-02	N
cg04386759	6q27	170245707	<i>IGR (LOC154449)</i>	-0.542	0.097	2.09E-08	5.91E-02	5	-0.186	0.116	1.08E-01	1.70E-01	5	5.580	1.82E-02	N
cg26180843	6q27	170248014	<i>IGR (LOC154449)</i>	-0.584	0.107	5.18E-08	1.14E-01	5	-0.200	0.125	1.09E-01	1.90E-01	5	5.432	1.98E-02	N
cg12035402	6q27	170250189	<i>IGR (LOC154449)</i>	-0.692	0.133	2.16E-07	7.79E-02	5	-0.237	0.149	1.11E-01	2.37E-01	5	5.179	2.29E-02	N
cg05438220	7q21.13	90643046	<i>CDK14</i>	-0.125	0.023	3.54E-08	2.11E-01	15	0.026	0.037	4.85E-01	3.21E-01	15	12.045	5.19E-04	Y
cg11399834	8p22	14566901	<i>SGCZ</i>	-0.348	0.054	1.20E-10	2.06E-01	20	-0.004	0.062	9.44E-01	5.44E-01	20	17.481	2.90E-05	Y
cg12185975	8q24.22	130761450	<i>IGR (ADCY8)</i>	-0.239	0.040	1.73E-09	6.17E-01	20	0.067	0.058	2.45E-01	1.62E-01	20	18.999	1.31E-05	Y
cg23402755	10p14	7702004	<i>ITIH2</i>	-0.453	0.089	3.85E-07	6.42E-01	12	-0.066	0.113	5.55E-01	4.38E-01	12	7.218	7.22E-03	N
cg14381908	10q11.21	43202369	<i>RASGEF1A</i>	0.204	0.040	4.90E-07	2.63E-01	18	0.095	0.045	3.62E-02	5.45E-01	18	3.181	7.45E-02	N
cg25422051	11q13.1	65916842	<i>C11orf68</i>	-0.658	0.094	2.43E-12	3.54E-01	7	0.115	0.161	4.75E-01	7.53E-02	7	17.242	3.29E-05	Y
cg15007809	12q21.2	75883289	<i>IGR (PHLDA1)</i>	-0.190	0.021	8.73E-20	4.99E-01	10	-0.033	0.039	4.02E-01	2.46E-01	10	12.674	3.71E-04	Y
cg19755435	14q31.3	88006657	<i>GPR65</i>	-0.462	0.087	1.04E-07	3.79E-01	20	0.002	0.093	9.84E-01	9.65E-01	20	13.282	2.68E-04	Y
cg20239174	15q24.1	73780023	<i>IGR (C15orf59)</i>	-0.160	0.025	2.42E-10	5.18E-01	7	0.018	0.057	7.51E-01	5.17E-02	7	8.047	4.56E-03	N
cg24801087	17q25.3	78485647	<i>DNAH17,DNAH17-AS1</i>	-0.573	0.106	6.81E-08	2.09E-01	13	0.197	0.152	1.94E-01	2.39E-01	13	17.293	3.20E-05	Y
cg08778119	17q25.3	78496484	<i>DNAH17,DNAH17-AS1</i>	-0.483	0.087	3.23E-08	3.68E-01	4	0.001	0.111	9.90E-01	1.58E-01	4	11.712	6.21E-04	Y
cg05206559	19q13.32	45913997	<i>NANOS2</i>	0.723	0.125	7.67E-09	3.28E-01	20	-0.048	0.138	7.26E-01	1.16E-01	20	17.132	3.49E-05	Y
cg25673584	19q13.32	45914293	<i>NANOS2</i>	0.849	0.152	2.45E-08	1.23E-01	20	-0.057	0.162	7.26E-01	2.33E-01	20	16.586	4.65E-05	Y
cg14192299	19q13.32	45914381	<i>NANOS2</i>	0.718	0.124	7.30E-09	1.08E-01	20	-0.048	0.137	7.26E-01	2.28E-01	20	17.155	3.45E-05	Y
cg19702802	19q13.32	45914471	<i>NANOS2</i>	0.743	0.129	9.10E-09	1.03E-01	20	-0.050	0.142	7.26E-01	1.95E-01	20	17.054	3.63E-05	Y
cg02345758	19q13.43	55837753	<i>NLRP4,NLRP11</i>	-0.443	0.067	3.06E-11	5.82E-02	5	0.001	0.096	9.90E-01	7.59E-01	5	14.402	1.48E-04	Y
Plan 3: Only Females																
cg25325322	2p11.2	84846591	<i>TRABD2A</i>	0.055	0.063	3.85E-01	4.69E-01	20	0.244	0.036	1.19E-11	2.20E-01	20	6.793	9.15E-03	N
cg18572898	6p21.32	32744326	<i>HLA-DQA2</i>	-0.014	0.046	7.65E-01	5.29E-01	20	-0.167	0.032	1.80E-07	1.60E-01	20	7.381	6.59E-03	N
cg10218546	6p21.32	32762046	<i>HLA-DQB2</i>	-0.025	0.084	7.65E-01	5.84E-01	20	-0.304	0.060	3.27E-07	6.43E-02	20	7.277	6.99E-03	N
cg02786056	8q13.2	69589075	<i>SULF1</i>	0.091	0.228	6.91E-01	1.02E-02	10	-0.421	0.062	1.22E-11	8.98E-01	10	4.685	3.04E-02	N
cg00222015	12q24.31	121795469	<i>LINC01089</i>	-0.106	0.034	1.51E-03	1.83E-01	20	-0.165	0.025	4.77E-11	1.93E-01	20	1.961	1.61E-01	N
cg13328209	12q24.31	124738956	<i>IGR (SCARB1)</i>	0.201	0.196	3.05E-01	8.15E-01	10	-0.515	0.102	4.89E-07	9.19E-02	10	10.453	1.22E-03	Y
cg17632299	13q14.3	52738831	<i>LECT1</i>	0.128	0.140	3.62E-01	1.81E-02	20	0.395	0.075	1.67E-07	6.33E-02	20	2.805	9.40E-02	N
cg18379295	14q22.1	51859437	<i>GNG2</i>	0.448	0.217	3.89E-02	4.01E-01	20	-0.597	0.116	2.79E-07	3.75E-01	20	18.038	2.17E-05	Y

Genomic coordinates are based on Human Genome version 38 (hg38).

