**Supp. Figure 1.** Conceptual framework of colocalization analysis. Approaches solely taking individual SNP association parameters into account may lead to false results in two ways (panels 1 and 2). A SNP associated with a trait A may be falsely associated with the general factor of Trait A and B because a causal SNP of Trait B is in Linkage disequilibrium (LD) with the SNP of Trait A (Panel 1). The general factor might miss some SNPs that are in fact associated with both traits. For example, a shared causal SNP strongly associated with Trait A but less strongly associated with Trait B may erroneously not be linked to the general factor (Panel 2).
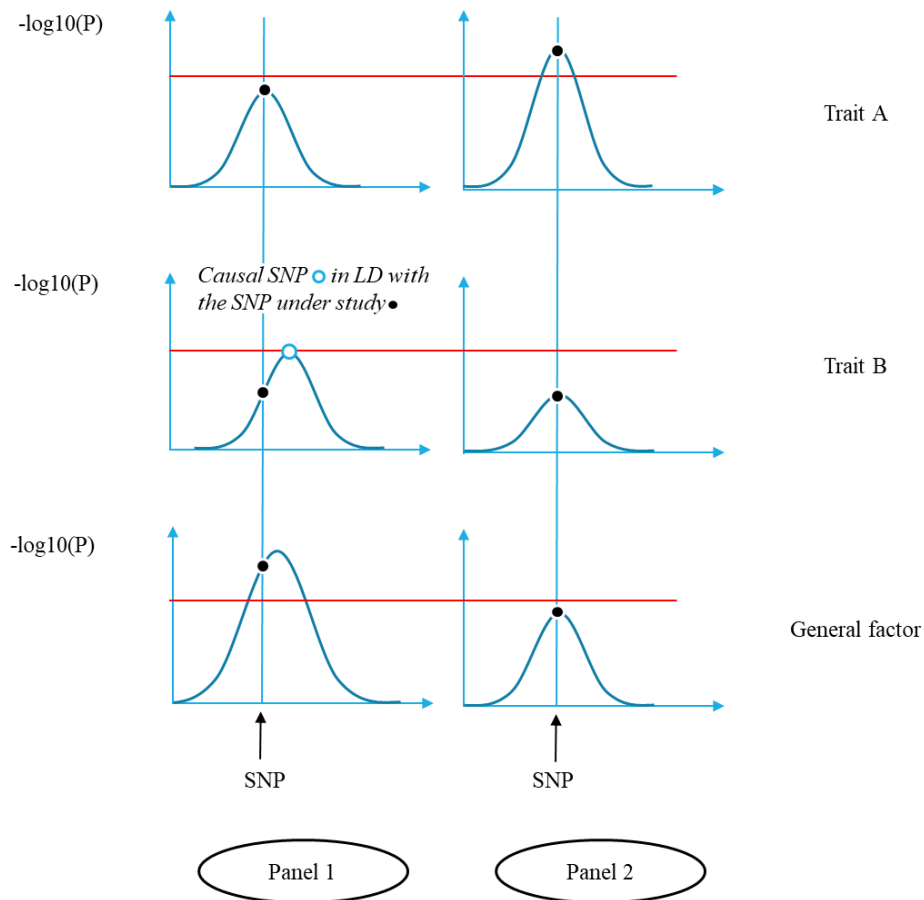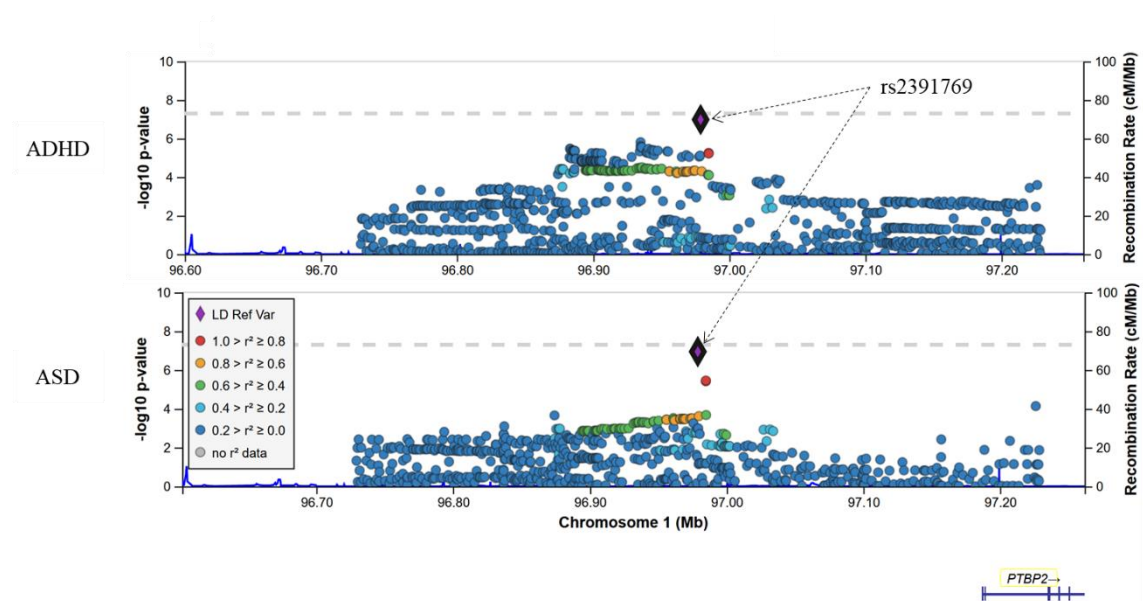
Supp. Figure 2. Region around rs6047310 (250kb around the SNP) in ADHD (upper figure) and ASD (lower figure) GWAS (chr = 20). *The genes INSM1 and PAX1 are not shown because they were mapped to* rs6047310 *using Chromatin interaction mapping which can involve long-range interactions.*
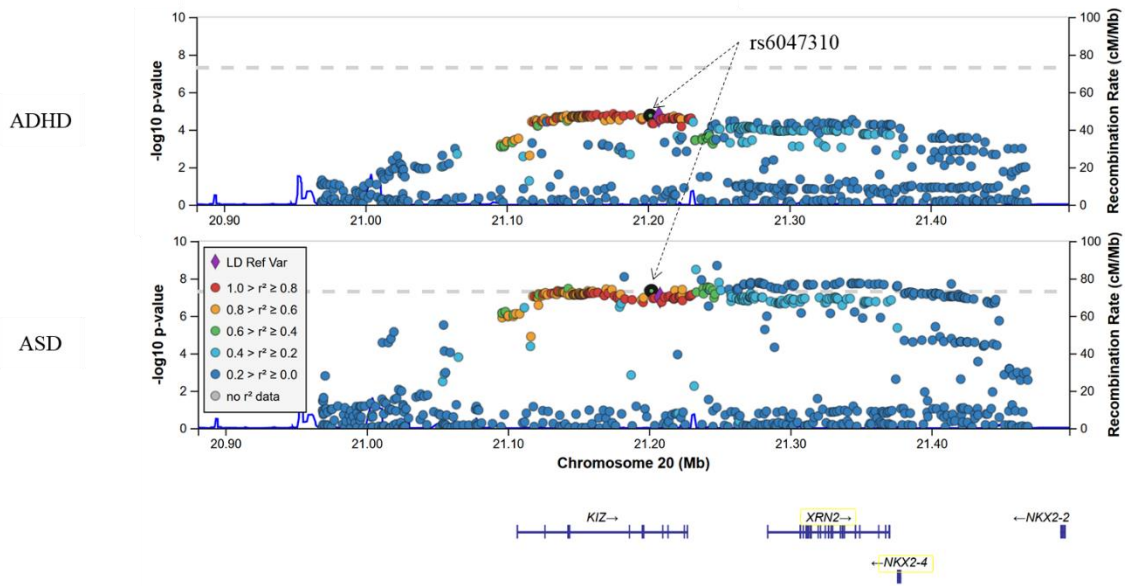
Supp. Figure 3. Region around rs6584649 and rs11591402 (250kb around the SNP) in ADHD (upper figure) and ASD (lower figure) GWAS (chr = 10).
