

SUPPLEMENTAL INFORMATION

Table S1: Characteristics of human-evolution focused genome annotations in 1000 Genomes Phase 3 (EUR)

Name	# Regions	Total Size (kb)	# 1KG† SNPs	Avg. MAF†	Reference
Human Accelerated Regions	2,737	702	1,874	0.213	(Capra et al. 2013)
Human Gained Enhancers - 7PCW	7,742	22,195	57,059	0.205	(Reilly et al. 2015)
Human Gained Enhancers - 8.5PCW	5,101	12,277	29,985	0.203	(Reilly et al. 2015)
Human Gained Enhancers - 12PCW (Frontal)	3,110	8,079	20,741	0.203	(Reilly et al. 2015)
Human Gained Enhancers - 12PCW (Occipital)	4,994	12,297	29,344	0.203	(Reilly et al. 2015)
Human Gained Enhancers - Adult human vs macaque (prefrontal cortex)	2852	12,692	32,009	0.206	(Vermunt et al. 2016)
Human Gained Promoters - Adult human vs macaque (prefrontal cortex)	358	2,048	5,111	0.213	(Vermunt et al. 2016)

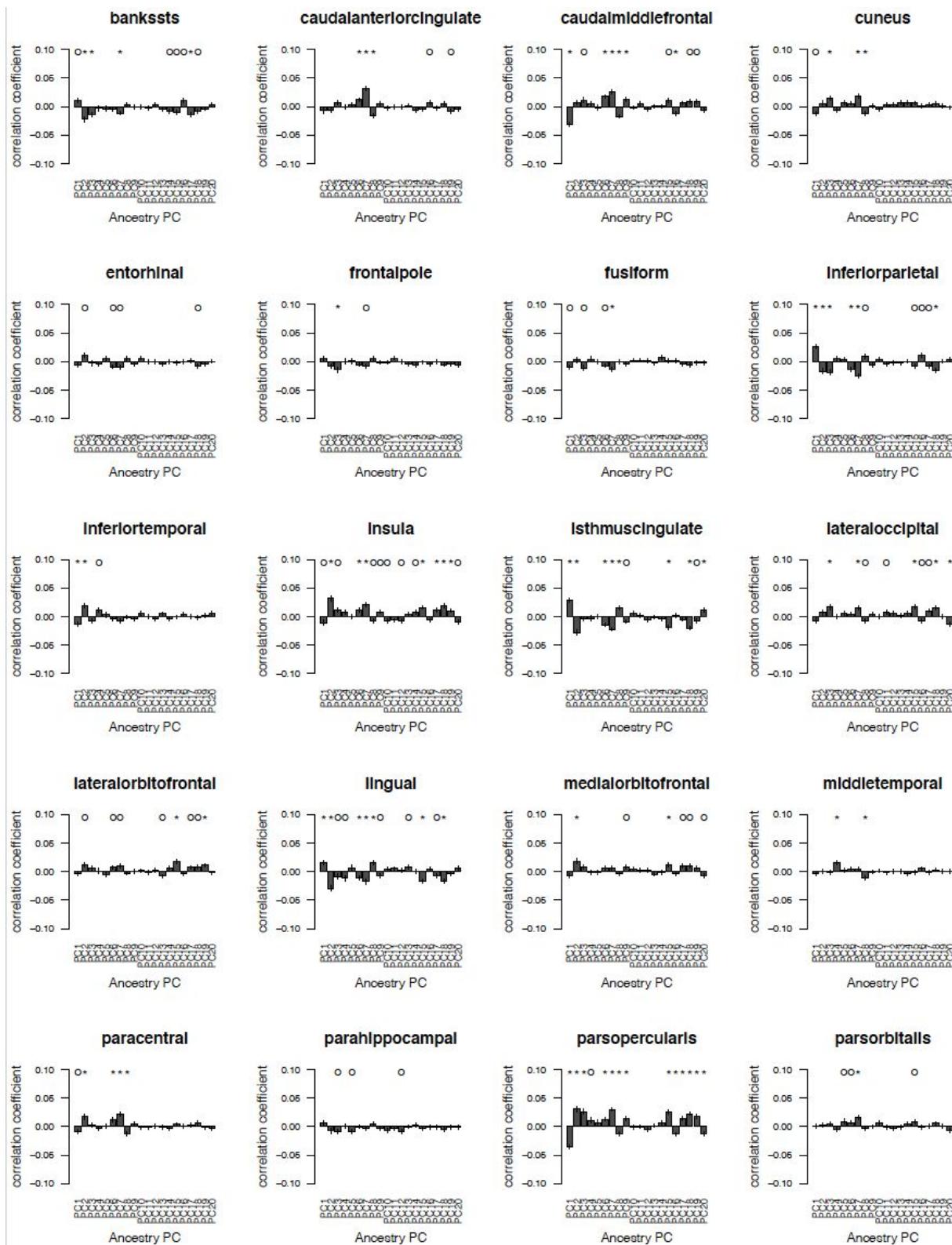
Human Gained Enhancers - Adult human vs chimpanzee (prefrontal cortex)	435	1,826	4,749	0.212	(Vermunt et al. 2016)
Human Gained Promoters - Adult human vs chimpanzee (prefrontal cortex)	28	129	329	0.242	(Vermunt et al. 2016)
Neanderthal Introgression SNPs	5,851	722,954	24,331	0.115	(Simonti et al. 2016)
Neanderthal Lineage Depleted Regions	6	84,440	175,377	0.208	(Vernot et al. 2016)
Selective Sweeps	314	19,064	23,744	0.196	(Peyrégne et al. 2017)

†Based on 1000 Genomes, phase 3 SNPs that were included in the ENIGMA3 meta-analysis

Table S2. eGenes impacted by loci within HGEs that are also associated with Regional or Global SA. See separate excel file.

Table S3. Irritable bowel disease heritability is not enriched in any of the evolution-focused annotations considered in this study. P-values are FDR-corrected for the number of annotations tested.

