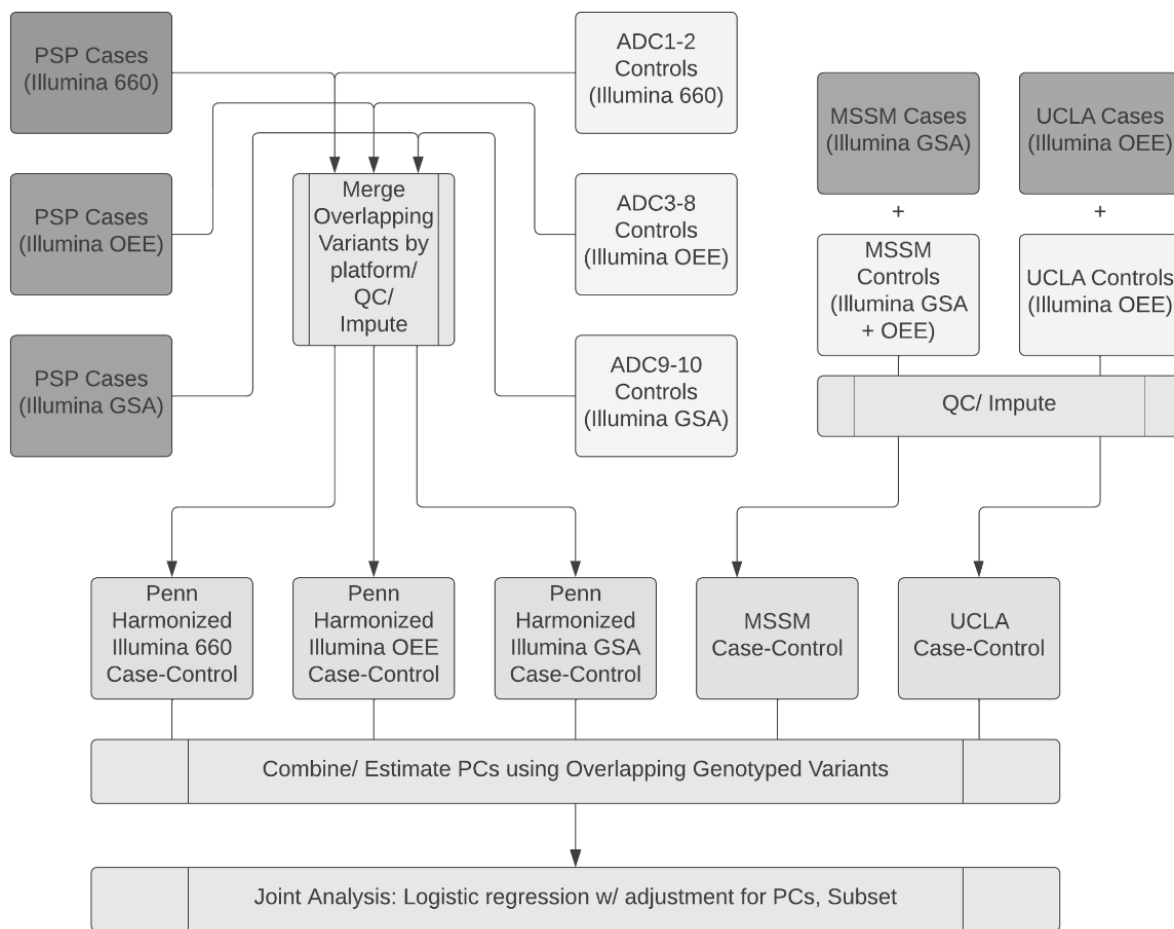
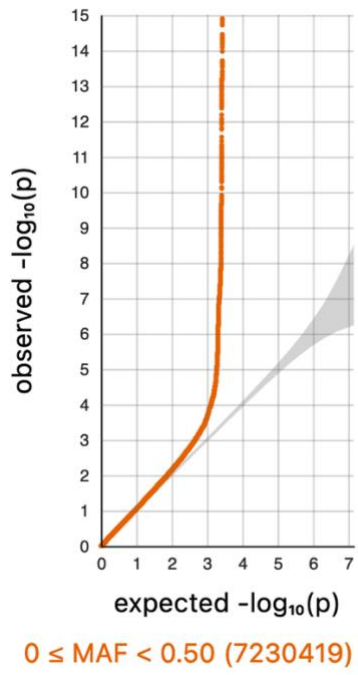


Supplementary Figures

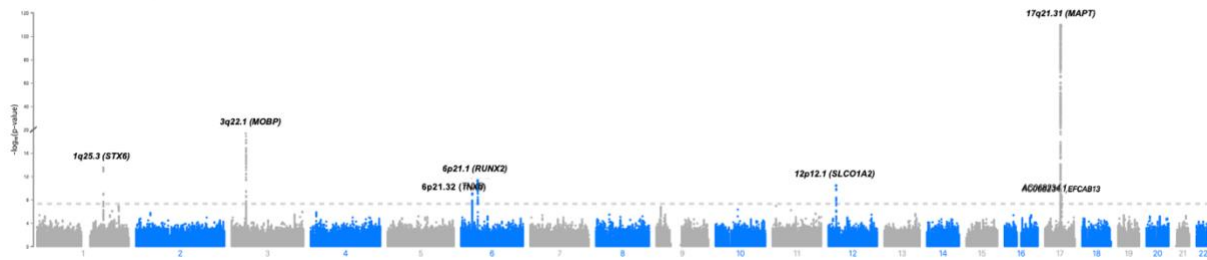


Supplementary Figure 1. Schematic overview of sample acquisition, genotyping and analysis of progressive supranuclear palsy cases and controls. Global Screening Array (GSA) Omni Express (OEE).

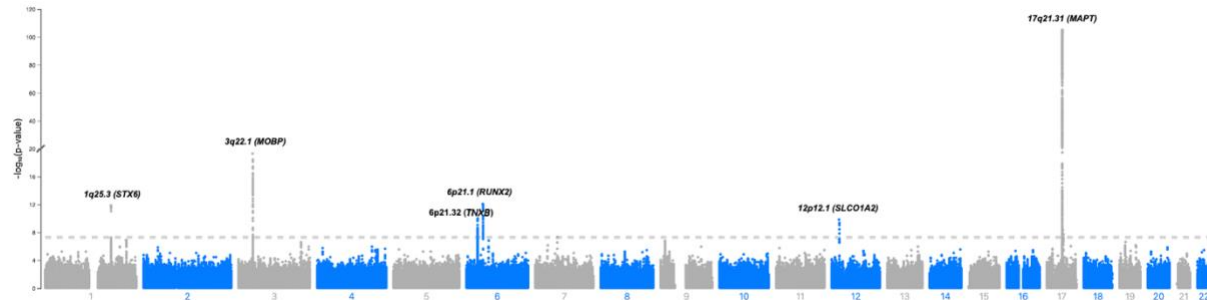


Supplementary Figure 2. Q-Q Plot of the main PSP Genome-wide associations.