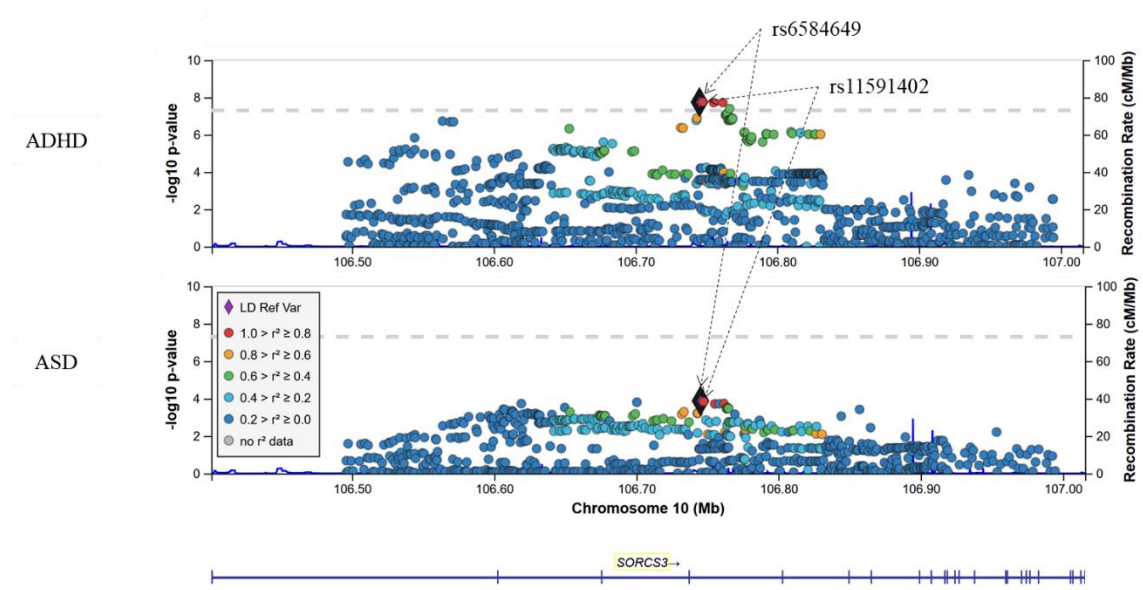
Supp. Figure 4. Region around rs2391769 (250kb around the SNP) in ADHD (upper figure) and ASD (lower figure) GWAS (chr = 1). *The gene DPYD is not shown because it was mapped to rs2391769 using Chromatin interaction mapping which can involve long-range interactions.*

Supp. Figure 5. Region around rs1222063 (250kb around the SNP) in ADHD (upper figure) and ASD (lower figure) GWAS (chr = 1).

Supp. Figure 6. Region around rs4916723 (250kb around the SNP) in ADHD (upper figure) and ASD (lower figure) GWAS (chr = 5).

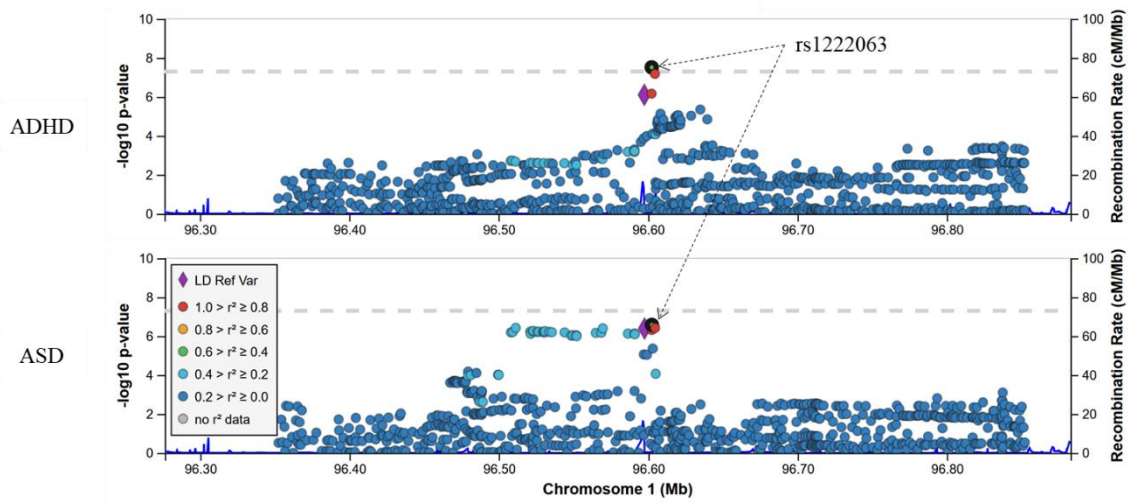**Supp. Figure 7.** Region around rs325506 (250kb around the SNP) in ADHD (upper figure) and ASD (lower figure) GWAS (chr = 5).