Annotation	Prop. <i>h</i> ²	Prop. <i>h</i> ² SE	Enrichment	Enrichment SE	FDR-corrected Enrichment <i>p</i>
HGE 12pcw - Frontal	-0.002	0.012	-0.715	3.840	0.833
HGE 12pcw - Occipital	0.025	0.017	5.602	3.945	0.629
HGE 7pcw	0.059	0.019	7.014	2.194	0.072
HGE 8.5pcw	0.024	0.017	5.463	3.797	0.629
Chimp PFC enhancers	0.001	0.004	1.781	5.344	0.884
Chimp PFC promoters	0.000	0.001	4.824	24.631	0.884
Macaque PFC enhancers	-0.007	0.012	-1.416	2.426	0.629
Macaque PFC promoters	-0.001	0.005	-1.668	6.811	0.833
HAR	-0.003	0.005	-11.108	18.704	0.775
Neanderthal lineage depleted regions	0.018	0.006	0.645	0.222	0.629
Neanderthal SNPs	0.002	0.004	0.309	0.664	0.629
Selective sweeps	0.001	0.003	0.288	0.788	0.629



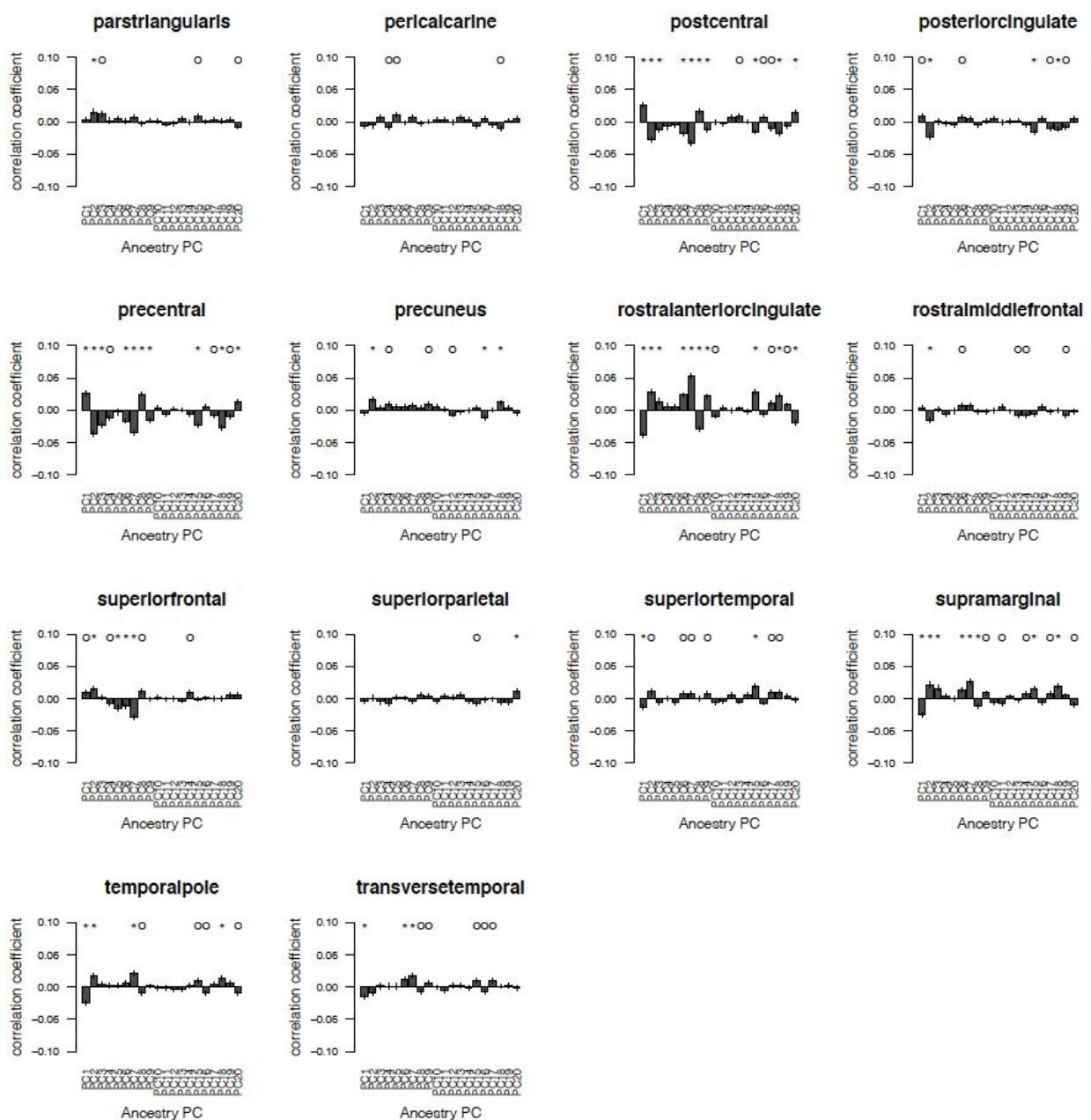
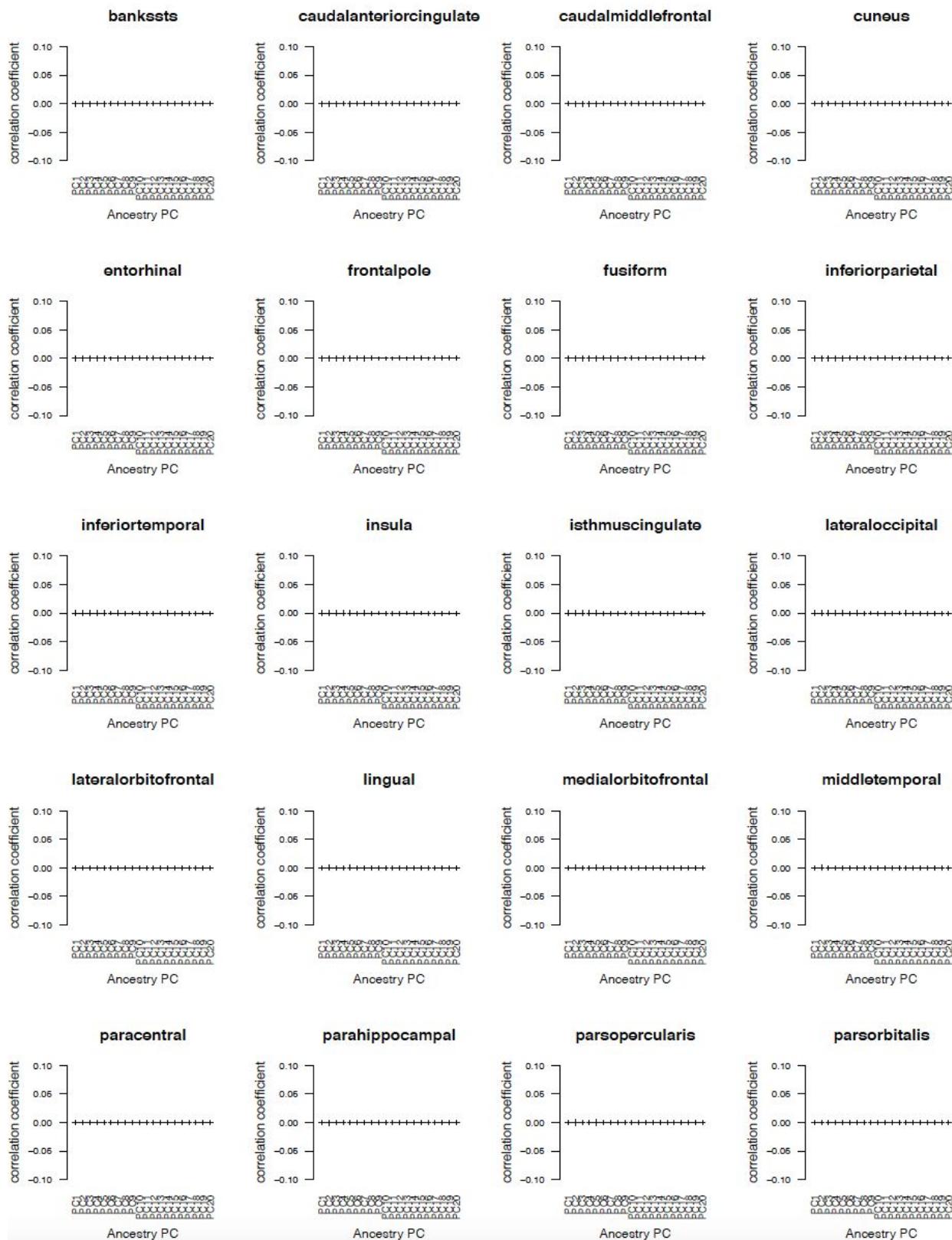


