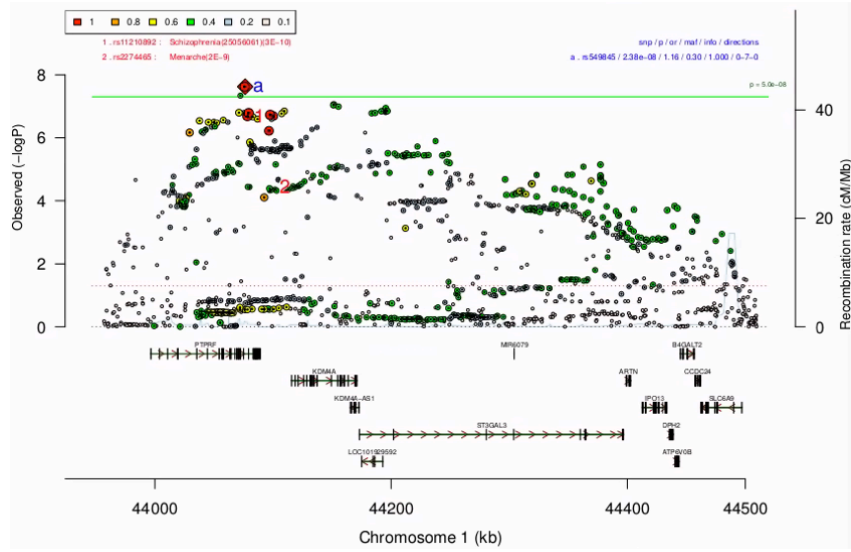


Supplementary Information

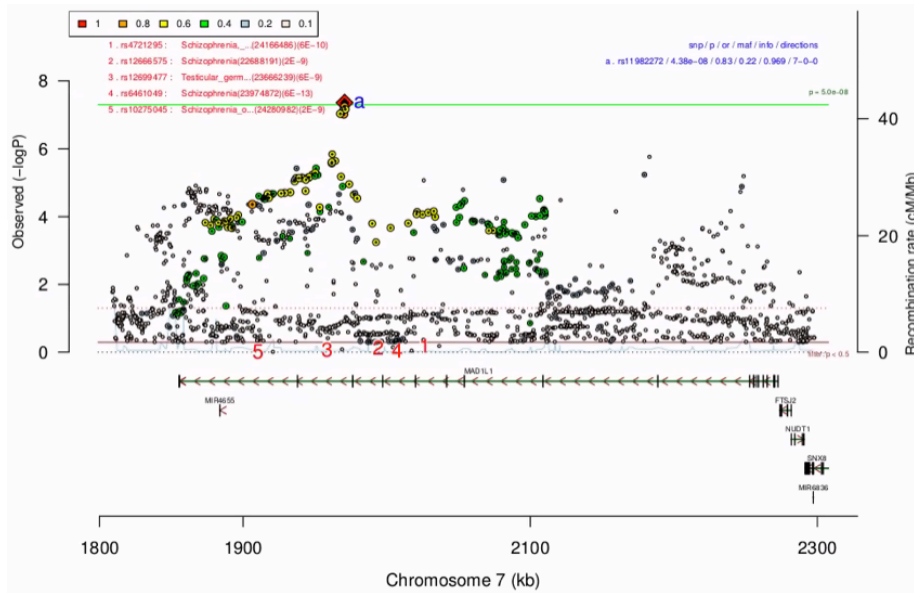
Risk variants and polygenic architecture of disruptive behavior disorders in the context of attention-deficit/hyperactivity disorder