Chr: chromosomal region (i.e., cytogenetic band); ProbePos: probe position; Gene: the gene or closest gene corresponding to the probe; b_{SMR}, SE_{SMR}, and P_{SMR}: beta coefficient, its standard error, and p-value of the probe in summary data-based Mendelian randomization (SMR) test; P_{HEIDI}: p-value of the heterogeneity in dependent instruments (HEIDI) test; N_{HEIDI}: number of single-nucleotide polymorphisms used for HEIDI test; Chisq and P: chi-square measure and its p-value from comparing the b_{SMR} of probe between the two groups; Sig?: if the probe has group-specific effects (Y: YES, N: NO) at the Bonferroni-adjusted significance level (i.e., 0.05/n.probes, where n.probes is the total number of probes in the Table).

Table S4: Wald chi-square test to compare probes effects between males and females for probes that were significant in brain-specific analyses of only one of the two groups

Significant Probes				Males					Females					Comparison		
ProbeID	Chr	ProbePos	Gene	b _{SMR}	SE _{SMR}	P _{SMR}	P _{HEIDI}	N _{HEIDI}	b _{SMR}	SE _{SMR}	P _{SMR}	P _{HEIDI}	N _{HEIDI}	Chisq	P	Sig?
Plan 2: Only Males																
cg17249452	2q37.3	239609813	<i>IGR (LOC150935)</i>	-0.192	0.031	9.13E-10	8.18E-01	13	0.082	0.055	1.36E-01	7.01E-01	13	18.724	1.51E-05	Y
cg23902610	2q37.3	239609910	<i>IGR (LOC150935)</i>	-0.355	0.065	4.35E-08	1.85E-01	15	0.152	0.102	1.39E-01	4.56E-01	15	17.456	2.94E-05	Y
cg23379309	9q22.33	99295046	<i>IGR (NAMA)</i>	-0.755	0.126	2.18E-09	7.02E-02	5	0.423	0.247	8.71E-02	6.56E-02	5	18.010	2.20E-05	Y
cg03080043	16q24.2	88484856	<i>ZFPM1</i>	-0.567	0.106	9.96E-08	8.10E-01	4	-0.042	0.114	7.08E-01	9.35E-01	4	11.359	7.51E-04	Y
cg05206559	19q13.32	45913997	<i>NANOS2</i>	0.272	0.043	2.96E-10	8.50E-01	19	-0.018	0.052	7.26E-01	1.81E-01	19	18.469	1.73E-05	Y
Plan 3: Only Females																
cg12833011	5q35.1	170503531	<i>KCNIP1</i>	-0.017	0.063	7.91E-01	1.70E-01	5	0.200	0.038	2.10E-07	8.90E-02	5	8.514	3.53E-03	Y
cg04322111	6p21.32	32761987	<i>HLA-DQB2</i>	-0.017	0.056	7.65E-01	5.04E-01	20	-0.201	0.039	2.21E-07	8.61E-02	20	7.346	6.72E-03	N
cg10218546	6p21.32	32762046	<i>HLA-DQB2</i>	-0.016	0.055	7.65E-01	4.98E-01	20	-0.198	0.038	2.18E-07	8.32E-02	20	7.349	6.71E-03	N

Please see the description provided below Table S3.

Table S5: Wald chi-square test to compare probes effects between hypertensive and non-hypertensive subjects for probes that were significant in blood-based analyses of only one of the two groups