a PSP- Main analysis

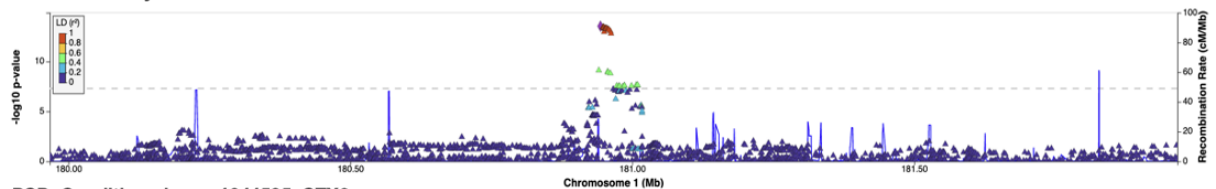


b PSP- 2654 cases, 5584 controls, 125 Non-Autopsy confirmed cases excluded

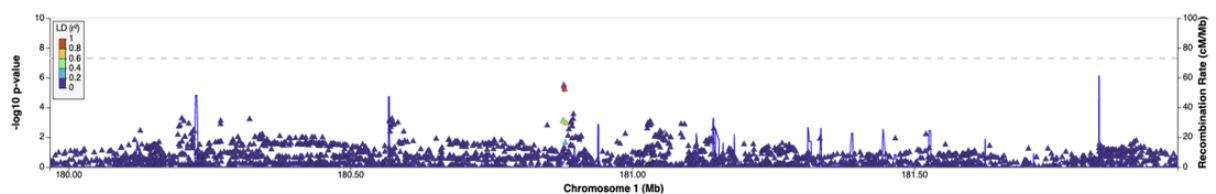


Supplementary Figure 3. Sensitivity analysis of the non-autopsy confirmed subjects. Results of the main association analysis (n=2779 cases, n=5584 controls) (a) compared to the results after excluding 125 non-autopsy confirmed samples confirm similar association signals (n=2654 cases, n=5584 controls).

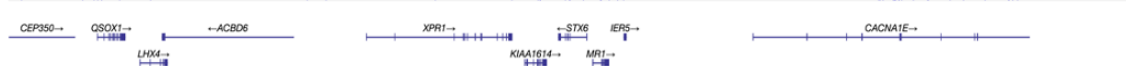
a PSP- Main analysis



b PSP- Conditioned on rs1044595: STX6

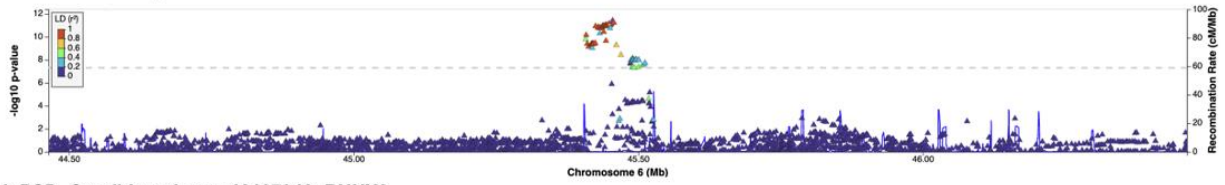


GWAS Catalog hits for PSP - Conditioned on rs1044595: STX6

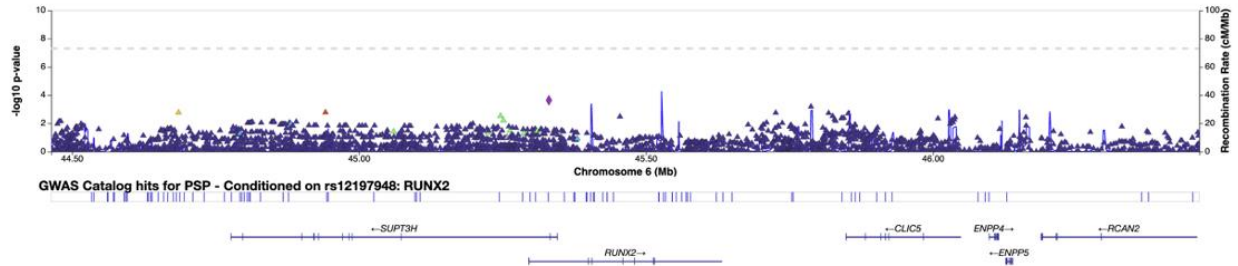


Supplementary Figure 4. Conditioning on rs1044595. The main association analysis (n=2779 cases, n=5584 controls) (a) and the conditioned analysis (n=2654 cases, n=5584 controls) (b) demonstrate there is no secondary signals in the locus containing STX6.

a PSP- Main analysis

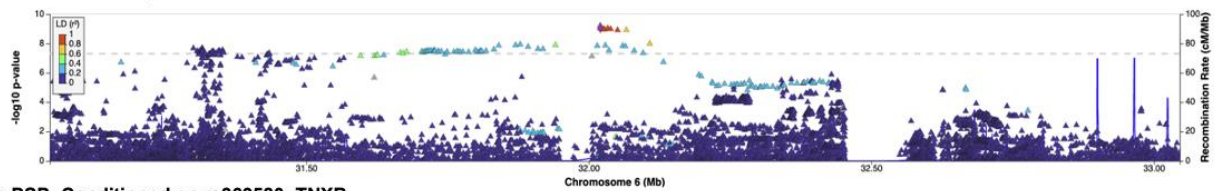


b PSP- Conditioned on rs12197948: RUNX2

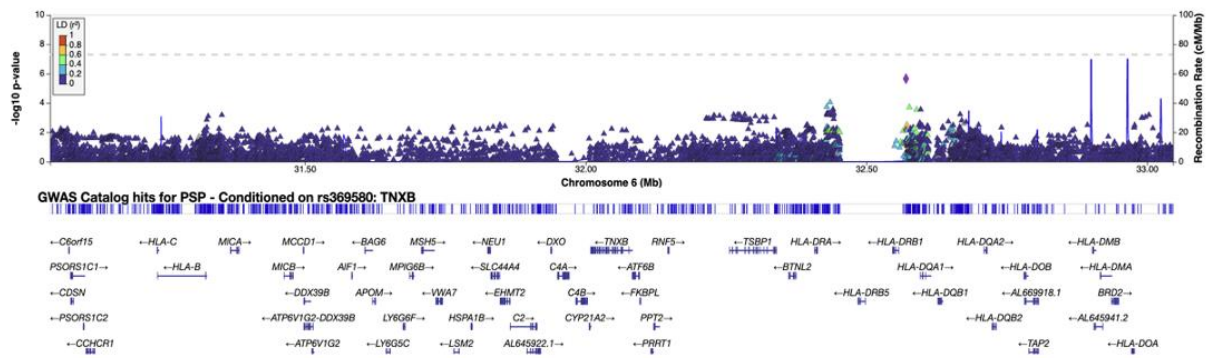


Supplementary Figure 5. Conditioning on rs12197948. The main association analysis (n=2779 cases, n=5584 controls) (a) and the conditioned analysis (n=2654 cases, n=5584 controls) (b) demonstrate there is no secondary signals in the locus containing RUNX2.

a PSP- Main analysis

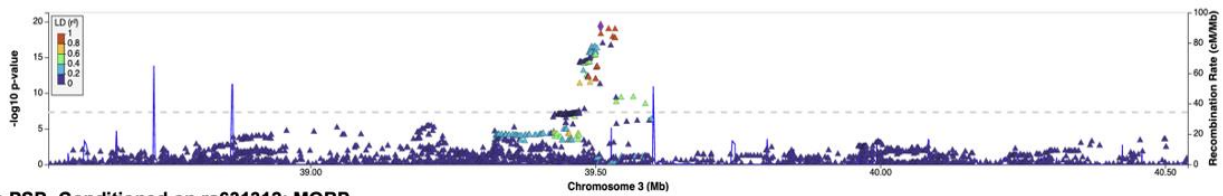


b PSP- Conditioned on rs369580: TNXB

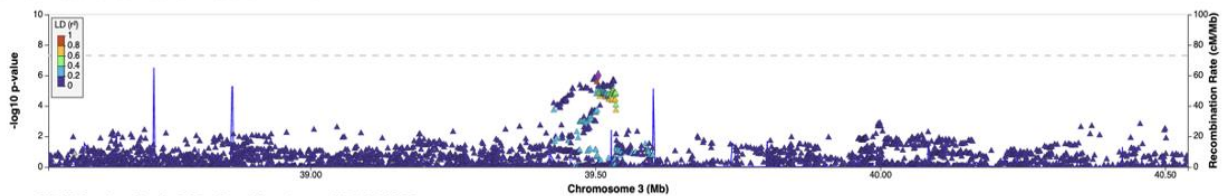


Supplementary Figure 6. Conditioning on rs369580. The main association analysis (n=2779 cases, n=5584 controls) (a) and the conditioned analysis (n=2654 cases, n=5584 controls) (b) demonstrate there are no secondary signals in the locus containing TNXB.