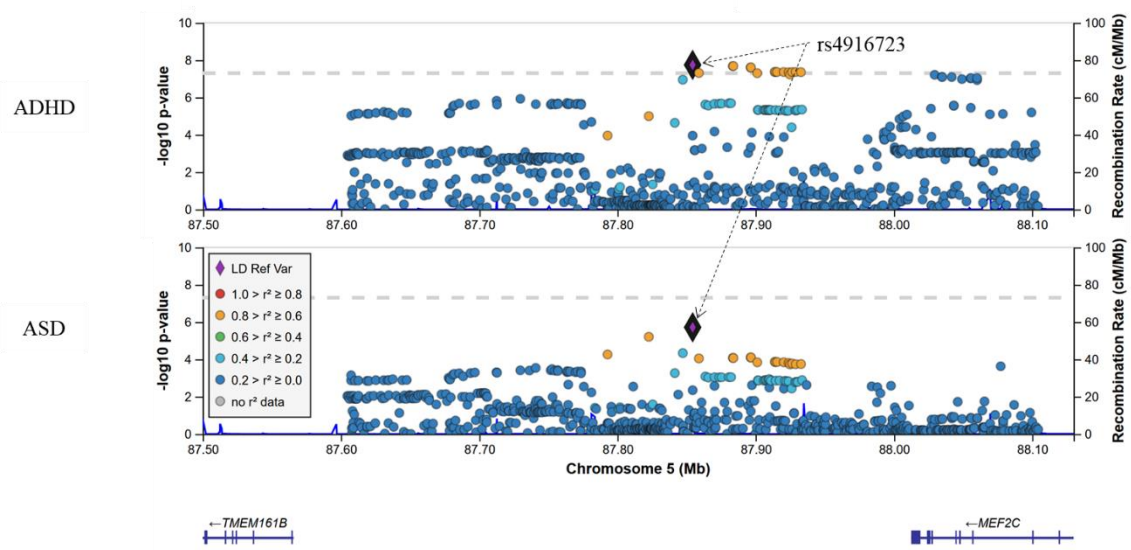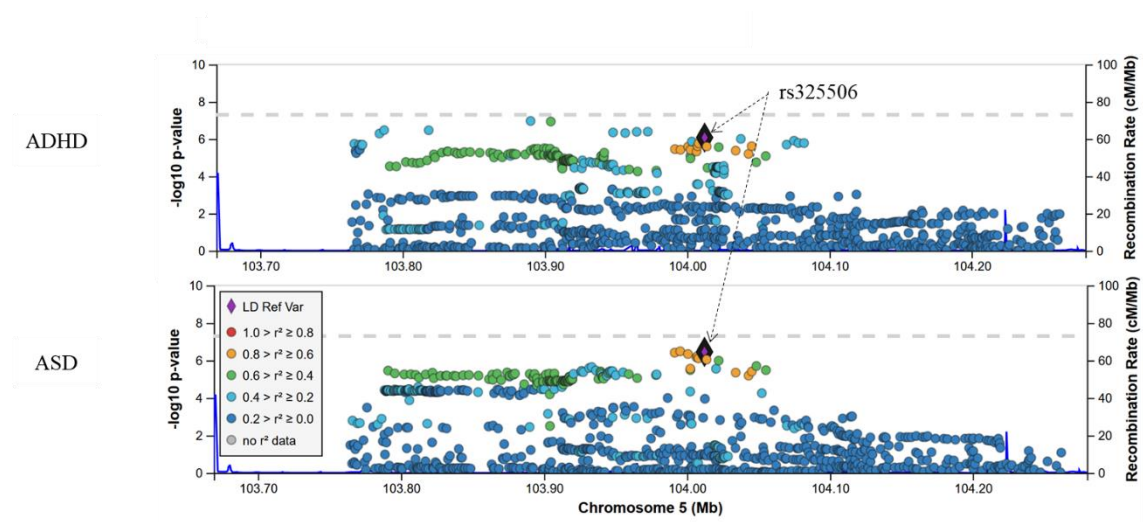**Supp. Figure 8.** Region around rs7318041 (250kb around the SNP) in ADHD (upper figure) and ASD (lower figure) GWAS (chr = 13).