Significant Probes				Hypertensive Subjects					Non-hypertensive Subjects					Comparison		
ProbeID	Chr	ProbePos	Gene	b _{SMR}	SE _{SMR}	P _{SMR}	P _{HEIDI}	N _{HEIDI}	b _{SMR}	SE _{SMR}	P _{SMR}	P _{HEIDI}	N _{HEIDI}	Chisq	P	Sig?
Plan 4: Hypertensive Subjects																
cg22472863	4q31.22	147096252	<i>IGR (TTC29)</i>	-0.314	0.048	7.53E-11	1.78E-01	17	-0.032	0.116	7.84E-01	1.56E-02	17	5.071	2.43E-02	N
cg23395749	5q35.3	177557245	<i>IGR (FAM193B)</i>	-0.484	0.088	3.08E-08	8.77E-02	5	-0.520	0.113	4.38E-06	5.79E-04	5	0.060	8.06E-01	N
cg06527438	6q27	170236746	<i>IGR (LOC154449)</i>	-0.470	0.092	3.40E-07	6.30E-01	5	-0.141	0.148	3.40E-01	1.29E-02	5	3.543	5.98E-02	N
cg05526015	6q27	170244757	<i>IGR (LOC154449)</i>	-0.397	0.075	1.22E-07	1.20E-01	6	-0.119	0.125	3.40E-01	3.27E-02	6	3.620	5.71E-02	N
cg00222015	12q24.31	121795469	<i>LINC01089</i>	-0.139	0.027	1.58E-07	1.84E-01	20	-0.104	0.040	1.03E-02	5.26E-01	20	0.547	4.60E-01	N
Plan 5: Non-hypertensive Subjects																
cg15076811	1p36.22	10940981	<i>IGR (C1orf127)</i>	0.057	0.129	6.59E-01	6.24E-01	4	-0.567	0.112	4.46E-07	7.68E-01	4	13.262	2.71E-04	Y
cg27535302	1p34.2	42165766	<i>GUCA2A</i>	0.009	0.043	8.35E-01	2.21E-01	13	-0.193	0.023	1.38E-16	3.99E-01	13	16.801	4.15E-05	Y
cg04510459	1p22.1	91582730	<i>IGR (CDC7)</i>	0.112	0.114	3.29E-01	9.23E-01	12	0.801	0.115	2.89E-12	3.22E-01	12	18.140	2.05E-05	Y
cg20306265	1p12	117615002	<i>FAM46C</i>	-0.058	0.077	4.54E-01	2.70E-01	20	-0.484	0.094	2.81E-07	6.42E-02	20	12.189	4.81E-04	Y
cg18342183	1q31.1	186763783	<i>IGR (PLA2G4A)</i>	0.002	0.080	9.80E-01	2.79E-01	18	-0.402	0.049	2.95E-16	1.40E-01	18	18.576	1.63E-05	Y
cg23924526	2p21	45771409	<i>PRKCE</i>	0.440	0.251	7.89E-02	6.05E-01	4	-0.431	0.078	3.34E-08	9.57E-02	4	11.018	9.02E-04	N
cg03063511	2p13.1	7930386	<i>DGUOK</i>	-0.009	0.047	8.51E-01	5.73E-01	11	-0.247	0.041	2.74E-09	1.09E-01	11	14.239	1.61E-04	Y
cg25325322	2p11.2	84846591	<i>TRABD2A</i>	0.126	0.044	4.16E-03	7.89E-01	20	0.265	0.051	1.86E-07	1.39E-01	20	4.291	3.83E-02	N
cg27608154	2q13	111124233	<i>BCL2L11</i>	-0.010	0.061	8.76E-01	2.43E-01	11	-0.310	0.056	3.03E-08	2.81E-01	11	13.223	2.76E-04	Y
cg25679431	3p22.3	32147516	<i>GPD1L</i>	0.072	0.071	3.14E-01	1.26E-01	9	-0.221	0.043	3.06E-07	1.62E-01	9	12.351	4.41E-04	Y
cg01317029	3q27.1	184345709	<i>FAM131A</i>	-0.072	0.172	6.76E-01	4.57E-01	11	0.616	0.122	4.98E-07	1.62E-01	11	10.622	1.12E-03	N
cg02951719	4p16.3	1518424	<i>IGR (NKX1-1)</i>	-0.009	0.113	9.37E-01	3.01E-01	20	-0.490	0.090	5.71E-08	1.46E-01	20	11.036	8.94E-04	N
cg05638493	5q31.3	141303800	<i>SLC25A2</i>	-0.111	0.095	2.45E-01	9.61E-01	19	-0.611	0.105	6.00E-09	2.78E-01	18	12.395	4.30E-04	Y
cg08631357	5q32	150209647	<i>SLC6A7</i>	0.093	0.048	5.47E-02	4.56E-02	20	0.288	0.056	3.18E-07	2.02E-01	20	6.937	8.44E-03	N
cg17781669	5q33.1	150488796	<i>IGR (NDST1)</i>	0.025	0.052	6.29E-01	6.02E-02	14	0.274	0.050	5.00E-08	1.30E-01	14	11.993	5.34E-04	Y