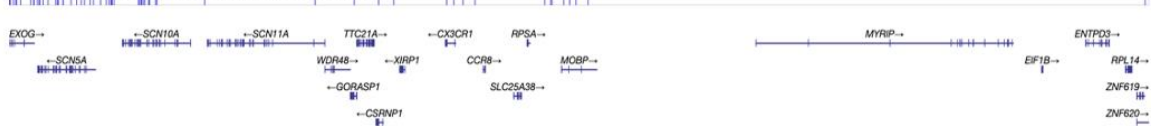
a PSP- Main analysis



b PSP- Conditioned on rs631312: MOBP

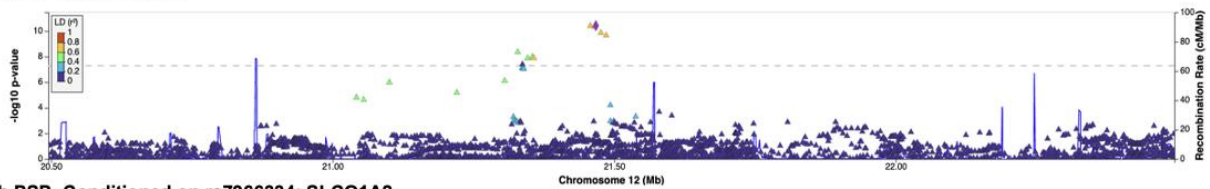


GWAS Catalog hits for PSP - Conditioned on rs631312: MOBP

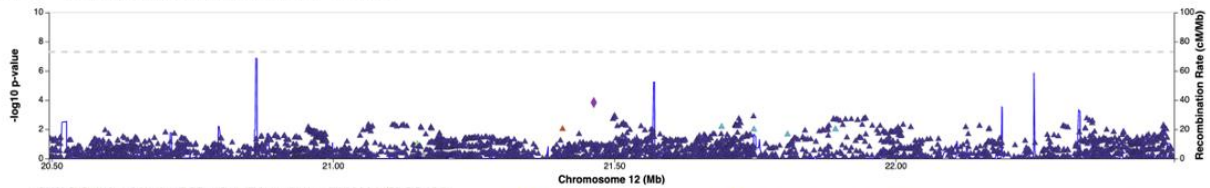


Supplementary Figure 7. Conditioning on rs631312. The main association analysis (n=2779 cases, n=5584 controls) (a) and the conditioned analysis (n=2654 cases, n=5584 controls) (b) demonstrate there are no secondary signals in the locus containing MOBP.

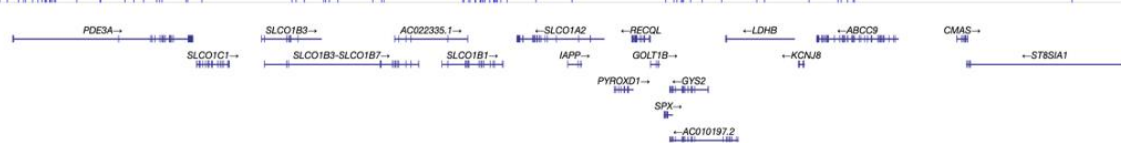
a PSP- Main analysis



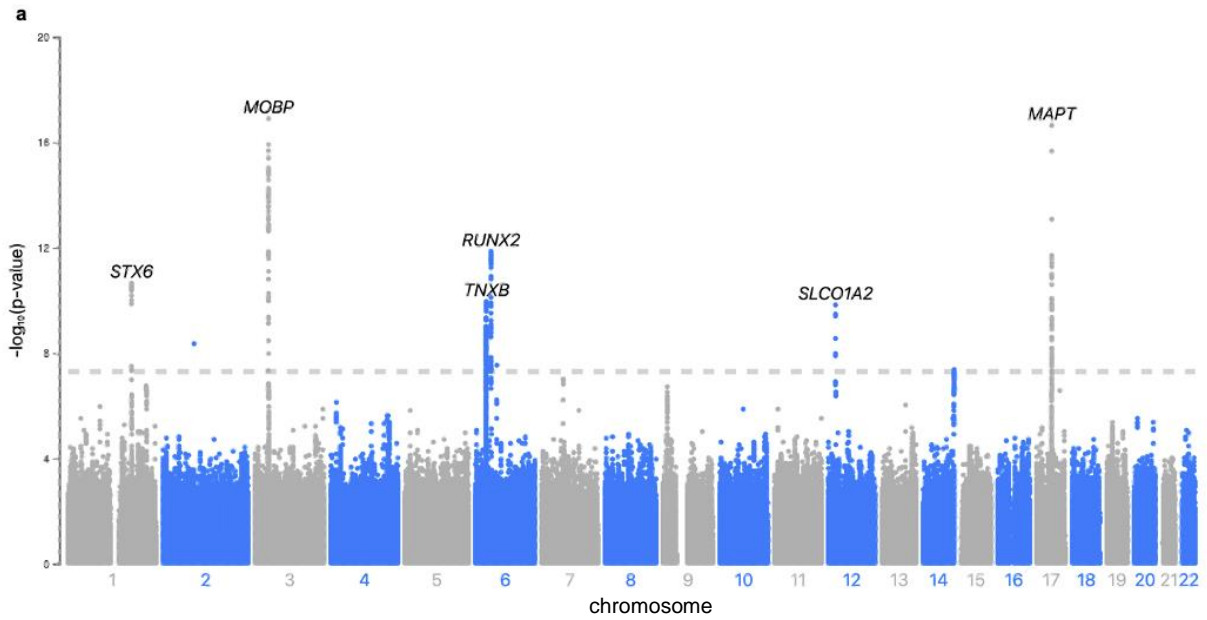
b PSP- Conditioned on rs7966334: SLCO1A2



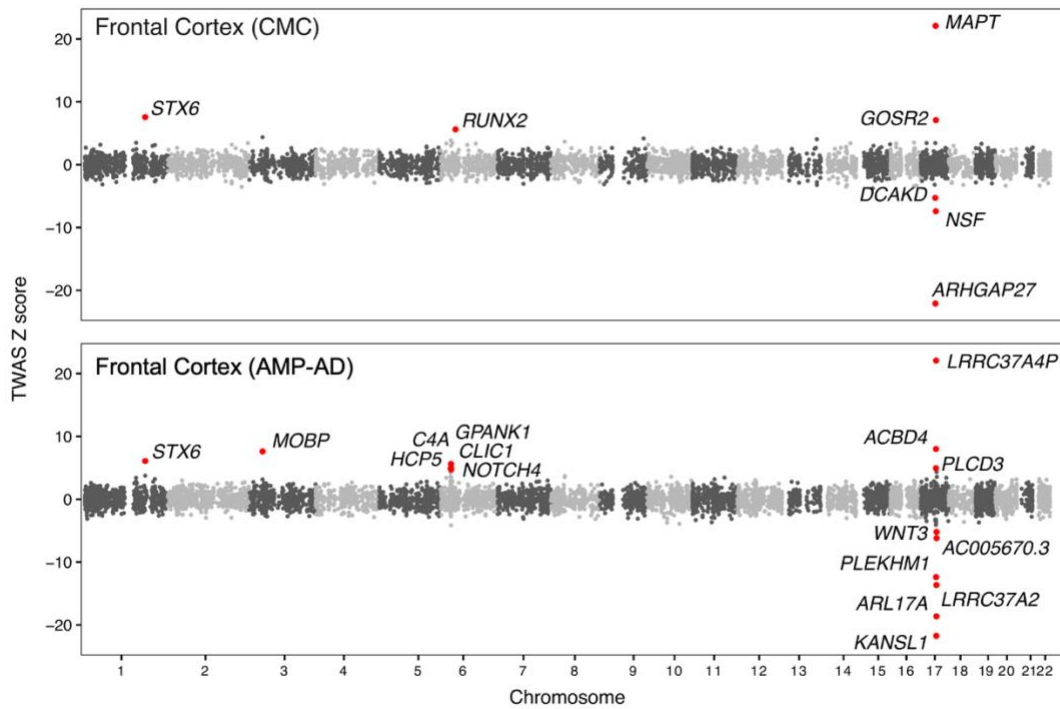
GWAS Catalog hits for PSP - Conditioned on rs7966334: SLCO1A2