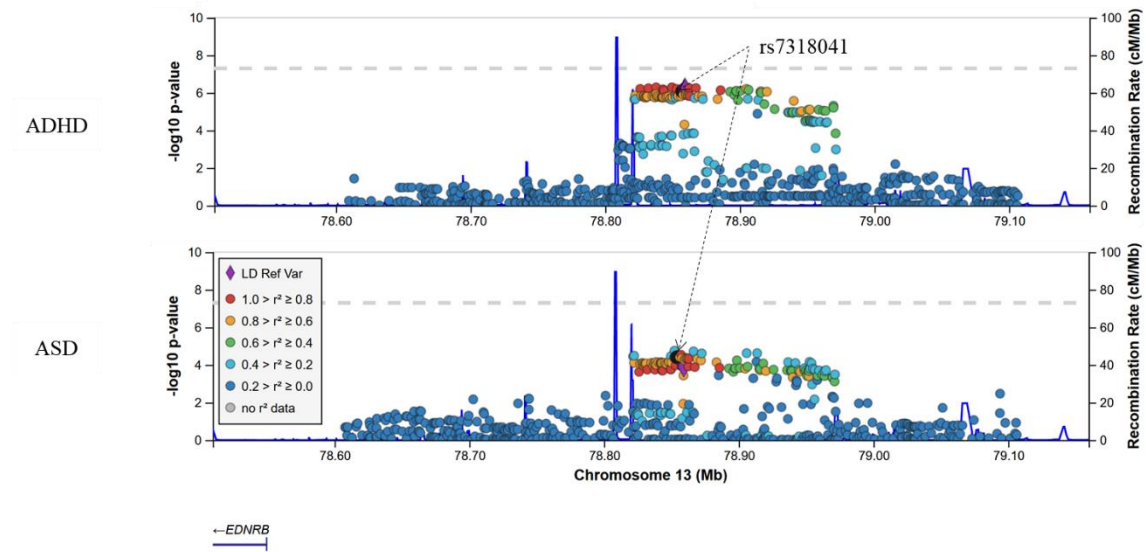
Supp. Figure 9. Tissue specific expression patterns (average expression per label (log2 transformed)) using GTEx v6 RNA-seq data (FUMA GENE2FUNC) of the SNPs (A) shared by ASD and ADHD and those that are specific to (B) ASD and (C) ADHD. Gray bars correspond to the significance after FDR correction.