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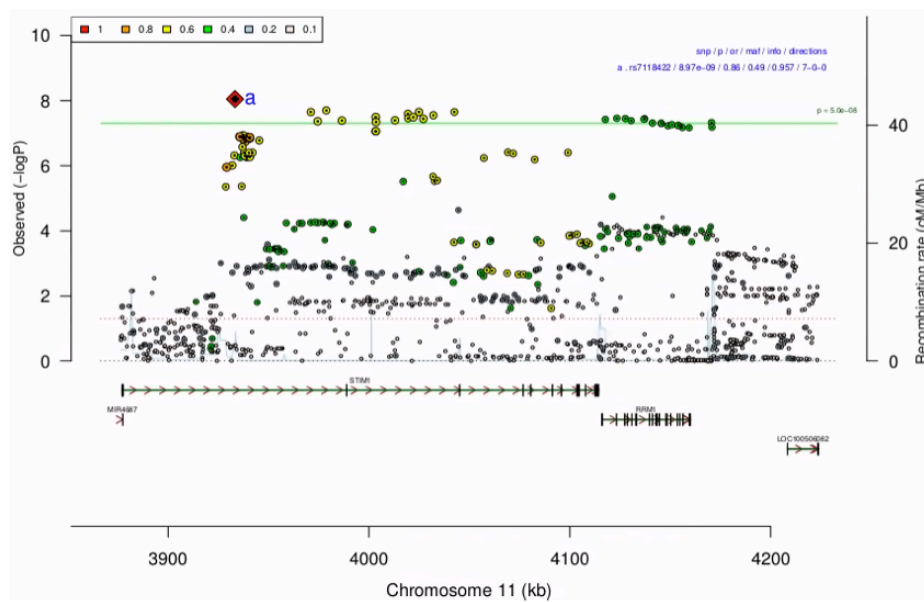
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A.



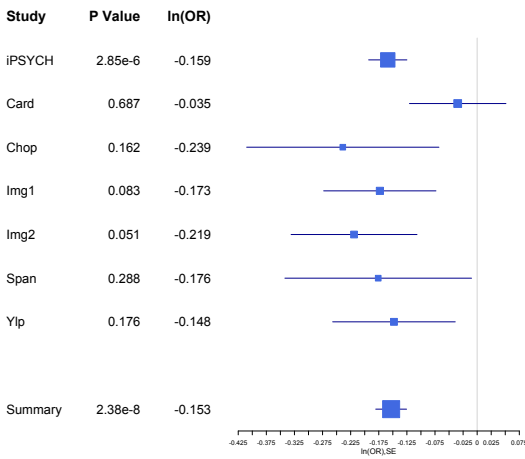
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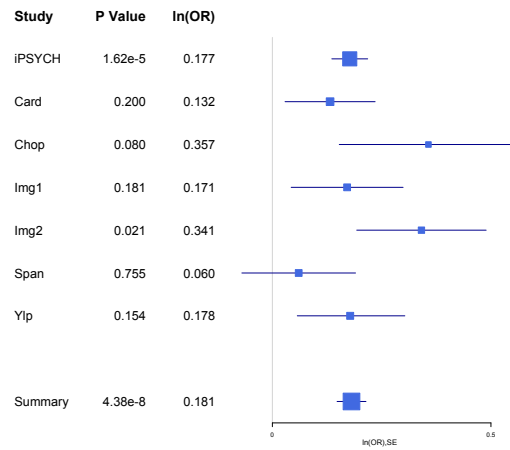
C.

Supplementary Figure 1.A-C. Regional association plots of the genome-wide significant loci

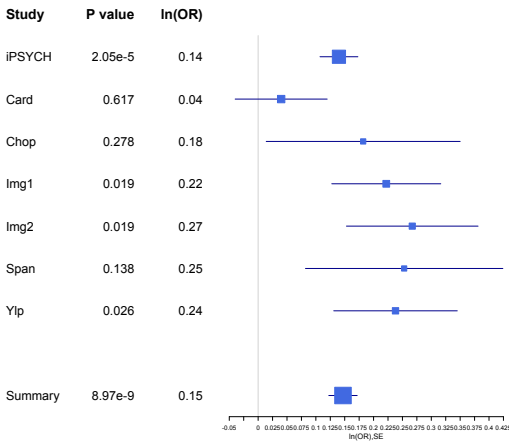
Regional association plots of the local association results from the three genome-wide significant loci identified in the GWAS meta-analysis of ADHD+DBDs (3,802 cases and 31,305 controls). The y-axis represents $-\log(P\text{-values})$ of variant association; the P-values are two-sided from meta-analysis using an inverse-variance weighted fixed effects model. The horizontal green line represents the threshold for genome-wide significance ($P = 5 \times 10^{-8}$). Location and orientation of the genes in the region is indicated, LD estimates of surrounding SNPs with the index SNP (r^2 values estimated based on 1KGP3) is indicated by colour (colour bar in upper left corner indicates r^2 values). Additionally, the local estimation of recombination rate is indicated in light blue (legend on vertical axis at right). Detailed SNP info in upper right corner (blue letters): SNP name (rsid), P-value (p), odds ratio (or), minor allele frequency(maf), imputation INFO score (info), directions in the analyzed cohorts (risk increasing - decreasing - missing). **A.** Regional association of the variants located the genome-wide significant locus on chromosome 1 **B.** Regional association of the variants located the genome-wide significant locus on chromosome 7 **C.** Regional association of the variants located the genome-wide significant locus on chromosome 11.



