Supplementary Materials

for

A structured brain-wide and genome-wide association study using ADNI PET images

by

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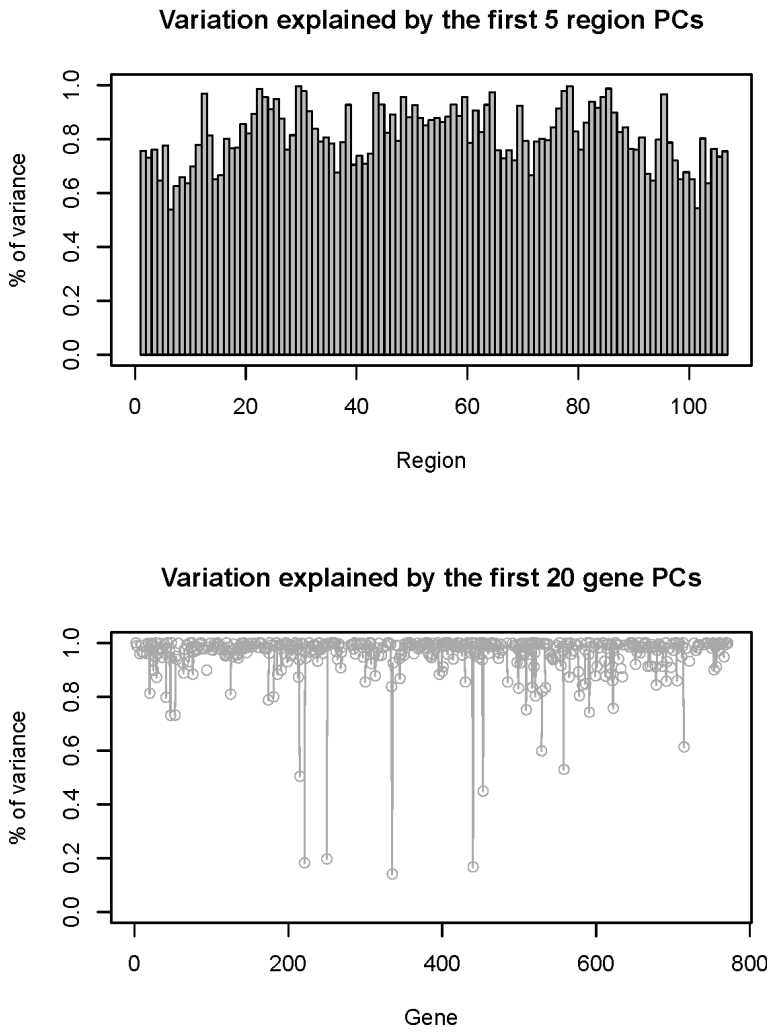
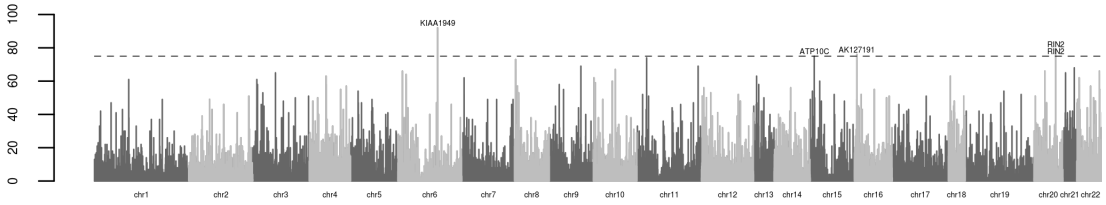
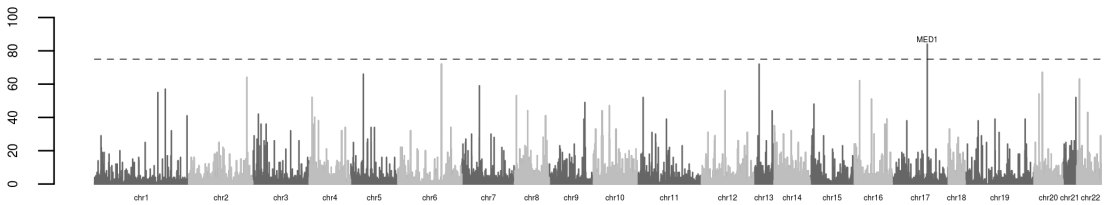