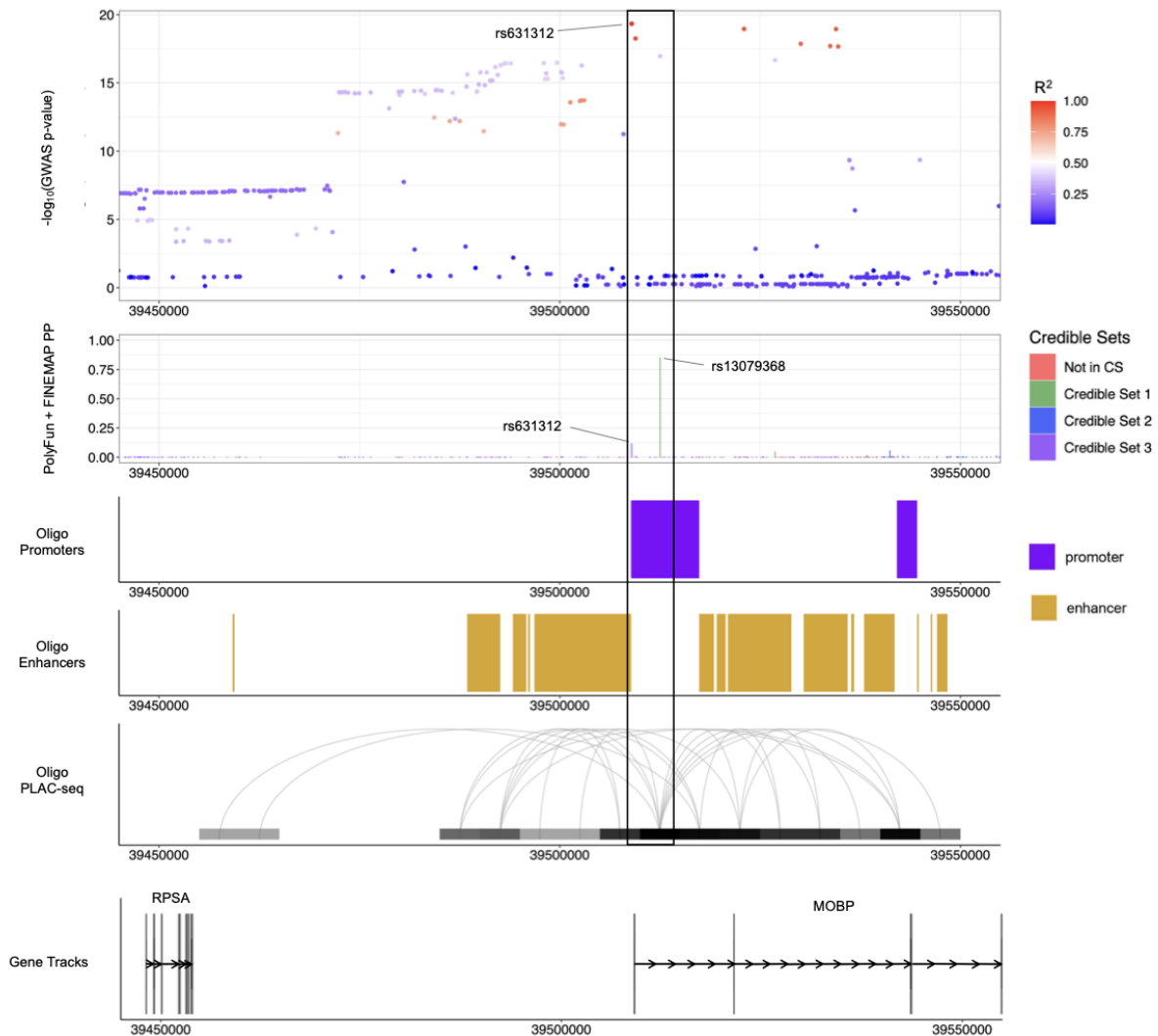
Supplementary Figure 8. Conditioning on rs7966334. The main association analysis (n=2779 cases, n=5584 controls) (a) and the conditioned analysis (n=2654 cases, n=5584 controls) (b) demonstrate there are no secondary signals in the locus containing SLCO1A2.



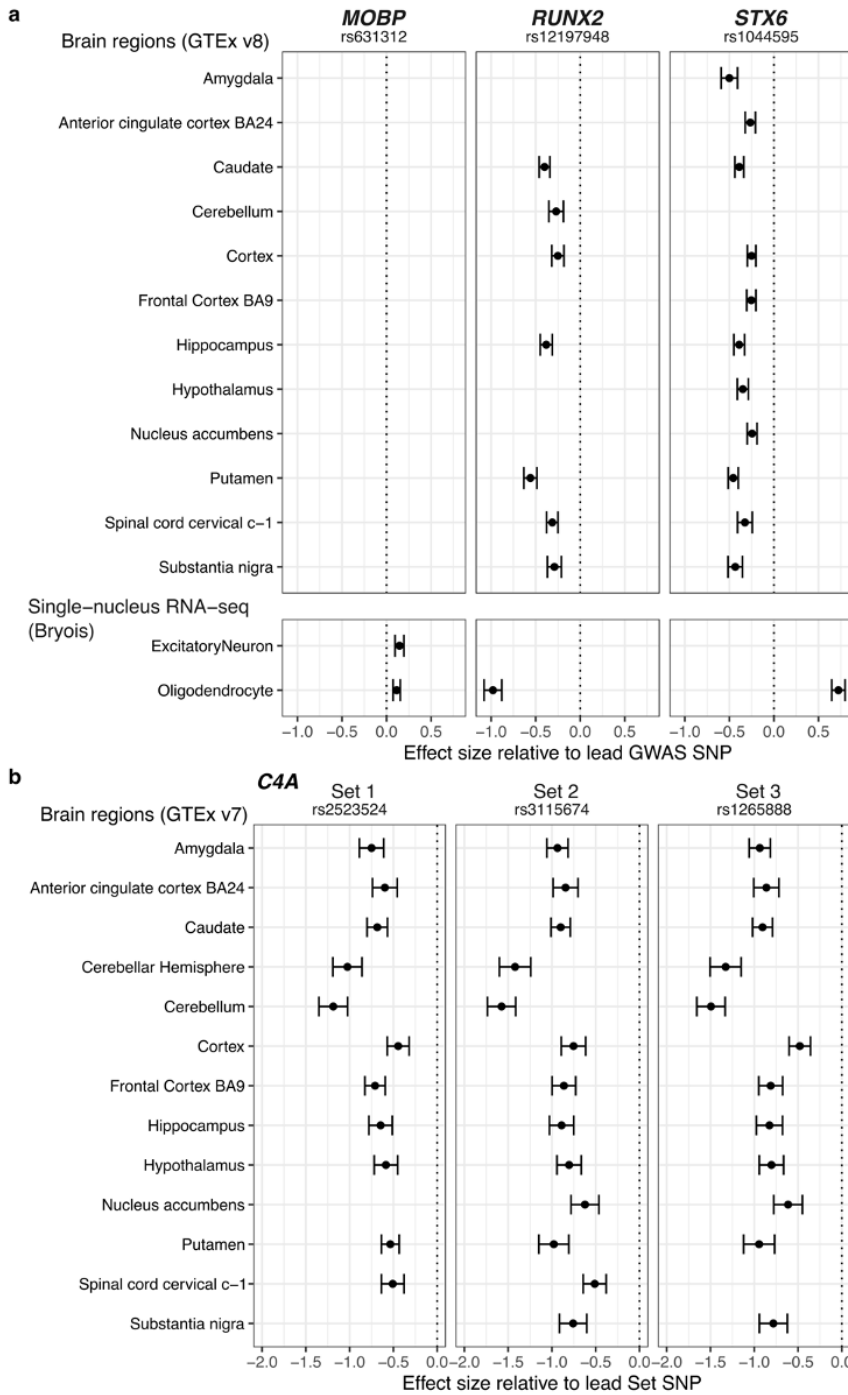
Supplementary Figure 9. Conditioning on MAPT sub haplotype (n=2654 cases, n=5584 controls). Adding the MAPT haplotypes as covariates in the association model reduces the MAPT signal but does change the five other association signals.