Figure S1. Detecting subtle ancestry regression in cortical SA regional GWASs. Error bars are standard errors.



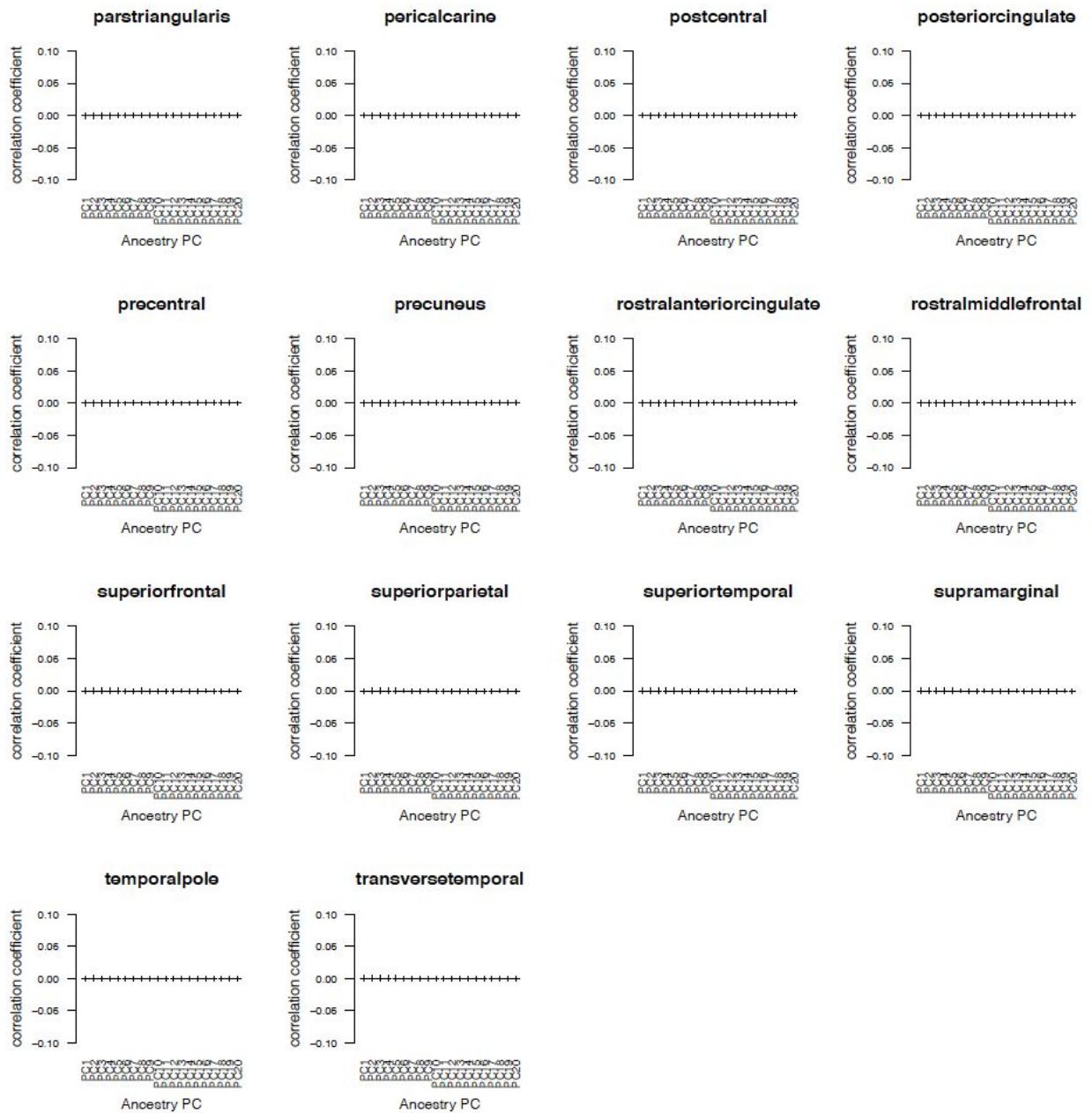
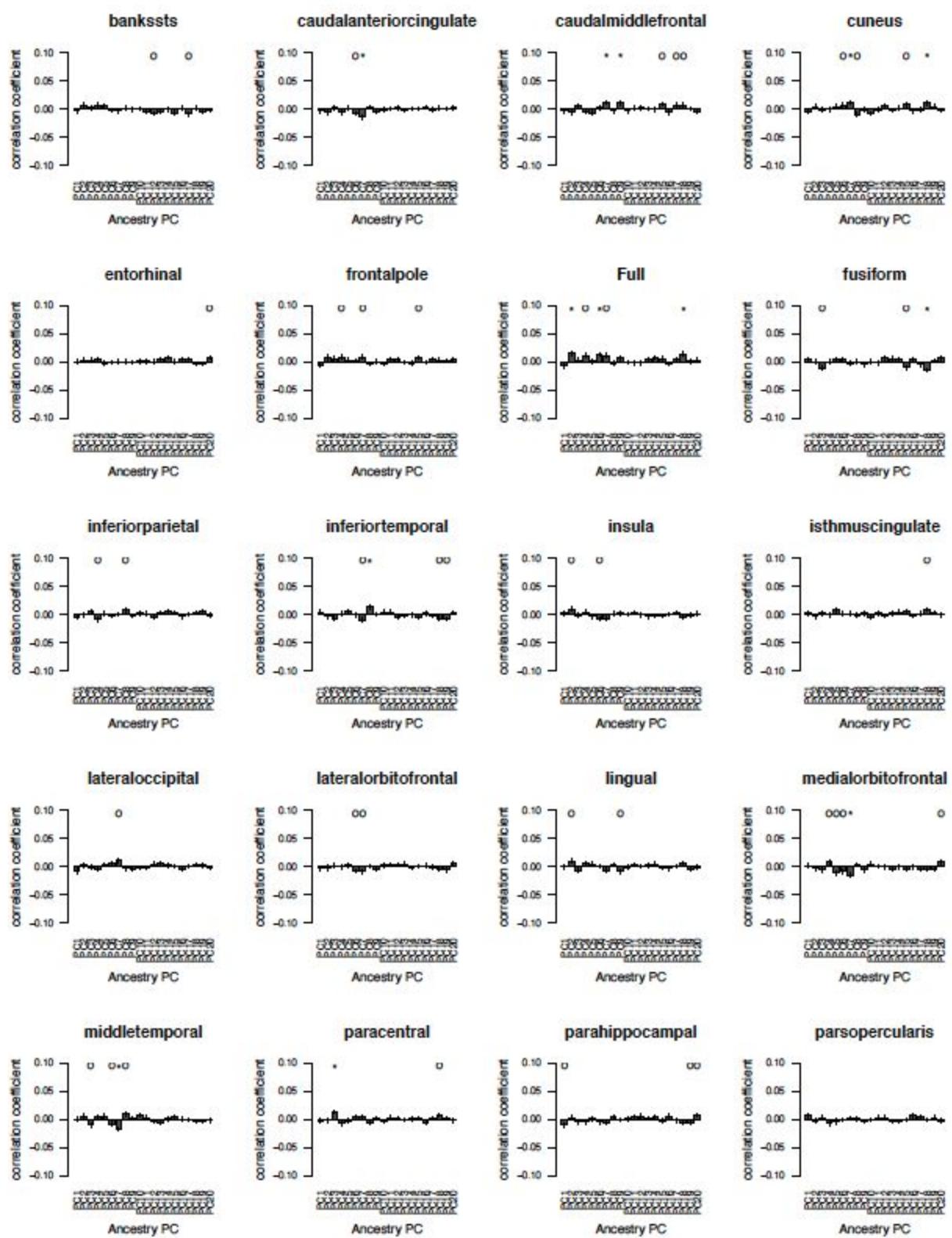