A.



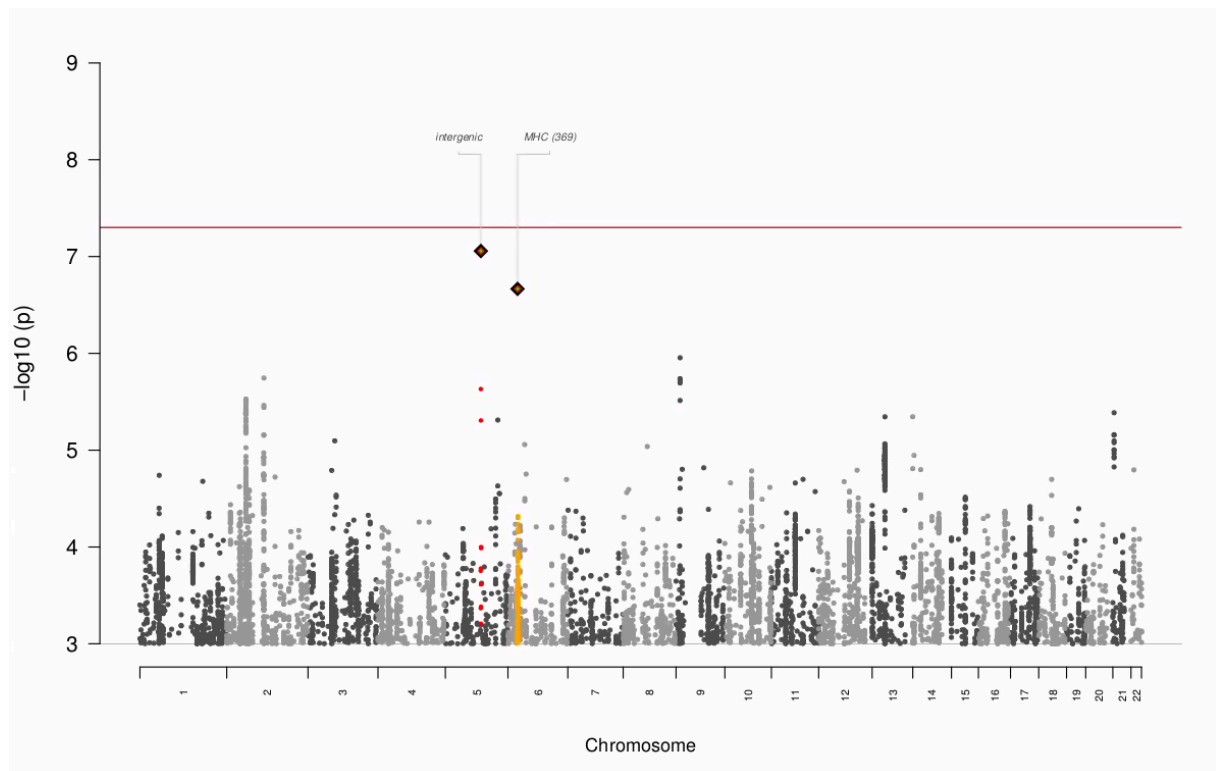
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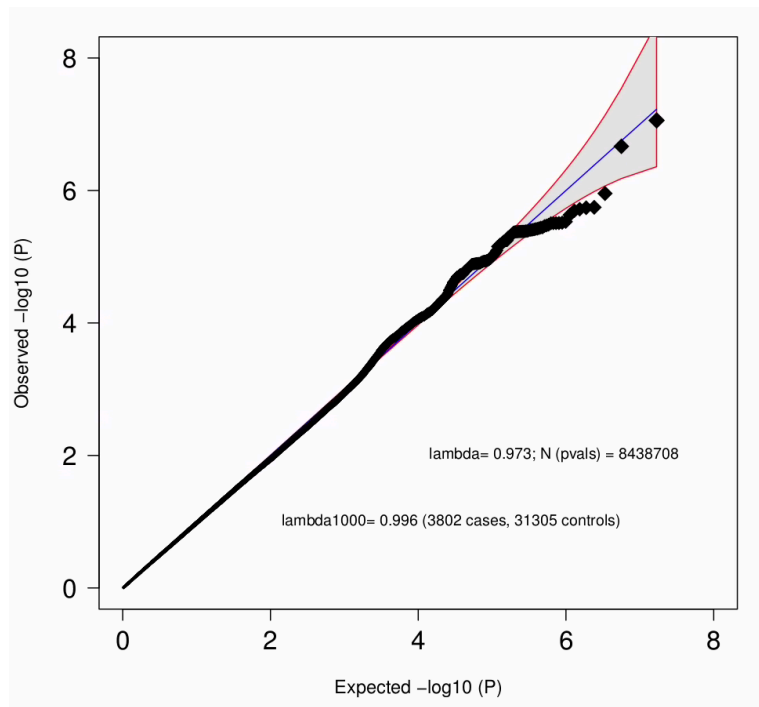
Supplementary Figure 2.A-C. Forest plots of genome-wide significant index variants