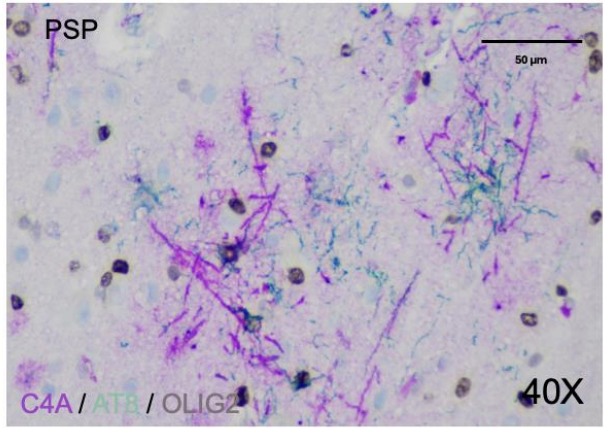
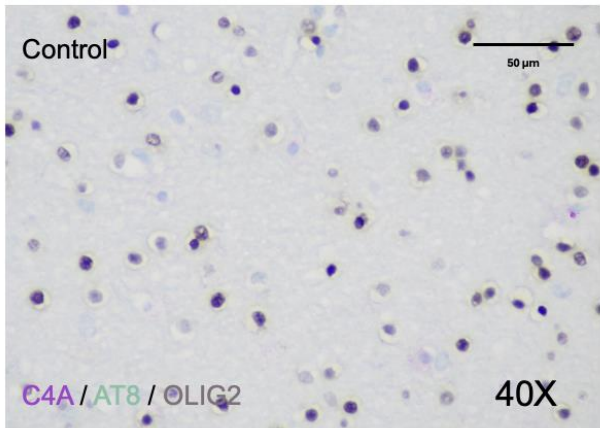
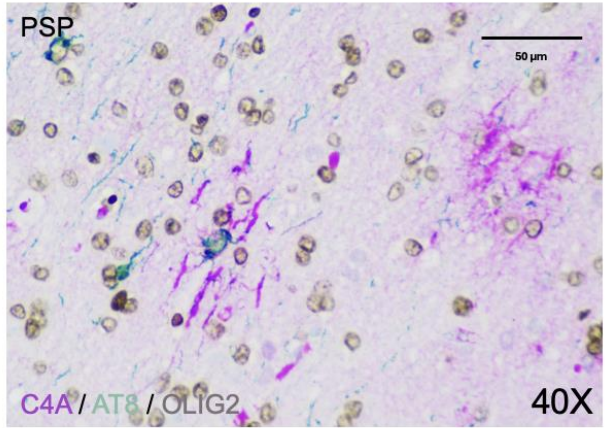
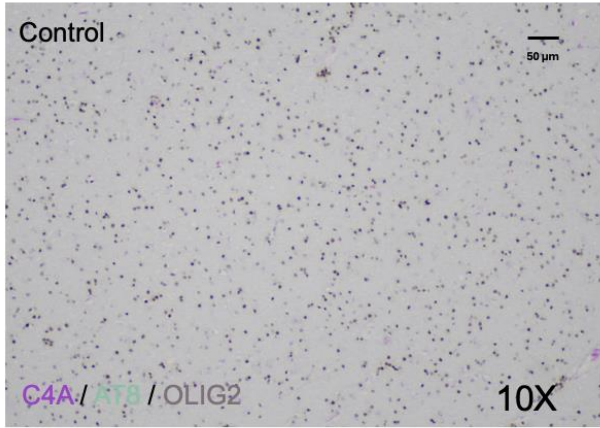
Supplementary Figure 10. Transcriptome-wide Association Study (TWAS) of PSP. Gene expression models were used from two studies of the dorsolateral prefrontal cortex. Upper panel: CommonMind Consortium (n=452). Lower panel: Accelerating Medicines Partnership in Alzheimer’s Disease (AMP-AD; n=888). Genes highlighted in red pass Bonferroni-adjusted $P < 0.05$.



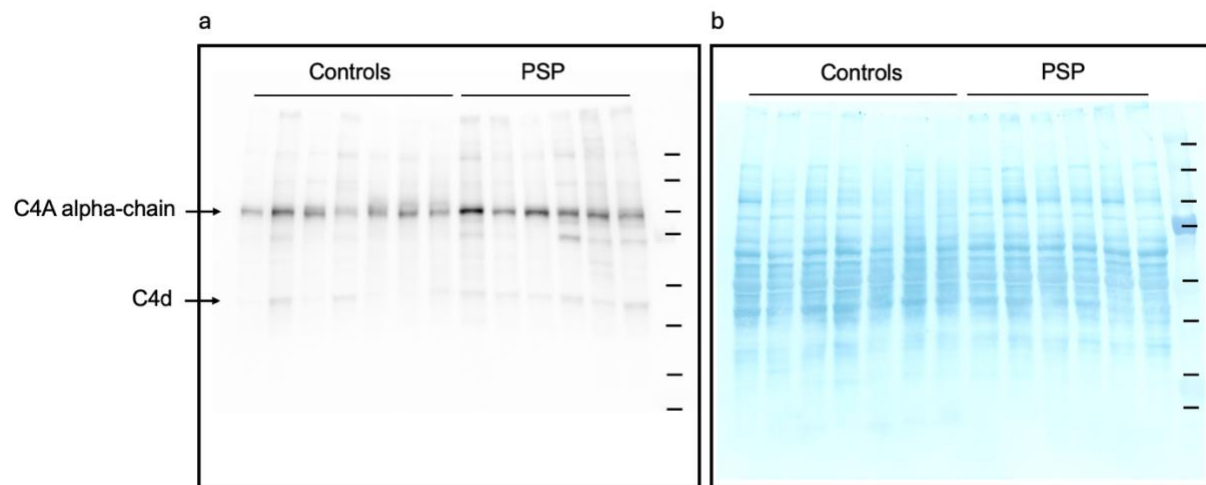
Supplementary Figure 11. Functional annotations from cell type-specific regulatory regions (enhancers and promoters) and cell type-specific DNA interactome anchors from proximity ligation-assisted ChIP-Seq (PLAC-seq) are shown in the locus containing MOBP SNPs are coloured by their LD with the lead GWAS SNP in Europeans (1000 Genomes European superpopulation).