Figure S2. Ancestry regressed cortical SA regional GWASs show diminished effects of subtle population stratification. Error bars are standard errors.



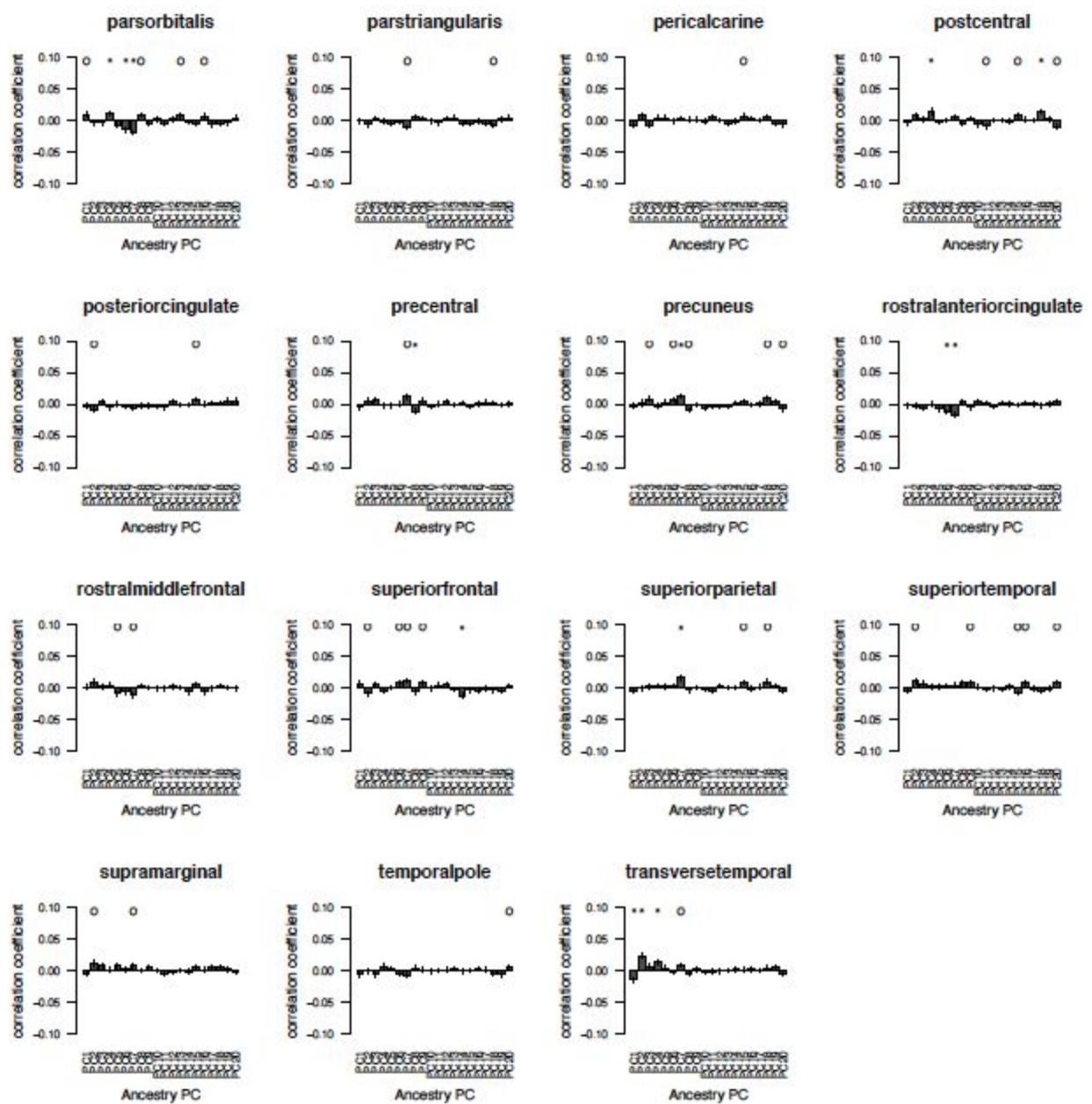
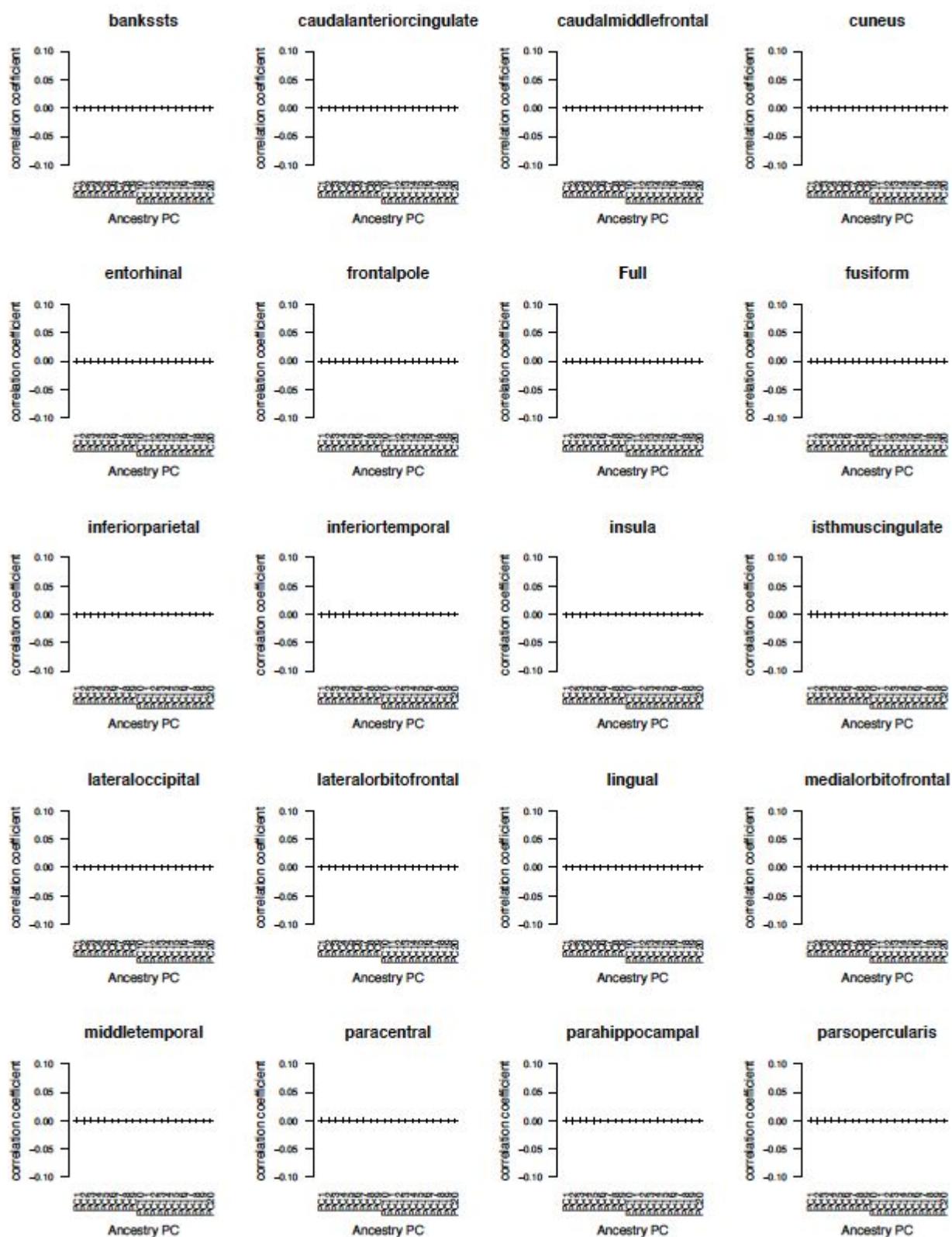