Forest plots for the index variants in the three genome-wide significant loci identified in the GWAS meta-analysis of ADHD+DBDs (3,802 cases and 31,305 controls). The plots provides a visualization of the effect size estimates, with the center representing the natural logarithm of the odds ratio (ln(OR)) in each included cohort, estimated from logistic regression and for the summary meta-analysis using an inverse-variance weighted fixed effects model. In addition, the standard error intervals for the effect size estimates represented by horizontal lines. **A.** Forest plot for the index variant rs549845 in the genome-wide significant locus on chromosome 1. **B.** Forest plot for the index variant rs11982272 in the genome-wide significant locus on chromosome 7. **C.** Forest plots for the index variant rs7118422 in the genome-wide significant locus on chromosome 11.



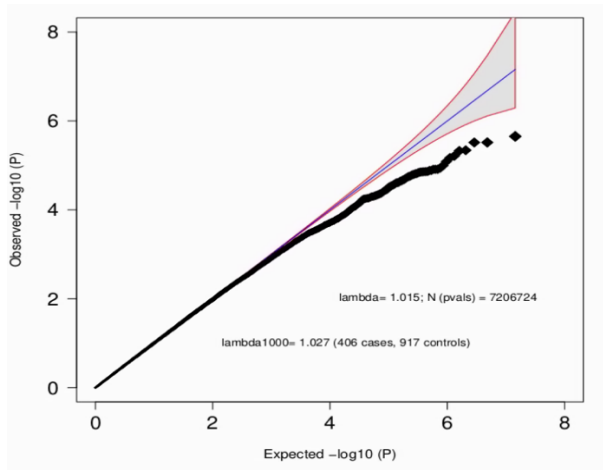
Supplementary Figure 3. Test for heterogeneity across cohorts in the meta-analysis of ADHD+DBDs

The y-axis represents $-\log(P\text{-values})$ from omnibus test of heterogeneity across cohorts tested with Cochran's Q test and quantified with the I^2 heterogeneity index. See Supplementary Table 2 for sample sizes. Red horizontal line indicates genome-wide significance threshold ($P = 5 \times 10^{-8}$).