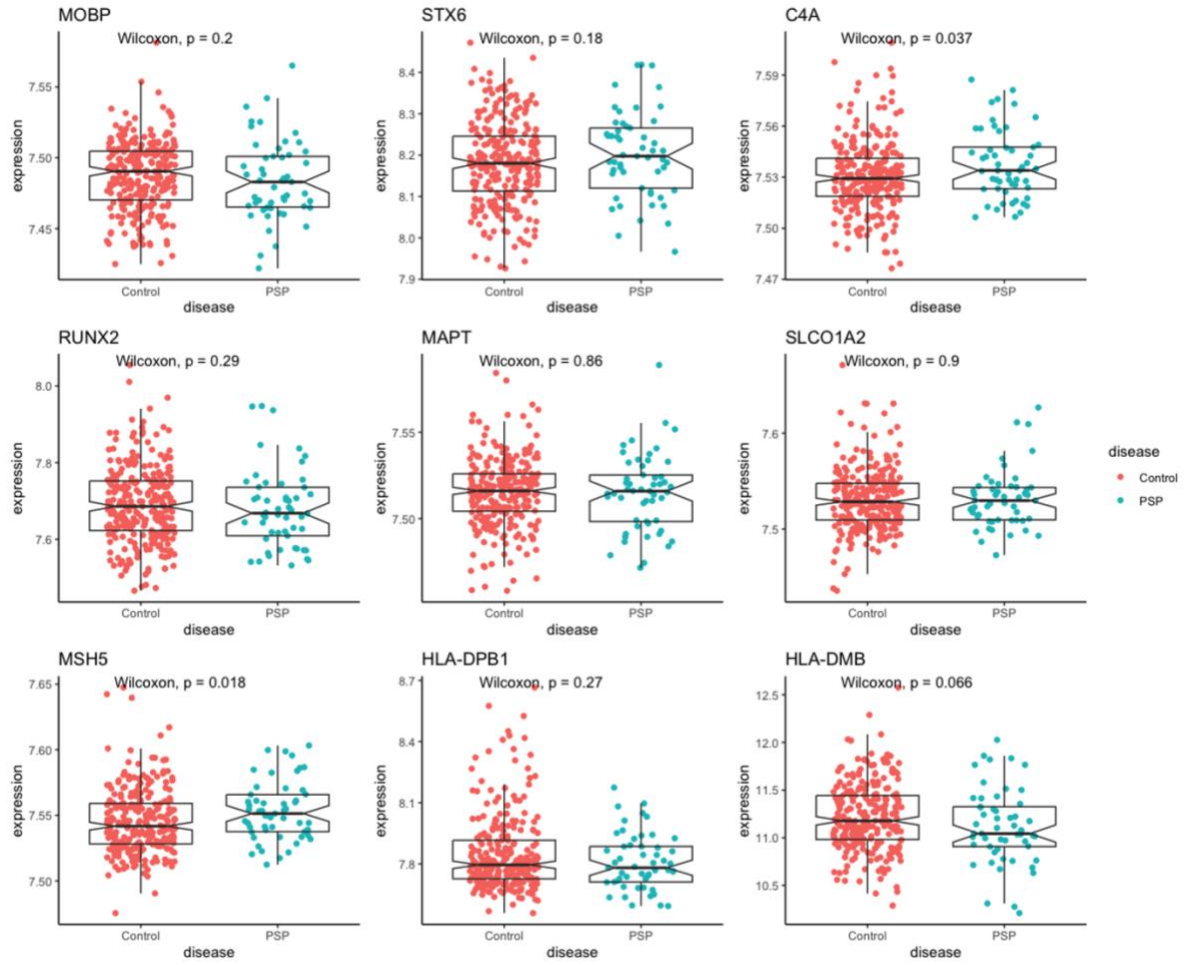
Supplementary Figure 12. Directions of effect of C4A eQTLs in GTEx brain regions using the lead SNP of the three SNP sets identified by INFERNO in the 6p21.32 locus.



Supplementary Figure 13. Additional representative staining images of C4A, AT8, and OLIG2 in frontal cortex of human postmortem progressive supranuclear palsy (PSP) and control brain tissue

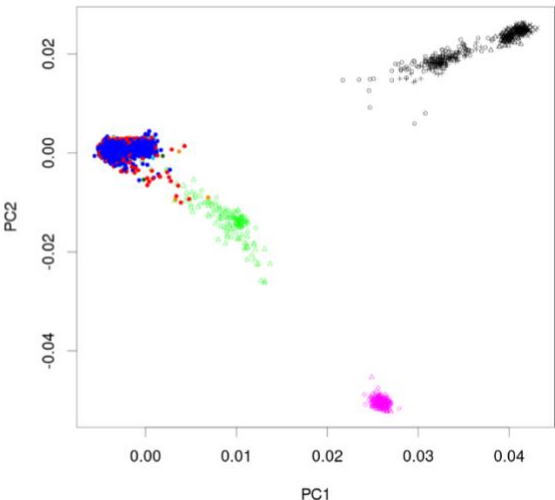
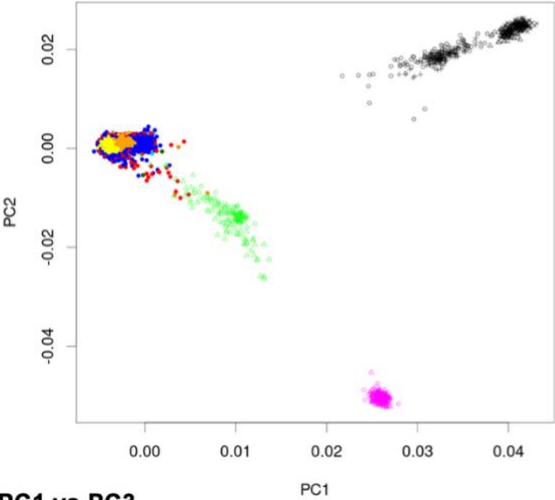


Supplementary Figure 14 Western Blot Analysis of C4A Protein Levels in Control (n=7) and PSP Samples (n=6) (a) Unedited C4A Western blot and (b) Amido Black-stained blot. Protein standards: 250, 150, 100, 75, 50, 37, 25, 20 (kDa).

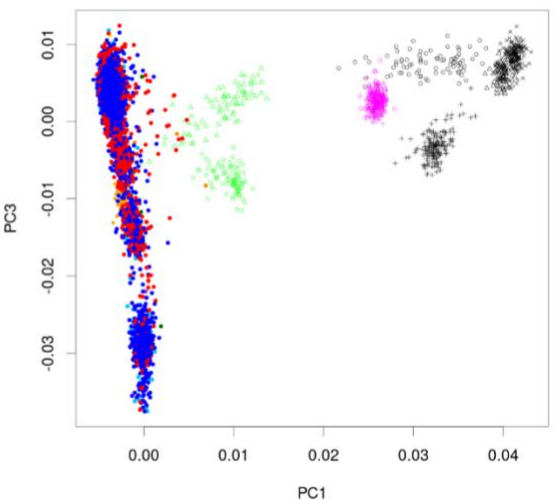
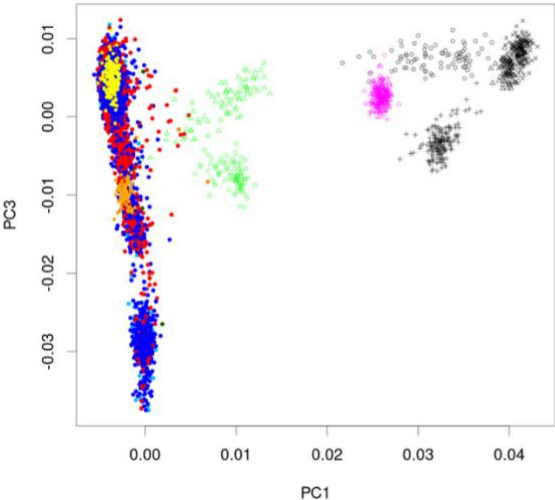


Supplementary Figure 15. Whole blood gene expression generated from microarray data on a select number of genes contained in significant loci.