cg15538767	5q33.1	150490833	<i>IGR (NDST1)</i>	0.050	0.104	6.30E-01	1.13E-01	7	0.552	0.108	3.27E-07	6.20E-01	7	11.223	8.08E-04	N
cg19810457	5q35.3	180247356	<i>MAPK9</i>	-0.005	0.079	9.46E-01	5.89E-01	6	-0.346	0.061	1.16E-08	1.18E-01	6	11.619	6.53E-04	N
cg09198601	6p24.3	10318947	<i>IGR (TFAP2A)</i>	-0.099	0.128	4.39E-01	2.26E-01	9	-0.742	0.117	2.37E-10	3.87E-01	9	13.746	2.09E-04	Y
cg14466923	6p21.32	33182959	<i>COL11A2</i>	-0.096	0.041	1.97E-02	1.22E-01	10	-0.226	0.045	4.59E-07	6.83E-02	10	4.602	3.19E-02	N
cg17430214	6p21.1	41279166	<i>TREM1</i>	0.065	0.120	5.88E-01	5.68E-01	10	0.672	0.123	4.60E-08	7.38E-02	10	12.541	3.98E-04	Y
cg00531924	6q21	110958687	<i>GTF3C6</i>	-0.148	0.160	3.57E-01	9.34E-01	12	-1.087	0.188	7.54E-09	1.38E-01	12	14.450	1.44E-04	Y
cg24039042	6q27	170271859	<i>IGR (LOC154449)</i>	-0.040	0.088	6.51E-01	6.26E-03	4	0.310	0.044	3.10E-12	1.63E-01	4	12.606	3.84E-04	Y
cg01766850	6q27	170271878	<i>IGR (LOC154449)</i>	-0.034	0.075	6.51E-01	6.10E-03	4	0.265	0.038	1.59E-12	2.13E-01	4	12.675	3.71E-04	Y
cg05973084	6q27	170271951	<i>IGR (LOC154449)</i>	-0.025	0.055	6.50E-01	5.67E-03	4	0.193	0.027	6.15E-13	4.25E-01	4	12.768	3.53E-04	Y
cg09344348	6q27	170271997	<i>IGR (LOC154449)</i>	-0.027	0.059	6.50E-01	5.71E-03	4	0.208	0.029	7.58E-13	4.10E-01	4	12.748	3.56E-04	Y
cg18555277	6q27	170272160	<i>IGR (LOC154449)</i>	-0.026	0.057	6.50E-01	5.54E-03	4	0.201	0.028	6.84E-13	3.90E-01	4	12.758	3.54E-04	Y
cg01209642	6q27	170272267	<i>IGR (LOC154449)</i>	-0.026	0.057	6.50E-01	5.43E-03	4	0.200	0.028	6.67E-13	3.49E-01	4	12.760	3.54E-04	Y
cg21138542	6q27	170272414	<i>IGR (DLL1)</i>	-0.035	0.077	6.51E-01	5.86E-03	4	0.271	0.038	1.75E-12	1.97E-01	4	12.665	3.73E-04	Y
cg03899510	6q27	170272602	<i>IGR (DLL1)</i>	-0.065	0.145	6.51E-01	1.06E-02	4	0.510	0.079	1.07E-10	9.71E-02	4	12.186	4.81E-04	Y
cg23988375	6q27	170275018	<i>IGR (DLL1)</i>	0.085	0.189	6.51E-01	1.21E-02	4	-0.665	0.111	1.97E-09	2.44E-01	4	11.754	6.07E-04	N
cg16108844	6q27	170275085	<i>IGR (DLL1)</i>	0.098	0.216	6.51E-01	1.10E-02	3	-0.760	0.133	1.06E-08	1.74E-01	3	11.455	7.13E-04	N
cg23534345	7p22.1	5639075	<i>RNF216</i>	-0.244	0.247	3.23E-01	1.36E-02	17	1.189	0.234	3.94E-07	5.89E-01	17	17.719	2.56E-05	Y
cg27103343	7p21.3	10779424	<i>IGR (NDUFA4)</i>	-0.063	0.032	4.79E-02	1.09E-01	20	-0.184	0.031	2.96E-09	6.12E-01	20	7.353	6.69E-03	N
cg07227187	7q11.21	64192342	<i>IGR (ZNF735P)</i>	-0.068	0.027	1.29E-02	2.91E-03	20	-0.149	0.027	3.66E-08	5.84E-01	20	4.370	3.66E-02	N
cg01391867	7q22.1	99500248	<i>ZNF394</i>	0.138	0.150	3.58E-01	2.80E-01	8	0.787	0.136	7.78E-09	4.44E-01	8	10.285	1.34E-03	N
cg23891049	7q33	134679117	<i>BPGM</i>	0.019	0.042	6.53E-01	1.05E-01	4	-0.156	0.030	1.70E-07	6.07E-01	4	11.487	7.01E-04	N
cg27057461	7q36.3	158343687	<i>PTPRN2</i>	0.140	0.167	4.03E-01	4.81E-01	5	-0.750	0.129	6.02E-09	4.46E-01	5	17.781	2.48E-05	Y
cg04035728	8p21.2	27465950	<i>CHRNA2</i>	0.082	0.061	1.79E-01	4.04E-01	20	-0.335	0.062	8.00E-08	5.36E-01	20	22.912	1.70E-06	Y