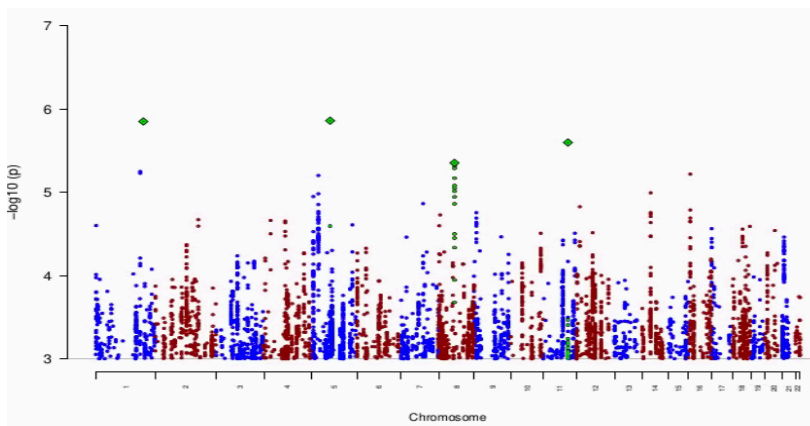
Supplementary Figure 4. Q-Q plot from test for heterogeneity between European cohorts

Quantile-quantile plot of P-values from the omnibus test of heterogeneity (I^2) between all cohorts in the GWAS meta-analysis of ADHD+DBDs. See Supplementary Table 2 for sample sizes of cohorts. Each dot represents the observed $-\log_{10}$ P-value, the blue line indicates the distribution under the null hypothesis and the shaded area indicates the 95% confidence interval.



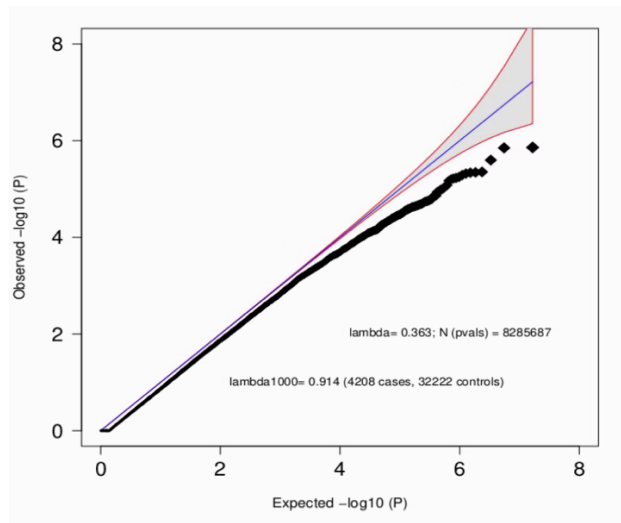
Supplementary Figure 5. Q-Q plot from GWAS of the Chinese Cohort

Quantile-quantile plot of the $-\log_{10}$ P-values from the GWAS of the Chinese cohort. Each dot represents the observed $-\log_{10}$ P-value, the blue line indicates the distribution under the null hypothesis and the shaded area indicates the 95% confidence interval.



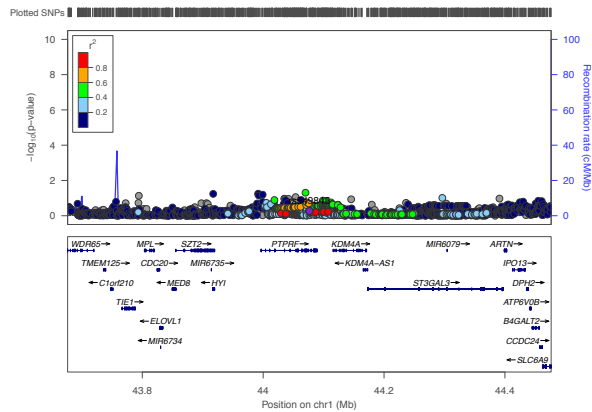
Supplementary Figure 6. Test for heterogeneity across cohorts in the cross ancestry GWAS

Manhattan plot from heterogeneity test of heterogeneity across the European iPSYCH and PGC cohorts and the Chinese cohort. The y-axis represents $-\log(P\text{-values})$ from omnibus test of heterogeneity across cohorts tested with Cochran's Q test and quantified with the I^2 heterogeneity index. See Supplementary Table 9 for sample sizes.