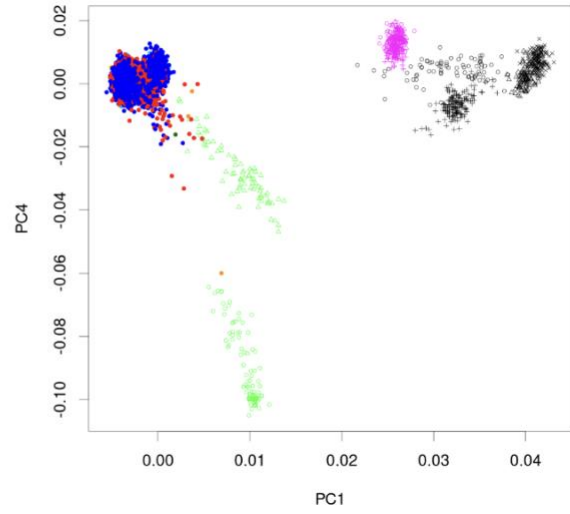
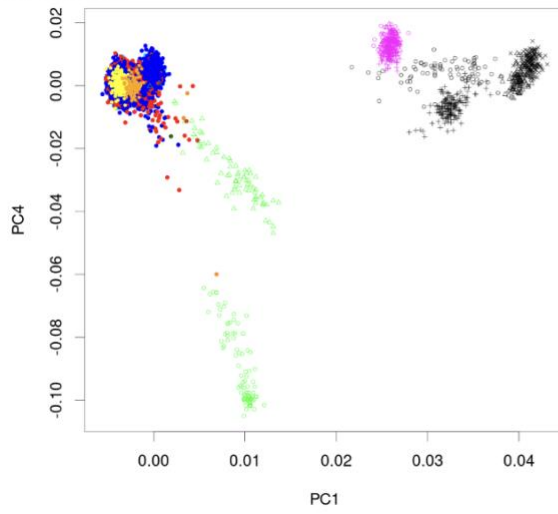
a) PC1 vs PC2



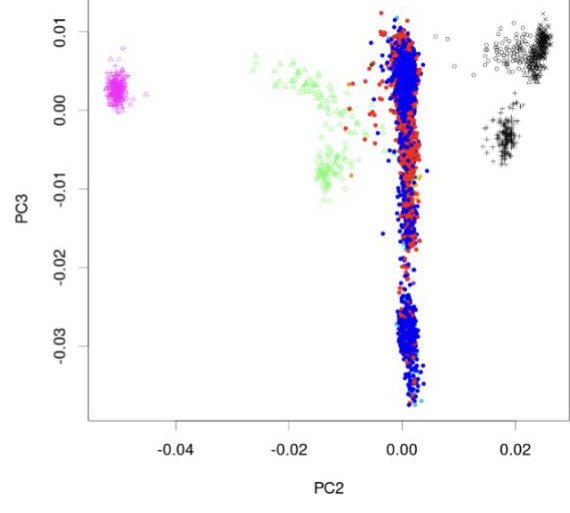
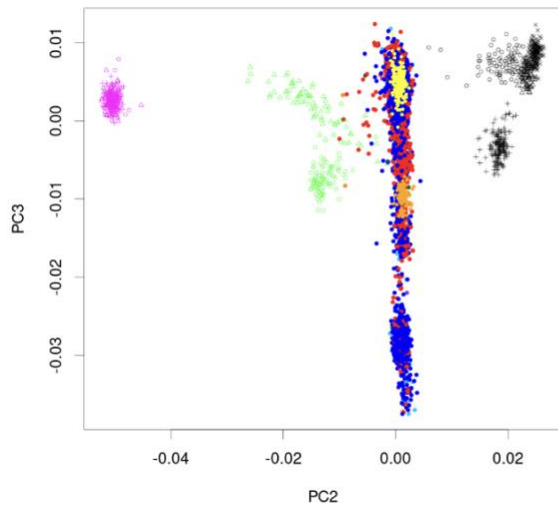
b) PC1 vs PC3



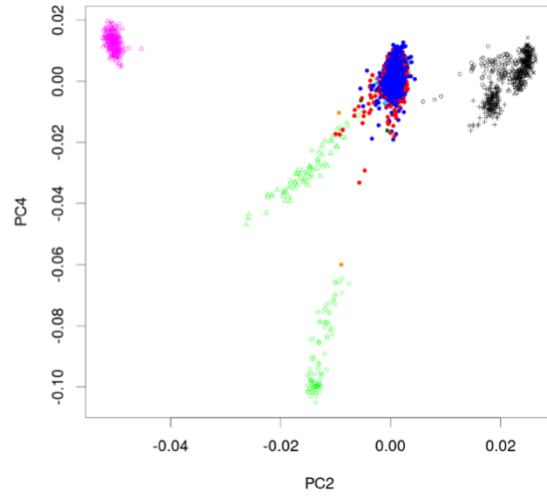
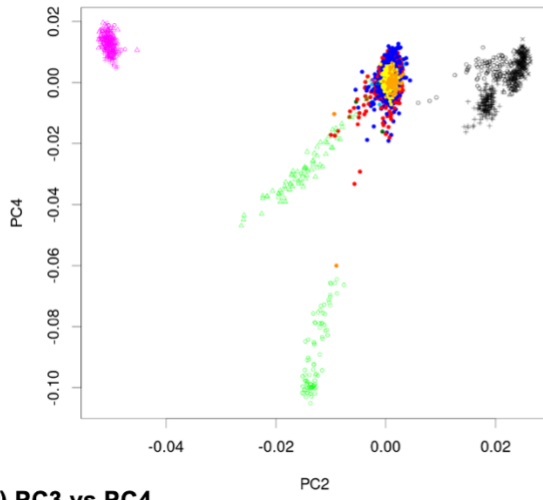
c) PC1 vs PC4



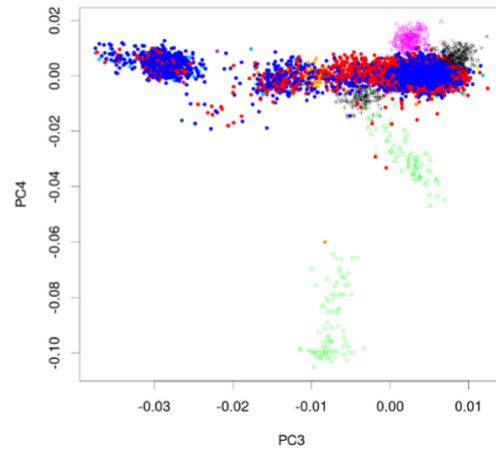
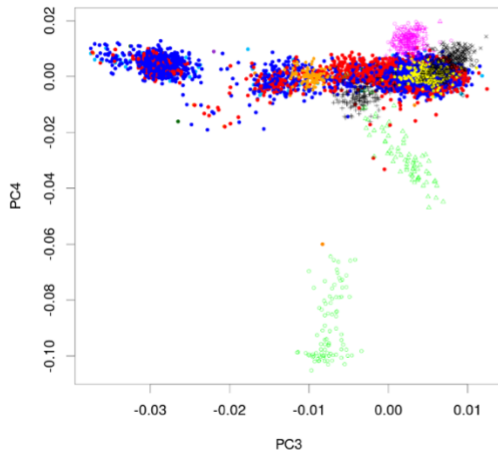
d) PC2 vs PC3