cg23277389	8q11.21	48921984	<i>SNAI2</i>	-0.222	0.100	2.58E-02	1.38E-01	7	-0.601	0.118	3.71E-07	3.16E-01	7	6.010	1.42E-02	N
cg26687619	8q24.22	133904113	<i>IGR (ST3GAL1)</i>	0.140	0.172	4.16E-01	3.67E-01	3	-0.716	0.124	8.59E-09	5.88E-01	3	16.247	5.56E-05	Y
cg23402755	10p14	7702004	<i>ITIH2</i>	-0.089	0.105	3.97E-01	7.78E-01	12	-0.726	0.099	2.53E-13	5.25E-01	12	19.424	1.05E-05	Y
cg23809813	10q23.31	88457915	<i>RNLS</i>	0.012	0.063	8.51E-01	3.54E-01	20	0.388	0.071	4.57E-08	5.26E-01	20	15.713	7.37E-05	Y
cg05399434	10q26.13	121609167	<i>IGR (FGFR2)</i>	0.010	0.156	9.48E-01	9.86E-02	20	-0.897	0.119	5.54E-14	5.26E-02	20	21.281	3.97E-06	Y
cg01628053	10q26.13	121609218	<i>IGR (FGFR2)</i>	0.011	0.165	9.48E-01	1.02E-01	20	-0.949	0.131	3.52E-13	1.40E-01	20	20.757	5.21E-06	Y
cg24635736	10q26.13	122979534	<i>PSTK</i>	-0.023	0.067	7.27E-01	4.75E-01	8	-0.346	0.060	6.12E-09	7.16E-01	8	12.948	3.20E-04	Y
cg16255663	10q26.3	129552735	<i>MGMT</i>	0.012	0.040	7.62E-01	9.49E-02	20	-0.204	0.036	8.69E-09	1.05E-01	20	16.444	5.01E-05	Y
cg17686260	10q26.3	129614500	<i>MGMT</i>	-0.011	0.038	7.70E-01	2.07E-02	20	-0.213	0.036	4.05E-09	3.03E-01	20	14.636	1.30E-04	Y
cg05741225	10q26.3	132103799	<i>JAKMIP3</i>	0.004	0.059	9.52E-01	2.23E-01	6	-0.218	0.039	2.91E-08	2.21E-01	6	9.673	1.87E-03	N
cg10427719	10q26.3	133334898	<i>CALY</i>	-0.010	0.061	8.73E-01	3.87E-01	20	-0.262	0.050	1.77E-07	1.21E-01	20	10.179	1.42E-03	N
cg02114346	10q26.3	133378038	<i>PAOX</i>	-0.039	0.133	7.70E-01	8.03E-01	11	0.688	0.137	5.26E-07	1.26E-01	11	14.457	1.43E-04	Y
cg11435872	11p11.2	45805924	<i>SLC35C1</i>	0.318	0.180	7.70E-02	3.05E-01	20	1.519	0.291	1.88E-07	2.73E-01	20	12.280	4.58E-04	Y
cg05360847	11q13.4	71576873	<i>IGR (KRTAP5-11)</i>	0.216	0.215	3.14E-01	6.68E-01	4	-0.942	0.159	3.50E-09	2.02E-01	4	18.758	1.48E-05	Y
cg02850715	11q24.3	130159317	<i>ST14</i>	0.204	0.149	1.72E-01	2.84E-01	20	-0.812	0.138	4.14E-09	7.87E-01	20	24.969	5.83E-07	Y
cg21029769	11q24.3	130159620	<i>ST14</i>	0.253	0.186	1.73E-01	3.12E-01	20	-1.006	0.184	4.58E-08	9.16E-01	20	23.191	1.47E-06	Y
cg19153300	11q25	134925086	<i>IGR (LOC283177)</i>	0.009	0.041	8.20E-01	5.44E-01	20	-0.201	0.033	1.18E-09	1.89E-01	20	15.904	6.66E-05	Y
cg21806090	12p13.33	20888868	<i>CACNA1C</i>	-0.123	0.034	2.60E-04	4.56E-01	6	-0.208	0.040	1.66E-07	5.05E-01	6	2.666	1.02E-01	N
cg11915525	12p11.23	27469767	<i>SMCO2</i>	0.052	0.094	5.78E-01	4.58E-01	20	-0.502	0.085	3.10E-09	5.37E-01	20	19.218	1.17E-05	Y
cg21922731	12q13.3	56763346	<i>HSD17B6</i>	-0.105	0.154	4.94E-01	2.53E-01	9	-0.920	0.167	3.47E-08	8.65E-01	9	12.874	3.33E-04	Y
cg05979241	12q21.2	77326379	<i>IGR (E2F7)</i>	0.056	0.069	4.22E-01	8.31E-01	18	0.424	0.068	3.95E-10	3.58E-01	18	14.469	1.42E-04	Y
cg24420742	12q21.2	77328028	<i>IGR (E2F7)</i>	-0.058	0.059	3.21E-01	7.77E-01	16	-0.369	0.057	1.24E-10	7.62E-01	16	14.289	1.57E-04	Y