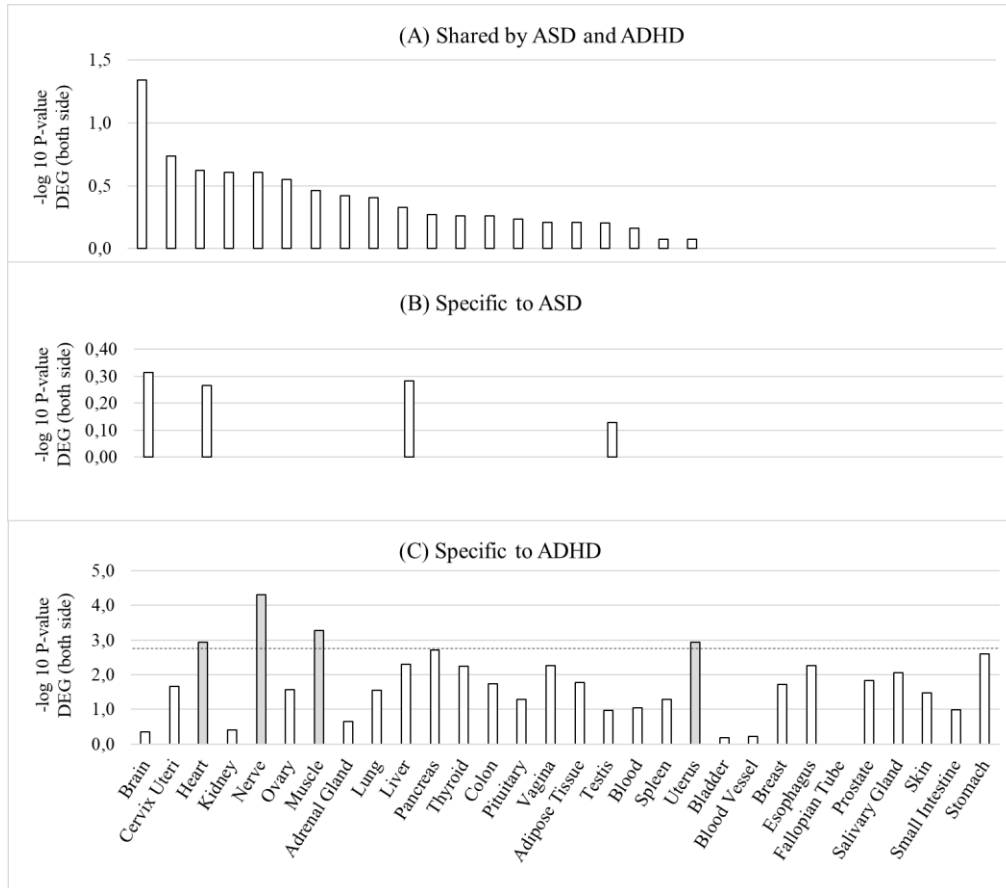
Supp. Figure 10. Temporal expression in the brain (average expression per label; log2 transformed p-values for the enrichment of Differentially Expressed Gene (DEG); based on 11 general developmental stages of brain samples from the BrainSpan data; FUMA GENE2FUNC) of genes that are (A) shared by ASD and ADHD and those that are specific to (B) ASD and (C) ADHD.

(A) Genes mapped to SNPs shared by ASD and ADHD

(B) Genes mapped to SNPs specific to ASD

(C) Genes mapped to SNPs specific to ADHD
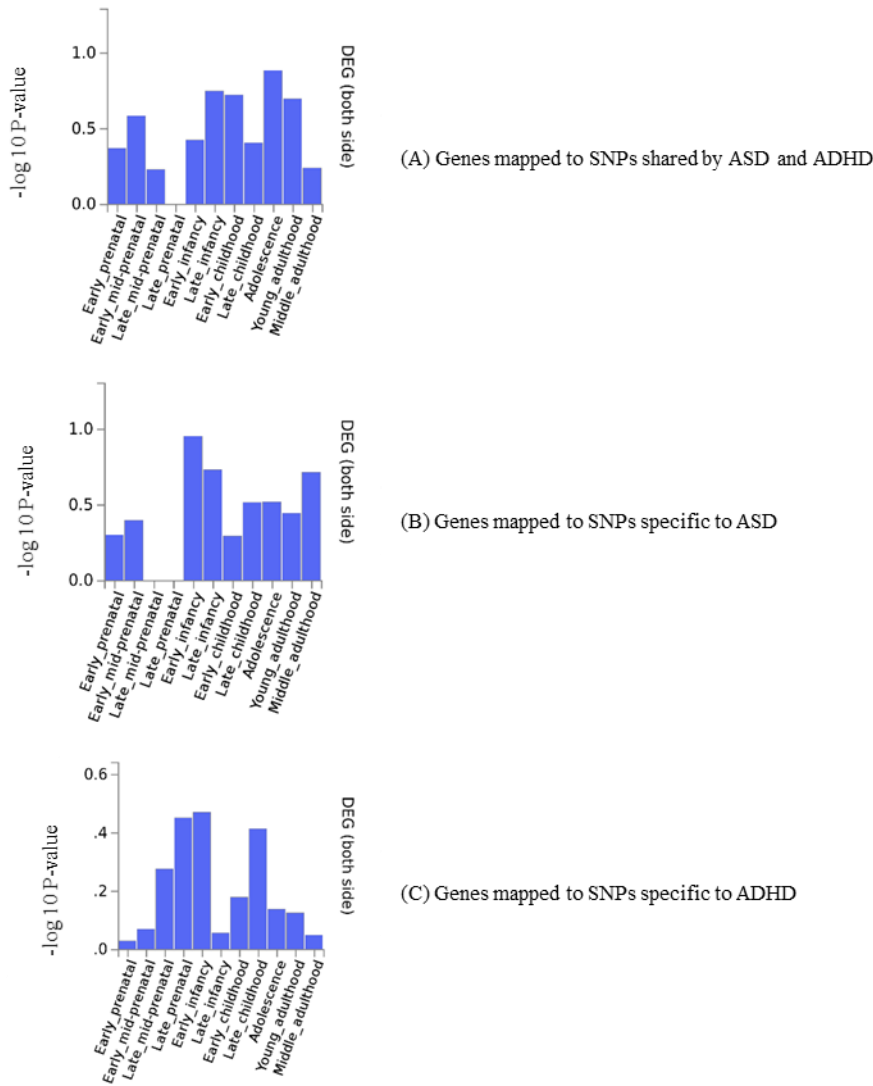
Supp. Figure 11. Leave-one-out sensitivity analysis of the MR analysis (IVW = Inverse Variance Weighted method). (A) The relationship between ASD as the exposure (*p*-value at 1e-6) and ADHD as the outcome. (B) The causal relationship between ADHD as the exposure (*p*-value at 1e-6) and ASD as the outcome.