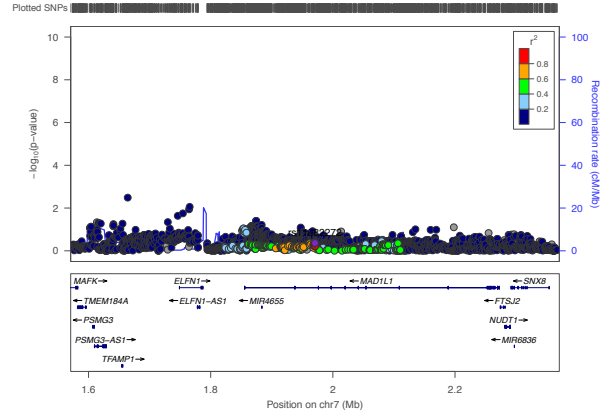


Supplementary Figure 7. Q-Q plot from test for heterogeneity between European and Chinese cohorts

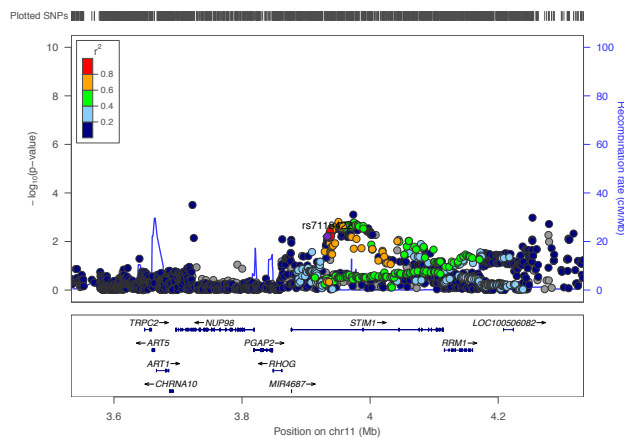
Quantile-quantile plot of P-values from the omnibus test of heterogeneity (I squared statistic (I²)) between cohorts. See Supplementary Table 9 for sample sizes of cohorts. Each dot represents the observed -log₁₀ P-value, the blue line indicates the distribution under the null hypothesis and the shaded area indicates the 95% confidence band.



A.