cg20090301	12q21.2	77362321	<i>IGR (E2F7)</i>	0.082	0.102	4.22E-01	9.00E-01	9	0.624	0.109	9.45E-09	2.98E-01	9	13.231	2.75E-04	Y
cg20045970	12q24.11	109881214	<i>GLTP</i>	0.206	0.185	2.65E-01	4.54E-01	17	-0.704	0.135	1.84E-07	4.11E-01	17	15.800	7.04E-05	Y
cg17632299	13q14.3	52738831	<i>LECT1</i>	0.159	0.099	1.10E-01	4.86E-03	20	0.592	0.085	2.67E-12	1.34E-01	20	11.048	8.88E-04	N
cg09557313	13q14.3	52739039	<i>LECT1</i>	0.181	0.113	1.11E-01	7.75E-03	20	0.675	0.100	1.37E-11	1.02E-01	20	10.708	1.07E-03	N
cg13822911	13q33.2	106376925	<i>LINC00460</i>	0.019	0.109	8.64E-01	4.05E-01	16	-0.649	0.125	2.03E-07	5.71E-02	16	16.167	5.80E-05	Y
cg05099145	16p13.3	1746332	<i>MAPK8IP3</i>	0.118	0.284	6.78E-01	1.77E-01	8	-1.613	0.196	2.07E-16	8.07E-01	8	25.120	5.39E-07	Y
cg11220950	16p13.3	1992692	<i>SYNGR3</i>	-0.051	0.164	7.54E-01	5.05E-01	17	-1.153	0.223	2.27E-07	5.53E-02	17	15.880	6.75E-05	Y
cg04519296	16p13.3	1993014	<i>SYNGR3</i>	0.049	0.167	7.69E-01	3.76E-01	17	-1.037	0.176	3.88E-09	9.73E-02	17	20.008	7.71E-06	Y
cg09397293	16p13.3	2005032	<i>ZNF598</i>	-0.052	0.119	6.64E-01	3.32E-01	20	0.688	0.116	3.06E-09	2.85E-01	20	19.765	8.76E-06	Y
cg26804891	16p13.3	2005241	<i>ZNF598</i>	-0.026	0.087	7.69E-01	3.38E-01	20	0.539	0.080	1.62E-11	7.60E-02	20	22.849	1.75E-06	Y
cg08576185	16p13.3	2005683	<i>ZNF598</i>	-0.056	0.128	6.64E-01	3.16E-01	20	0.740	0.126	4.76E-09	3.59E-01	20	19.524	9.94E-06	Y
cg10470208	16p13.3	2008700	<i>ZNF598</i>	-0.032	0.164	8.47E-01	4.74E-01	14	1.112	0.209	1.02E-07	7.58E-02	14	18.529	1.67E-05	Y
cg06998361	16q21	58110599	<i>IGR (C16orf80)</i>	-0.073	0.067	2.81E-01	4.37E-02	20	-0.442	0.069	1.35E-10	2.53E-01	20	14.707	1.26E-04	Y
cg15638306	17q21.33	49506292	<i>NGFR,LOC100288866</i>	-0.149	0.158	3.46E-01	2.83E-01	15	-1.047	0.206	3.96E-07	3.09E-01	15	11.898	5.62E-04	Y
cg25674938	19p13.3	1360982	<i>MUM1</i>	0.009	0.079	9.06E-01	1.26E-01	9	-0.315	0.053	2.97E-09	2.54E-01	8	11.536	6.82E-04	N
cg04698472	19q13.41	51497571	<i>SIGLEC12</i>	-0.019	0.031	5.46E-01	3.17E-01	20	-0.170	0.027	1.62E-10	8.24E-02	20	13.657	2.19E-04	Y
cg18795732	19q13.42	55549968	<i>IGR (SBK3)</i>	-0.072	0.062	2.44E-01	4.61E-01	8	-0.310	0.051	1.12E-09	3.97E-01	8	8.805	3.00E-03	N
cg02345758	19q13.43	55837753	<i>NLRP4,NLRP11</i>	-0.114	0.081	1.56E-01	3.16E-01	5	-0.463	0.070	2.75E-11	7.09E-01	5	10.725	1.06E-03	N
cg23062096	20p13	2747930	<i>EBF4</i>	0.028	0.161	8.64E-01	8.72E-01	6	0.912	0.180	3.89E-07	5.32E-01	6	13.430	2.48E-04	Y
cg18120111	21q22.3	42496937	<i>RSPH1</i>	0.023	0.070	7.40E-01	1.90E-01	20	-0.400	0.078	2.64E-07	2.44E-01	20	16.304	5.40E-05	Y
cg20460554	21q22.3	42497150	<i>RSPH1</i>	0.016	0.048	7.40E-01	1.42E-01	20	-0.273	0.052	1.57E-07	1.21E-01	20	16.636	4.53E-05	Y
cg04903116	22q11.21	21443870	<i>HIC2</i>	-0.078	0.072	2.77E-01	2.31E-01	13	-0.356	0.058	9.59E-10	3.16E-01	13	9.011	2.68E-03	N
cg22846809	22q11.21	21646831	<i>IGR (SDF2L1)</i>	0.075	0.069	2.77E-01	2.54E-01	13	0.340	0.055	7.80E-10	3.66E-01	13	9.051	2.63E-03	N