Figure S3. Detecting subtle ancestry regression in cortical thickness regional GWASs. Error bars are standard errors.



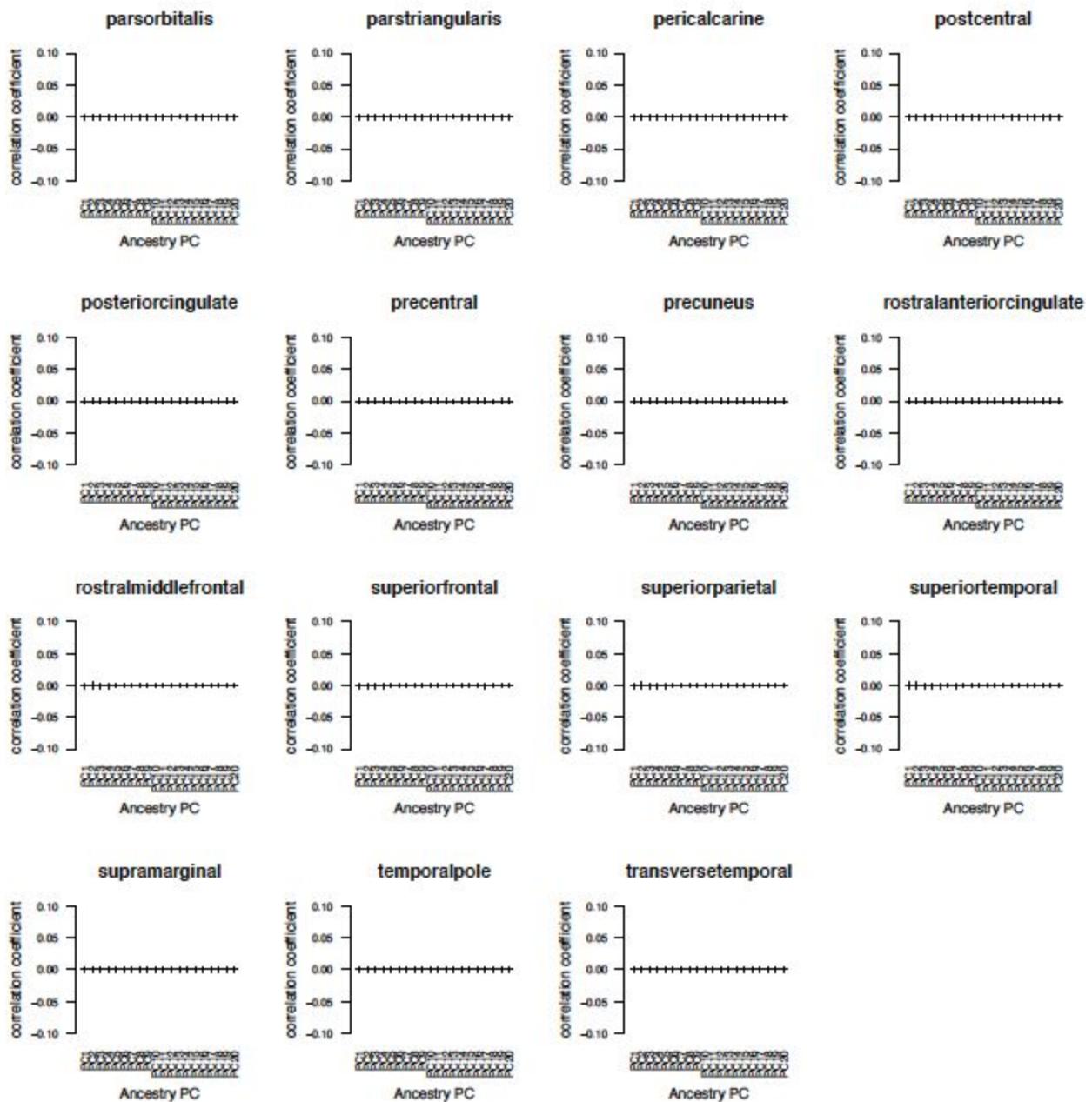


Figure S4. Ancestry regressed cortical thickness regional GWASs show diminished effects of subtle population stratification. Error bars are standard errors.