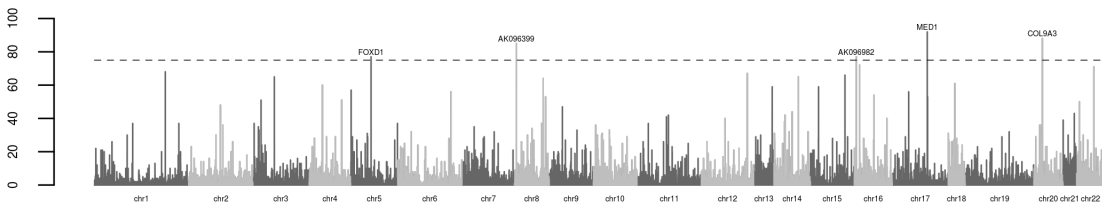
Figure S.1: (a) Percent of variation explained by the first five PCs in each of the 106 ROIs. (b) Percent of variation explained by up to the first 20 PCs for each gene on chromosome 20.



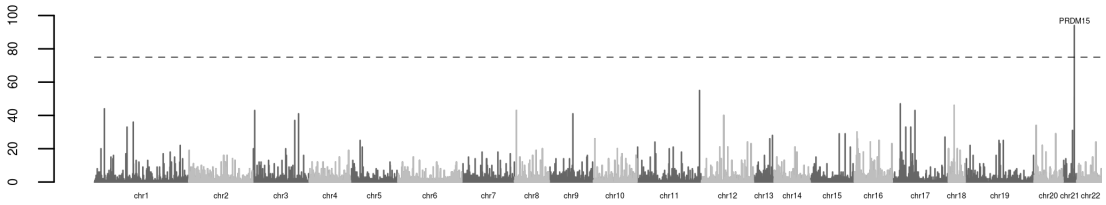
(a) Region: CERHEM(L)



(b) Region: Superior parietal cortex BA39(L)



(c) Region: Superior parietal cortex BA39(R)



(d) Region: Occipital cortex BA17(R)

Figure S.2: Stability selection frequencies. ROI versus the genome. (a) The gene PC effect selection frequency for region CERHEM(L), where the gene *RIN2* has two independent PCs with selection frequencies more than 75% and is therefore selected and passed to the second-stage selection. (b) and (c) The gene×AD interaction effect selection frequencies on regions BA39(L) and BA39, where the genes *MED1* and *COL9A3* are selected, among a few others. (d) The gene×MCI interaction effect on region BA17; the gene *PRDM15* is selected into the second stage.