Please see the description provided below Table S3.

Table S6: Wald chi-square test to compare probes effects between hypertensive and non-hypertensive subjects for probes that were significant in brain-specific analyses of only one of the two groups

Significant Probes				Hypertensive Subjects					Non-hypertensive Subjects					Comparison		
ProbeID	Chr	ProbePos	Gene	b _{SMR}	SE _{SMR}	P _{SMR}	P _{HEIDI}	N _{HEIDI}	b _{SMR}	SE _{SMR}	P _{SMR}	P _{HEIDI}	N _{HEIDI}	Chisq	P	Sig?
Plan 4: Hypertensive Subjects																
cg11750962	1p36.22	11134621	<i>MTOR</i>	-0.411	0.075	5.14E-08	9.76E-02	4	0.373	0.291	1.99E-01	8.52E-01	4	6.812	9.06E-03	N
cg12833011	5q35.1	170503531	<i>KCNIP1</i>	0.215	0.038	1.91E-08	4.09E-01	5	-0.046	0.076	5.43E-01	7.12E-01	5	9.408	2.16E-03	N
cg23395749	5q35.3	177557245	<i>IGR (FAM193B)</i>	-0.791	0.157	5.17E-07	1.01E-01	5	-0.848	0.198	1.83E-05	7.04E-03	5	0.051	8.21E-01	N
Plan 5: Non-hypertensive Subjects																
cg09127005	1p34.1	43950718	<i>IPO13</i>	-0.041	0.103	6.89E-01	5.47E-01	11	-0.668	0.123	5.13E-08	5.72E-01	11	15.279	9.28E-05	Y
cg11003133	1q23.1	159076601	<i>AIM2</i>	-0.077	0.060	2.00E-01	8.94E-01	18	-0.312	0.062	4.62E-07	3.40E-01	18	7.443	6.37E-03	N
cg04198912	1q32.1	205567693	<i>MFSD4</i>	0.135	0.091	1.38E-01	3.05E-02	3	0.654	0.123	1.08E-07	7.41E-01	3	11.544	6.80E-04	Y
cg03706720	3q27.1	184513150	<i>IGR (EPHB3)</i>	0.190	0.066	3.76E-03	2.09E-01	20	-0.328	0.048	1.05E-11	2.27E-01	20	40.490	1.98E-10	Y
cg06691616	4q31.1	138609944	<i>IGR (LINC00499)</i>	-0.027	0.099	7.85E-01	4.62E-01	8	0.522	0.094	2.84E-08	1.65E-01	8	16.114	5.96E-05	Y
cg08631357	5q32	150209647	<i>SLC6A7</i>	0.074	0.039	5.45E-02	2.02E-01	18	0.230	0.045	2.76E-07	2.24E-01	18	6.983	8.23E-03	N
cg02769614	6p21.32	32167275	<i>PPT2-EGFL8, EGFL8</i>	-0.051	0.110	6.41E-01	6.44E-03	3	0.535	0.089	1.58E-09	2.46E-01	3	17.166	3.42E-05	Y
cg08288383	7q21.3	98051318	<i>IGR (LMTK2)</i>	0.057	0.097	5.59E-01	7.22E-01	19	0.658	0.128	2.86E-07	8.87E-02	19	14.012	1.82E-04	Y
cg10308629	7q33	134670051	<i>BPGM</i>	0.010	0.128	9.35E-01	1.79E-01	3	-0.520	0.101	2.88E-07	2.57E-01	3	10.584	1.14E-03	Y
cg04388919	7q36.1	149422042	<i>IGR (ZNF777)</i>	0.325	0.123	8.01E-03	4.69E-02	10	1.421	0.229	4.97E-10	2.44E-01	10	17.872	2.36E-05	Y
cg07189157	7q36.1	149422316	<i>IGR (ZNF777)</i>	0.268	0.099	6.77E-03	9.95E-02	9	1.172	0.166	1.52E-12	4.69E-01	9	21.933	2.82E-06	Y
cg24635736	10q26.13	122979534	<i>PSTK</i>	-0.017	0.072	8.11E-01	2.45E-01	3	-0.374	0.072	1.68E-07	8.24E-01	3	12.286	4.56E-04	Y
cg25214093	10q26.13	124447241	<i>IGR (NKX1-2)</i>	-0.020	0.054	7.05E-01	6.30E-01	10	0.260	0.047	3.31E-08	5.00E-01	10	15.461	8.42E-05	Y
cg15567360	11q13.4	71611653	<i>IGR (KRTAP5-11)</i>	0.156	0.155	3.16E-01	4.87E-01	3	-0.679	0.130	1.67E-07	3.71E-01	3	17.014	3.71E-05	Y
cg03249590	12q13.3	56646415	<i>ATP5B, SNORD59A</i>	0.097	0.056	8.22E-02	8.53E-01	3	0.331	0.059	2.00E-08	5.50E-02	3	8.311	3.94E-03	N
cg06679265	12q13.3	56646420	<i>ATP5B, SNORD59A</i>	0.105	0.061	8.31E-02	9.59E-01	3	0.359	0.066	4.72E-08	2.41E-01	3	8.053	4.54E-03	N
cg09557313	13q14.3	52739039	<i>LECT1</i>	0.135	0.115	2.38E-01	1.78E-01	7	0.547	0.103	1.06E-07	5.67E-01	7	7.138	7.55E-03	N
cg04870949	13q34	113455542	<i>IGR (DCUN1D2)</i>	-0.050	0.044	2.52E-01	4.14E-01	18	-0.270	0.053	4.21E-07	1.29E-01	18	10.119	1.47E-03	Y
cg07011318	16p13.3	2004943	<i>ZNF598</i>	-0.022	0.050	6.64E-01	3.31E-01	17	0.291	0.046	1.96E-10	1.12E-01	17	21.132	4.29E-06	Y
cg09397293	16p13.3	2005032	<i>ZNF598</i>	-0.021	0.049	6.64E-01	3.35E-01	18	0.282	0.044	1.86E-10	1.13E-01	18	21.156	4.23E-06	Y
cg05211189	16p13.3	2005402	<i>ZNF598</i>	0.013	0.040	7.54E-01	4.61E-01	18	0.283	0.043	7.47E-11	1.01E-01	18	20.877	4.90E-06	Y
cg08576185	16p13.3	2005683	<i>ZNF598</i>	-0.022	0.051	6.64E-01	4.94E-01	16	0.295	0.046	2.00E-10	9.02E-02	16	21.122	4.31E-06	Y
cg06998361	16q21	58110599	<i>IGR (C16orf80)</i>	-0.098	0.091	2.77E-01	1.32E-01	11	-0.591	0.109	5.49E-08	6.81E-01	11	12.131	4.96E-04	Y
cg10191399	16q23.3	81693451	<i>CMIP</i>	0.034	0.040	3.89E-01	4.55E-01	20	0.246	0.041	1.54E-09	8.86E-02	20	13.820	2.01E-04	Y
cg20002045	21q22.3	42499561	<i>SLC37A1</i>	0.027	0.080	7.40E-01	3.21E-01	20	-0.456	0.090	4.49E-07	1.87E-01	20	15.950	6.51E-05	Y
cg01716252	21q22.3	45132690	<i>ADARB1</i>	0.104	0.129	4.21E-01	4.86E-01	17	0.827	0.164	4.46E-07	1.32E-01	17	12.007	5.30E-04	Y

Please see the description provided below Table S3.