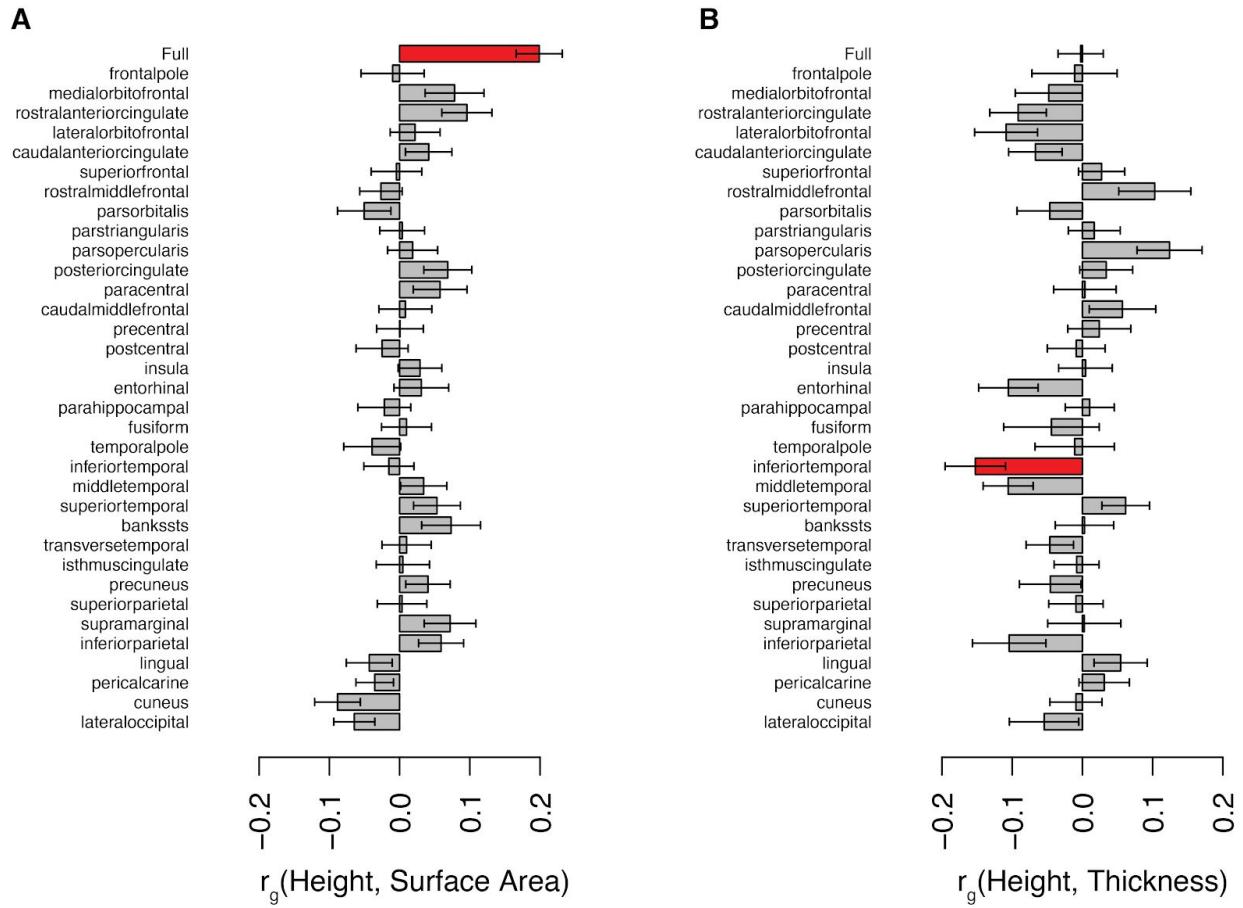


Figure S6. Genetic correlations between cortical surface area **(a)** and thickness **(b)** with height (Wood et al. 2014). Red bars indicate a significant correlation after FDR correction for multiple comparisons within the 35 traits of either surface area or thickness.

Surface area (cor=0.635;P=4.2e-05)