(A) MR-IVW: ASD on ADHD
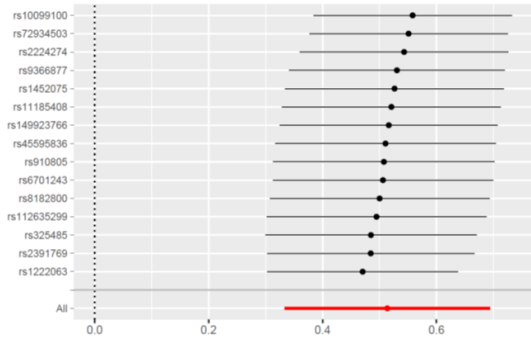
(B) MR-IVW: ADHD on ASD
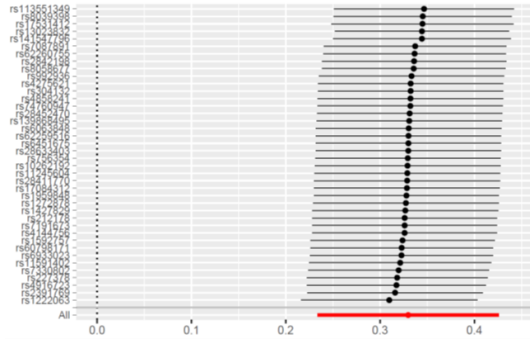
Supp. Figure 12. Funnel plot of MR causal estimates against their precision (inverse of standard error) when examining (A) the relationship between ASD as the exposure (*p*-value at 1e-6) and ADHD as the outcome and (B) the relationship between ADHD as the exposure (*p*-value at 1e-6) and ASD as the outcome. Each data point corresponds to an individual genetic variant. The x axis corresponds to the coefficient of the genetic variant-outcome association divided by the coefficient of the genetic variant-exposure association.