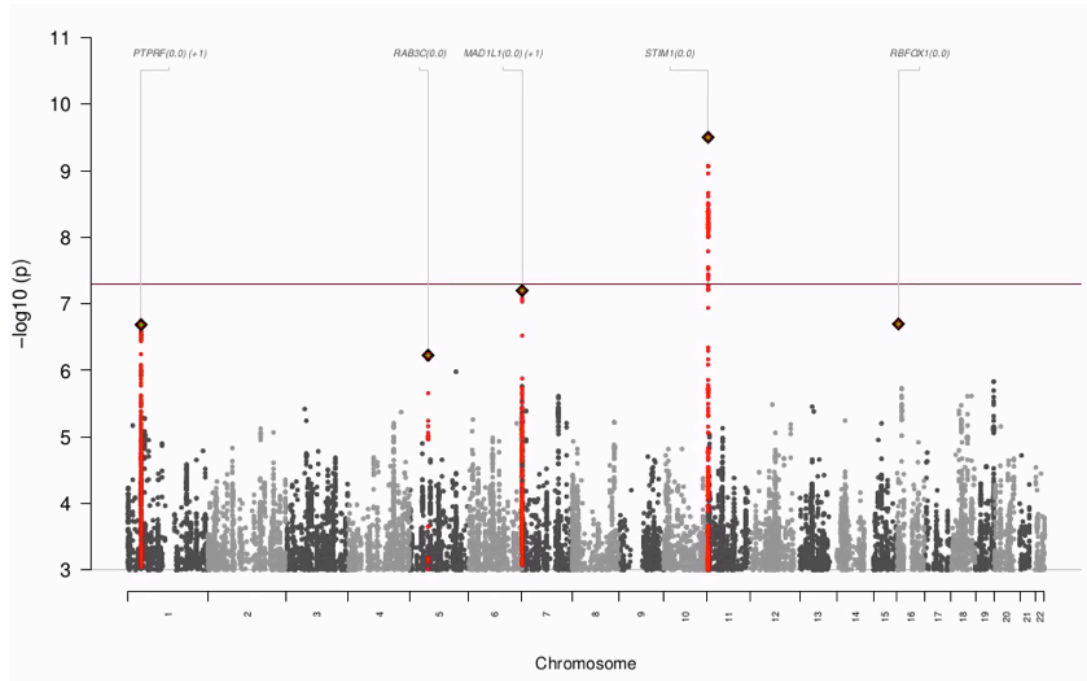
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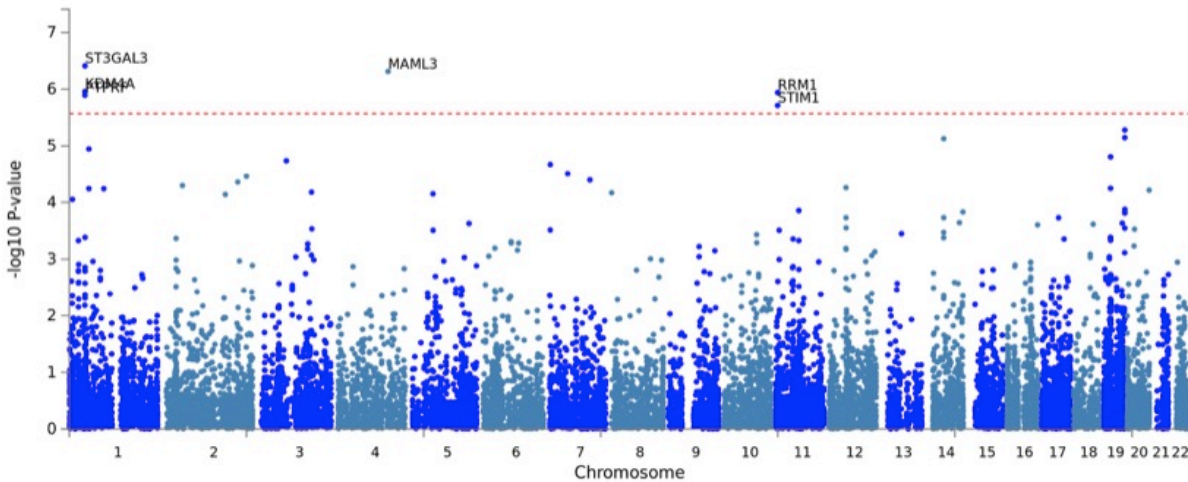
Supplementary Figure 8.A-C. Regional association in the Chinese cohort

Regional association plots of the local association results for the Chinese cohort in the three genome-wide significant loci identified in the GWAS meta-analysis of ADHD+DBDs. The y-axis represents $-\log(P\text{-values})$ of variant association; the P-values are two-sided from logistic regression. Location and orientation of the genes in the region is indicated, LD estimates of surrounding SNPs with the index SNP (r^2 values estimated based on 1KGP3) is indicated by color (color bar in upper left corner indicates r^2 values). Additionally, the local estimation of recombination rate is indicated in light blue (legend on vertical axis at right). **A.** Local association surrounding the index variant rs549845 on chromosome 1 **B.** Local association surrounding the index variant rs11982272 on chromosome 7 **C.** Local association surrounding the index variant rs7118422 on chromosome 11.



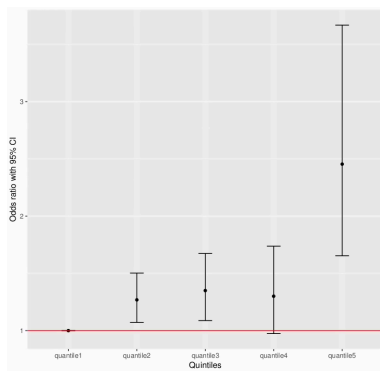
Supplementary Figure 9. Manhattan plot of GWAS meta-analysis of European and Chinese cohorts

Results from cross-ancestry GWAS meta-analysis of iPSYCH and PGC cohorts with European and Chinese ancestries. Two-sided P-values from meta-analysis using an inverse-variance weighted fixed effects model, and a sample size of 4,208 cases and 32,222 controls. The red horizontal line represents the threshold for genome-wide significant association ($P = 5 \times 10^{-8}$).