Table S7: List of Abbreviations

Abbreviation	Explanation
<i>ABCA7</i>	ATP Binding Cassette Subfamily A Member 7
AD	Alzheimer's Disease
<i>ADCY8</i>	Adenylate Cyclase 8
<i>AIM2</i>	Absent in Melanoma 2
<i>ANK1</i>	Ankyrin 1
<i>AP2A2</i>	Adaptor Related Protein Complex 2 Subunit Alpha 2
<i>APOC1</i>	Apolipoprotein C1
<i>APOE</i>	Apolipoprotein E
<i>APP</i>	Amyloid Beta Precursor Protein
A β	Amyloid- β
<i>BIN1</i>	Bridging Integrator 1
<i>BPGM</i>	Bisphosphoglycerate Mutase
<i>BRD2</i>	Bromodomain Containing 2
<i>BUG22</i>	Basal Body Upregulated Gene 22
<i>C10orf54</i>	Chromosome 10 Open Reading Frame 54
<i>C16orf80</i>	Chromosome 16 Open Reading Frame 80
<i>CDH23</i>	Cadherin Related 23
<i>CFAP20</i>	Cilia and Flagella Associated Protein 20
<i>CHRNA2</i>	Cholinergic Receptor Nicotinic Alpha 2 Subunit
CHS	Cardiovascular Health Study
<i>CLIC1</i>	Chloride Intracellular Channel 1
<i>CLU</i>	Clusterin
<i>CMIP</i>	C-Maf Inducing Protein
<i>COL11A2</i>	Collagen Type XI Alpha 2 Chain
dbGaP	The Database of Genotypes and Phenotypes
<i>DGUOK</i>	Deoxyguanosine Kinase
<i>DUSP22</i>	Dual Specificity Phosphatase 22
<i>EBF4</i>	Early B Cell Factor Family Member 4
<i>EGFL8</i>	Epidermal Growth Factor-Like Like Domain Multiple 8
eQTL	Expression Quantitative trait Locus
<i>FAM193B</i>	Family with Sequence Similarity 193 Member B
FDR	False Discovery Rate
FHS	Framingham Heart Study
GABA	Gamma-Aminobutyric Acid
GRASP	Genome-Wide Repository of Associations Between SNPs and Phenotypes
GSA	Gene Set Analysis
GSA-SNP2	Gene Set Analysis-Single-Nucleotide Polymorphisms-2
GSEA	Gene Set Enrichment Analysis
GWAS	Genome-Wide Association Study
HEIDI	Heterogeneity in Dependent Instruments
<i>HLA-DPB1</i>	Human Leukocyte Antigen Class II, DP Beta 1
<i>HLA-DQA2</i>	Human Leukocyte Antigen Class II, DQ Alpha 2
<i>HLA-DQB2</i>	Human Leukocyte Antigen Class II, DQ Beta 2
<i>HLA-DRB1</i>	Human Leukocyte Antigen Class II, DR Beta 1
<i>HLA-DRB5</i>	Human Leukocyte Antigen Class II, DR Beta 5
HRS	Health and Retirement Study

HTN	Hypertension
ICD-9	International Classification of Disease codes, Ninth revision
IGR	Inter-Genic Region
<i>IL-18</i>	Interleukin 18
<i>IL-1β</i>	Interleukin 1 Beta
IRB	Institutional Review Board
<i>ITIH2</i>	Inter-Alpha-Trypsin Inhibitor Heavy Chain 2
KEGG	Kyoto Encyclopedia of Genes and Genomes
<i>KRTAP5-11</i>	Keratin Associated Protein 5-11
<i>L1CAM</i>	L1 Cell Adhesion Molecule
<i>LECT1</i>	Leukocyte Cell Derived Chemotaxin 1
LOADFS	Late-Onset Alzheimer's Disease Family Study
<i>LOC100288866</i>	Uncharacterized LOC100288866
<i>LOC154449</i>	Uncharacterized LOC154449
<i>MAPT</i>	Microtubule Associated Protein Tau
MB	Methylene Blue
<i>MHC</i>	Major Histocompatibility Complex
mQTL	Methylation Quantitative trait Locus
<i>MUM1</i>	Melanoma Ubiquitous Mutated Protein 1
MWA	Methylome-Wide Association
NABA	Matrisome Project
<i>NANOS2</i>	Nanos C2HC-Type Zinc Finger 2
<i>NDUFA4</i>	NDUFA4 Mitochondrial Complex Associated
<i>NGFR</i>	Nerve Growth Factor Receptor
NHGRI-EBI GWAS	National Human Genome Research Institute-European Bioinformatics Institute Genome-Wide Association Studies Catalog
NINCDS-ADRDA	National Institute of Neurological and Communicative Disorders and Stroke of the United States-the Alzheimer's Disease and Related Disorders Association
<i>NLR4</i>	Nucleotide-Binding Oligomerization Domain, Leucine Rich Repeat and Caspase Recruitment Domain Containing 4
<i>NLRP3</i>	Nucleotide-Binding Oligomerization Domain, Leucine Rich Repeat and Pyrin Domain Containing 3
<i>PHLDA1</i>	Pleckstrin Homology Like Domain Family A Member 1
PID	Pathway Interaction Database
<i>PPT2-EGFL8</i>	Palmitoyl-Protein Thioesterase 2-Epidermal Growth Factor-Like Like Domain Multiple 8 Readthrough
<i>PSEN1</i>	Presenilin 1
<i>PSTK</i>	Phosphoseryl-TRNA Kinase
<i>RHBDF2</i>	Rhomboid 5 Homolog 2
<i>RPL13</i>	Ribosomal Protein L13
<i>SIGLEC12</i>	Sialic Acid Binding Immunoglobulin Like Lectin 12
<i>SLC24A4</i>	Solute Carrier Family 24 Member 4
<i>SLC25A2</i>	Solute Carrier Family 25 Member 2
<i>SLC35C1</i>	Solute Carrier Family 35 Member C1
<i>SLC6A7</i>	Solute Carrier Family 6 Member 7
SMR	Summary Data-Based Mendelian Randomization
SNP	Single-Nucleotide Polymorphism
<i>SORBS3</i>	Sorbin And SH3 Domain Containing 3
<i>SORL1</i>	Sortilin Related Receptor 1
<i>ST14</i>	Suppression of Tumorigenicity 14
TCA	Tricarboxylic Acid
<i>TOMM40</i>	Translocase of Outer Mitochondrial Membrane 40
<i>TREM1</i>	Triggering Receptor Expressed on Myeloid Cells 1
TWA	Transcriptome-Wide Association

ZNF394
ZNF598

Zinc Finger Protein 394
Zinc Finger Protein 598