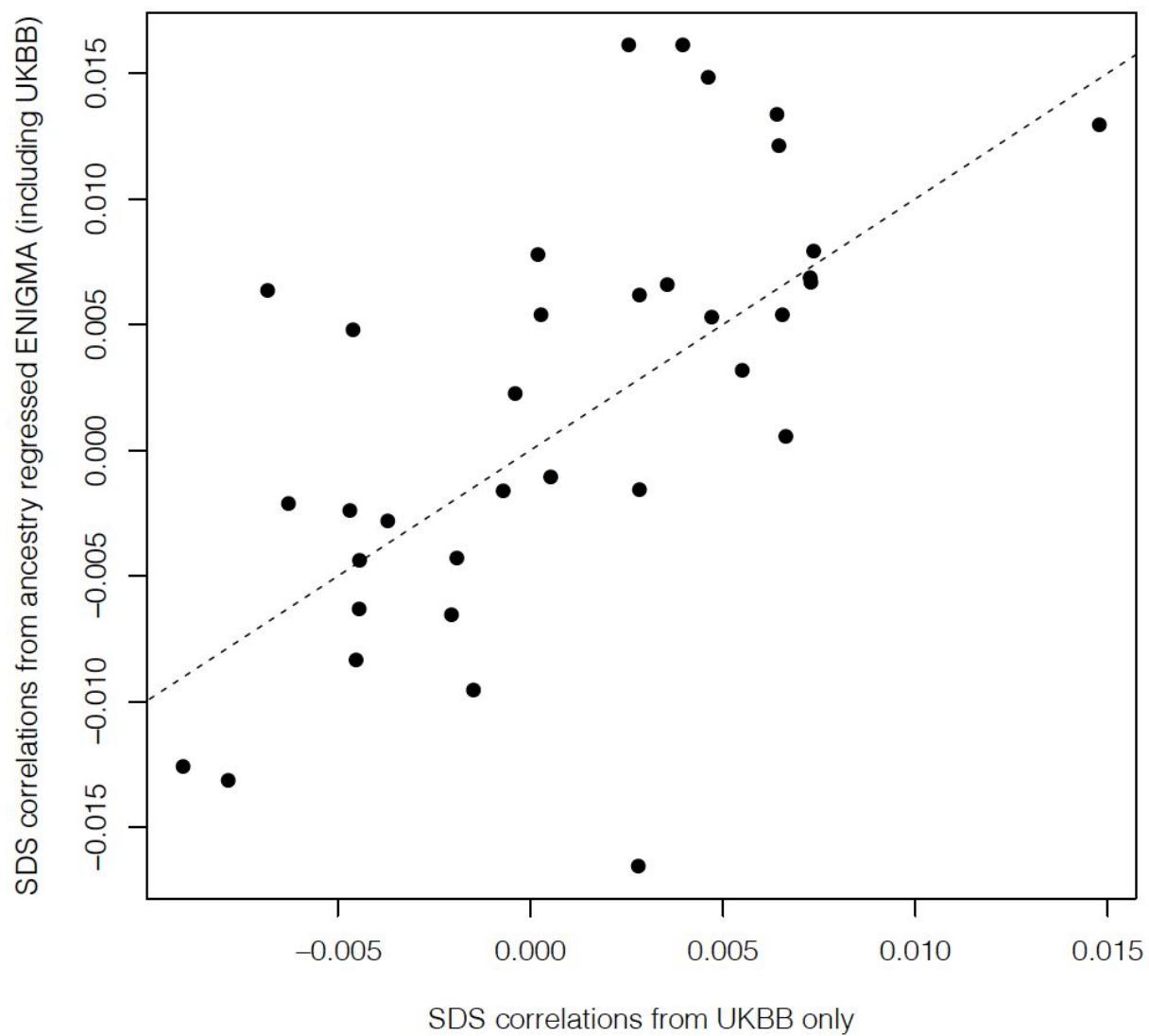


Figure S7. SDS correlations to cortical surface area in a population less susceptible to subtle population stratification (UKBB EUR) and the ancestry regressed ENIGMA data. The $y=x$ line is shown.

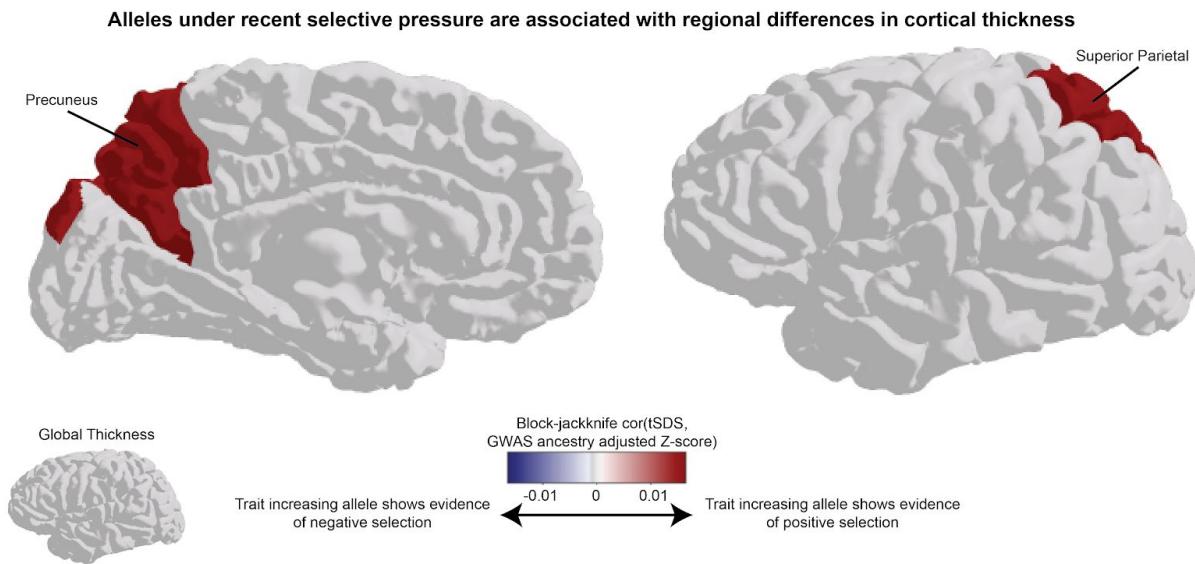


Figure S8. Evidence for haplotypes under recent polygenic selection (~2000-3000 years) impacting cortical thickness. (a) A block-jackknife correlation of ancestry regressed effect sizes from GWAS (Z-scores) with scores of recent selection (t_{SDS}) demonstrates evidence for polygenic alleles under selective pressure also influencing both global and regional thickness (colored regions indicate $FDR < 0.05$). Colder colors indicate that the trait increasing alleles (associated with increased thickness) are generally associated with negative selection (decreasing allele frequencies in the population), whereas warmer colors indicate that trait increasing alleles are associated with positive selection.