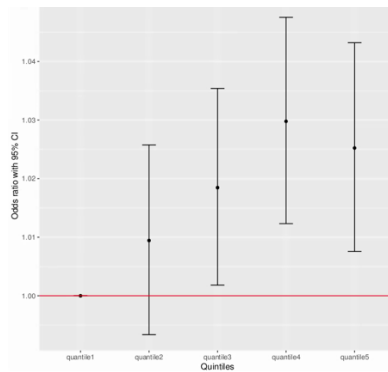


Supplementary Figure 10. Manhattan plot from gene-based MAGMA association analysis

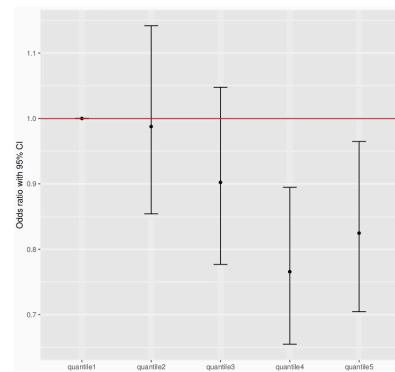
The y-axis represents $-\log(P\text{-values})$ of gene-based association with ADHD; P-values are two-sided from MAGMA analysis based on summary statistics from the GWAS meta-analysis of 3,802 cases and 31,305 controls. The horizontal red dotted line represents the threshold for exome-wide significance ($P = 2.7 \times 10^{-6}$).



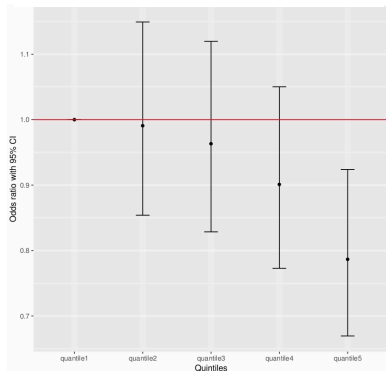
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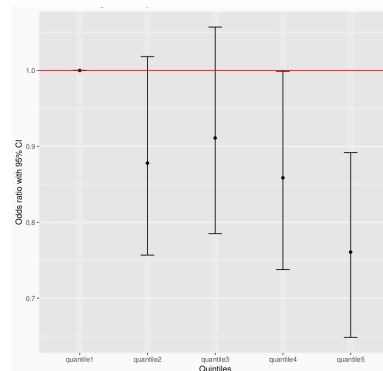
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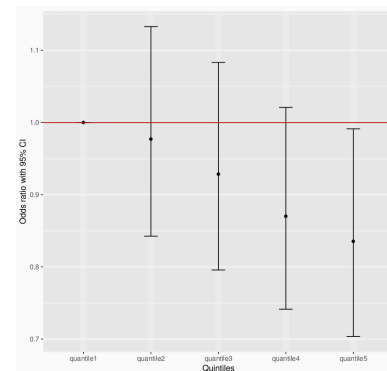
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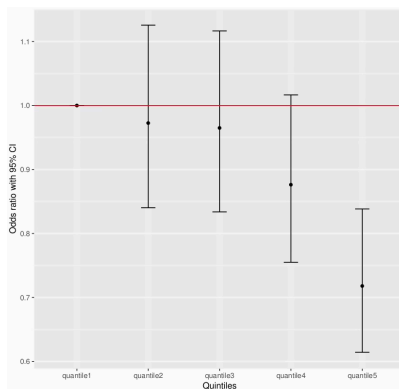
D.



E.



F.



G.

Supplementary Figure 11.A-G. Quintile plots of odds ratio for ADHD+DBDs by PRS

Odds Ratio (OR) by PGS within each quintile for ADHD+DBDs compared to ADHDwoDBDs. The plots represent the seven phenotypes (detailed results on Supplementary Table 8) demonstrating significant association of PGS with ADHD+DBDs after correcting for multiple testing. The center represents the odds ratio and error bars indicate 95% confidence limits **A.** PGS for ADHD **B.** PGS for aggression in children **C.** PGS for number of educational years **D.** PGS for college completion. **E.** PGS for human intelligence **F.** PGS for verbal numerical reasoning. **G.** PGS for age at first birth.

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