e) PC2 vs PC4

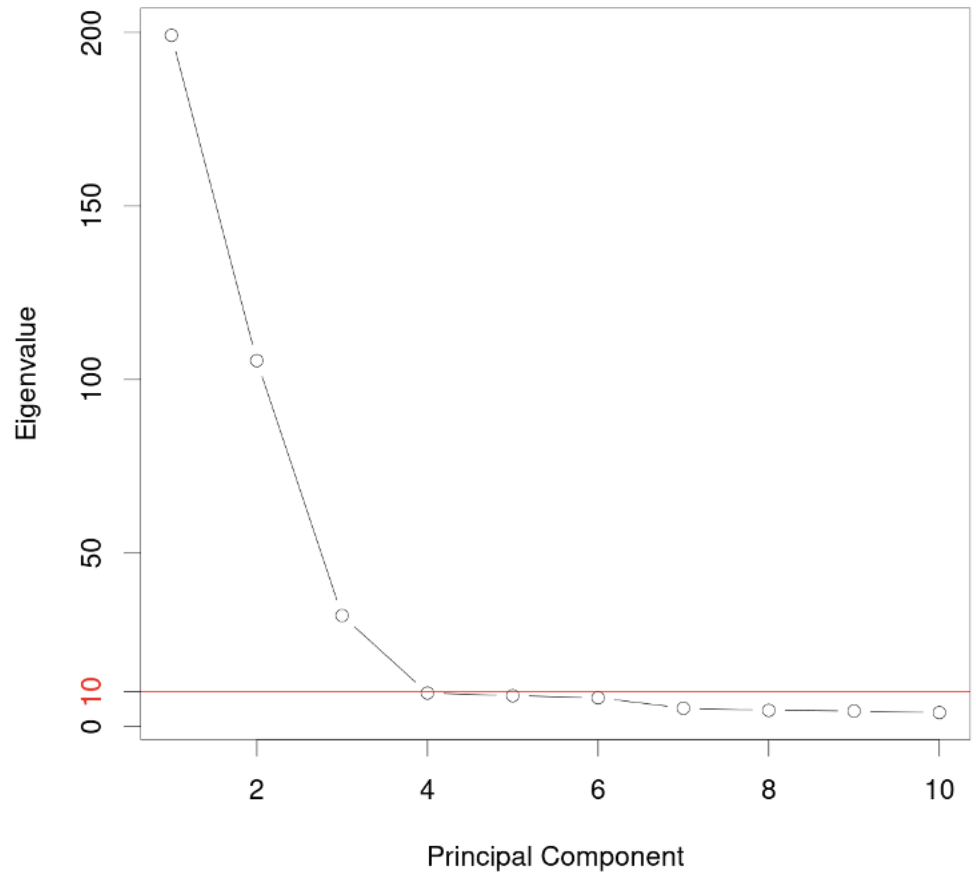


f) PC3 vs PC4



- UPENN Cases
 - UPENN Controls
 - UCLA Cases
 - UCLA controls
 - MSSM Cases
 - MSSM Controls
 - ASW - African ancestry in Southwest USA
 - CEU - Utah residents with Northern and Western European ancestry from the CEPH collection
 - CHB - Han Chinese in Beijing, China
 - △ CHD - Chinese in Metropolitan Denver, Colorado
 - GIH - Gujarati Indians in Houston, Texas
 - + JPT - Japanese in Tokyo, Japan
 - △ LWK - Luhya in Webuye, Kenya
 - △ MEX - Mexican ancestry in Los Angeles, California
 - + MKK - Maasai in Kinyawa, Kenya
 - TSI - Toscani in Italia
 - × YRI - Yoruba in Ibadan, Nigeria
-

Supplementary Figure 16. Plots of Principal Components against 1,000 Genomes (1kG) Reference Samples. Shown are plots of PC1 vs. PC2 (a), PC1 vs. PC3 (b), PC1 vs. PC4 (c), PC2 vs. PC3 (d), PC2 vs. PC4 (e), and PC3 vs. PC4 (f) for the combined dataset. All population substructure outliers have been excluded. The figure legend including shape representations and coloring are shown after the plots (g). Plots on the left depict case-control samples in the background to allow overlapping reference samples to be distinguishable while plots on the right depict case-control samples in the foreground above reference samples.



Supplementary Figure 17. Scree Plot for Principal Components Analysis (PCA). The selection threshold for principal components (PCs) to be include in covariate adjustment was a PC eigenvalue>10.

	Penn Harmonized Illumina 660 Case-Control	Penn Harmonized Illumina OEE Case-Control	Penn Harmonized Illumina OE Case-Control	Penn Harmonized Illumina GSA Case-Control	MSSM Illumina GSA Case-Control	UCLA Illumina OE Case-Control	UCLA Illumina O2.5 Case-Control
Pre-QC Total SNPs and Samples	535,373 SNPs	685,175 SNPs	713,053 SNPs	689,780 SNPs	453,831 SNPs	1,277,721 SNPs	2,345,083 SNPs
	1,928 Samples	1,766 Samples	1,581 Samples	2,333 Samples	390 Samples	524 Samples	382 Samples
Genotyping Calling QC: Drop SNPs with call rate <90% & Re-cluster	26,542 SNPs	90,876 SNPs	185,920 SNPs	20,651 SNPs	115,396 SNPs	8 SNPs	19,386 SNPs
Sample-level QC: Drop samples with call rate <98%	2 Samples	0 Samples	0 Samples	0 Samples	0 Samples	0 Samples	0 Samples
Variant-level QC: Drop SNPs with call rate <98%	49 SNPs	7 SNPs	9 SNPs	28 SNPs	6,756 SNPs	23,936 SNPs	45,658 SNPs
Variant-level QC: Drop SNPs with MAF<0.02	1,202 SNPs	325 SNPs	431 SNPs	166,333 SNPs	0 SNPs	0 SNPs	0 SNPs
Variant-level QC: Drop SNPs with HWE $P < 10^{-6}$ if MAF > 0.01	10 SNPs	77 SNPs	67 SNPs	56 SNPs	19 SNPs	74 SNPs	1,048 SNPs
Variant-level QC: Drop SNPs with case-control differential missigness $P < 10^{-6}$	564 SNPs	0 SNPs	0 SNPs	0 SNPs	0 SNPs	0 SNPs	0 SNPs
Sample-level QC: Drop sex-mismatched individuals	0 Samples	0 Samples	0 Samples	0 Samples	0 Samples	0 Samples	0 Samples
Sample-level QC: Drop duplicate or excessively related samples ($\text{Pi-Hat} < 0.4$)	1 Sample	3 Samples	0 Samples	1 Sample	0 Samples	0 Samples	92 Samples
Sample-level QC: Drop population substructure outliers	11 Samples	15 Samples	16 Samples	10 Samples	3 Samples	0 Samples	2 Samples
Post-QC Total SNPs and Samples	507,096 SNPs	593,890 SNPs	498,840 SNPs	669,045 SNPs	331,660 SNPs	1,253,703 SNPs	2,278,991 SNPs
	1,914 Samples	1,748 Samples	1,565 Samples	2,322 Samples	385 Samples	488 Samples	285 Samples

Supplementary Figure 18. Quality Control by Genotyping Platform for Each Dataset. Pre- and Post-QC SNP and sample counts are shown for each genotyping platform subset, and the number of SNPs or of samples removed at each QC step is depicted in italics.