Surface Area

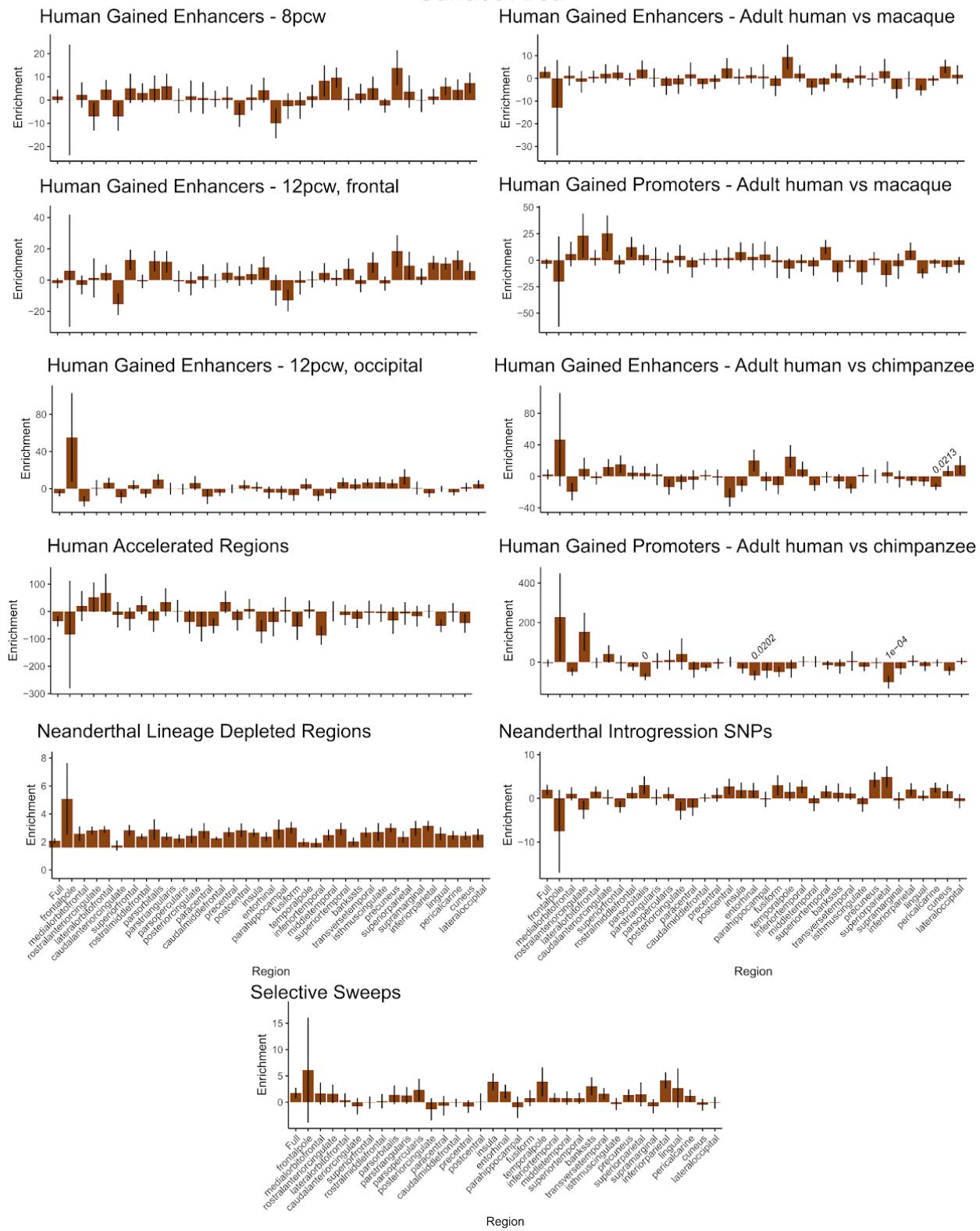


Figure S9. Cortical surface area enrichment scores for Human Accelerated Regions (HARs), fetal and adult HGEs, selective sweeps, Neanderthal introgressed regions, and Neanderthal depleted regions. Error bars represent standard errors, numbers above bars indicate FDR corrected p-values less than 0.05.

Thickness

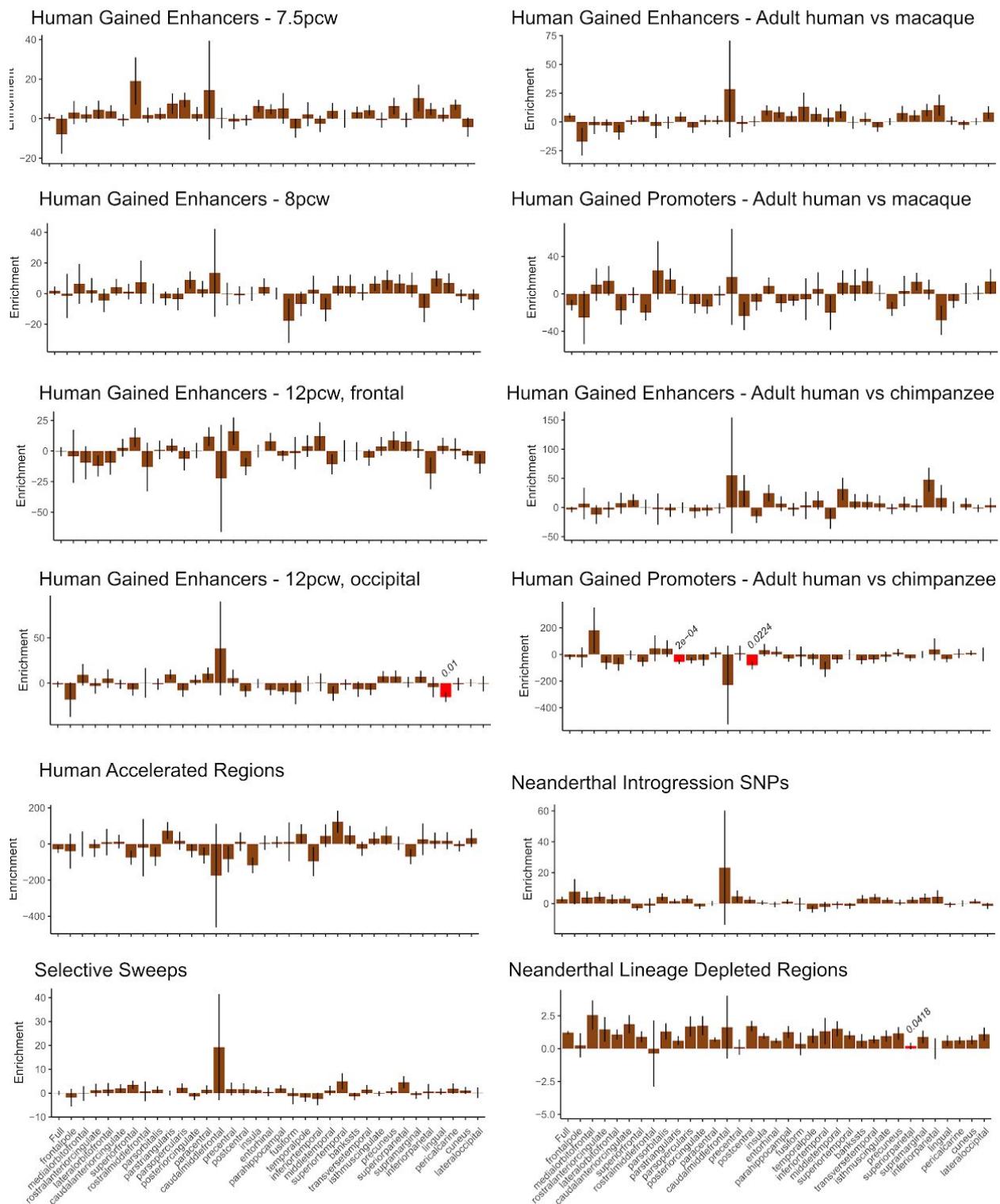


Figure S10. Cortical thickness enrichment scores for Human Accelerated Regions (HARs), fetal and adult HGEs, selective sweeps, Neanderthal introgressed regions, and Neanderthal depleted regions. Error bars represent standard errors, numbers above bars indicate FDR corrected p-values less than 0.05. Negative significant enrichment scores are labeled with the FDR corrected p-values, but are not discussed due to difficulty in interpretation.

Figure S11. GViz plots for 60 GWAS loci are available as a separate PDF.

References

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