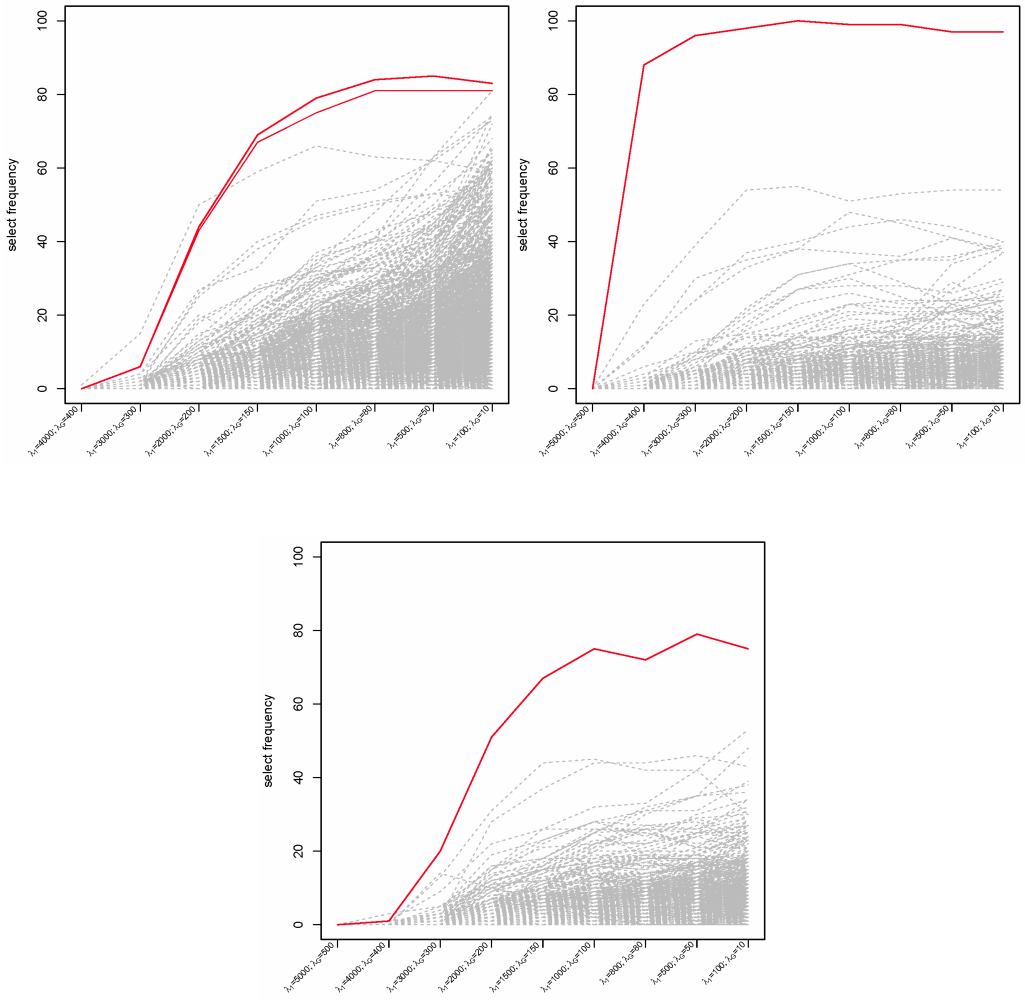


Figure S.3: Illustrating robustness to the tuning parameters of stability selection. Depicted are the selection paths of the regions CERHEM(L) and the occipital cortex BA19(R) on chromosome 20 in the first stage selection. The vertical axis is the select frequency out of 100 bootstrap datasets and the horizontal axis indicates the different settings of the tuning parameter values. We fixed the ratio of the individual level tuning parameter λ to the group level tuning parameter λ_1 at 10. The highlighted selection paths are for the top selected regression coefficients. Notice that the top signals are consistently selected from the bootstrapped datasets. (a) The gene effect of the region CERHEM(L). (b) The gene AD interaction effect of the region occipital cortex BA19(R). (c) The gene MCI interaction effect of the region occipital cortex BA19(R).

Table S.1: Some other gene×AD and gene×MCI interaction effects of top SNPs that have a p-value more significant than 10^{-5} and a selection frequency exceeding 80%.

gene information				top selective SNP in gene		associated	effect type	reference
name	chr	num. SNP in gene	% variance by 20 PCs	SNP name	most sig. p-value	region		
HOXD4	2	11	100%	rs2072590	1.6e-06	Medial frontal cortex_BA9(L)	G×AD	Nolte et al. [10],
AK096399	8	40	98.6%	rs6436025	1.3e-06	Primary somatosensory cortex_BA5(R)	G×MCI	Cannon et al. [2]
TBC1D4	13	86	87.1%	rs1864726	2.4e-06	Medial frontal cortex_BA8(L)	G×MCI	Talbot et al. [13], Yang, Li, & Liu [14], Dai et al. [4], Sakamoto & Holman [12]
GPR108	19	27	98%	rs2250656	6.4e-06	Occipital cortex_BA18(L)	G×MCI	Goltz, Brüggemeier, & Geerts [6]
BTG3	21	26	99.5%	rs2849896	6.3e-06	Pre-motor cortex_BA6(L)	G×MCI	Carson [3]

Table S.2: The top selected *APOE-ϵ4* effects for voxels that have a selection frequency exceeding 80% and a p-value not exceeding 0.1.

ROI	rank within ROI	$\hat{\beta}$	*APOE4* p-value	effect type	reference
Lateral frontal	1	315.3	0.10	G	Murphy et al. [9],
BA44 (R)	2	310.4	0.07	G	Harwood et al. [7],
	3	296.1	0.09	G	Johnson et al. [8]
	4	292.8	0.08	G	
	5	291.5	0.10	G	
BA43 (R)	1	223.4	0.07	G×AD	
	2	218.8	0.10	G×AD	
	3	216.9	0.09	G×AD	
BA42 (R)	1	−303.7	0.06	G	
	2	−299.7	0.08	G	
	3	−292.8	0.07	G	
Superior parietal	1	−395.8	0.09	G×MCI	Ross et al. [11],
BA39 (R)	2	−395.2	0.09	G×MCI	Alexander et al. [1],
	3	−395.2	0.10	G×MCI	Duara et al. [5]

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