(A) MR-IVW: ASD on ADHD
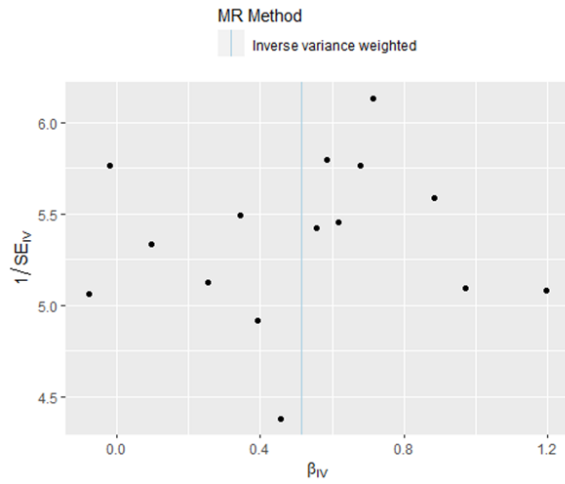
(B) MR-IVW: ADHD on ASD
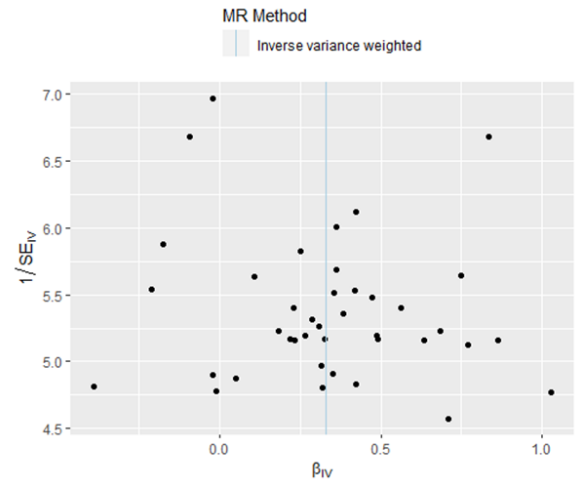
Supp. Figure 13. Log-likelihood from the contamination mixture method as a function of the causal estimate for (A) ASD on ADHD and (B) ADHD on ASD.

(A) MR-IVW: ASD on ADHD

(B) MR-IVW: ADHD on ASD
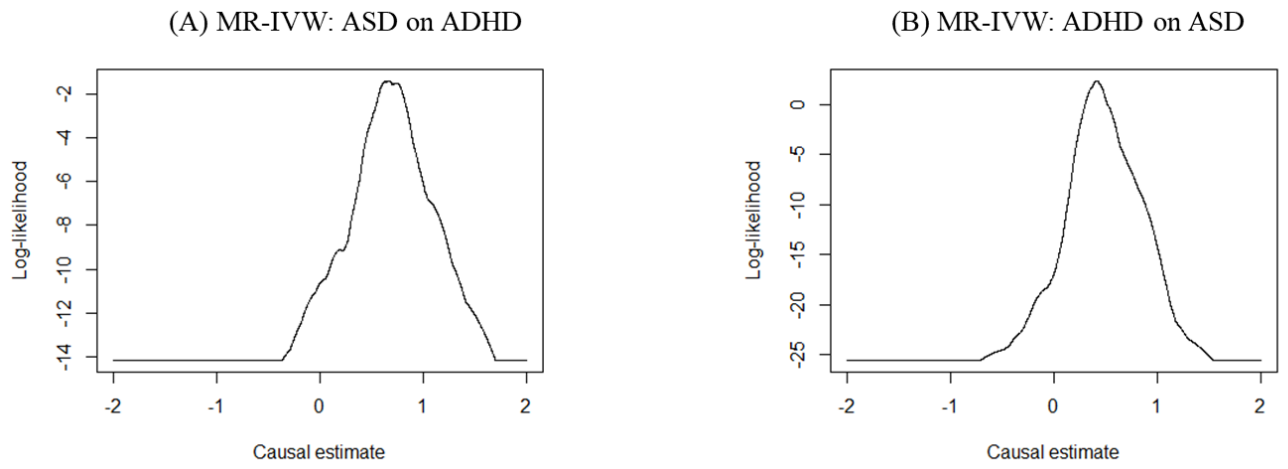
Supp. Figure 14. Bidirectional MR using multiple MR methods after excluding SNPs shared by ASD and ADHD. The left scatter plot depicts the relationship between the genetic instruments indexing ASD (p-value at 1e-6) and ADHD as the outcome (left graphs). The right scatter plot depicts the relationship between genetic instruments indexing ADHD (p-value at 1e-6) and ASD as the outcome. Upper graphs: of SNP regression coefficients quantifying the level of association using different methods.
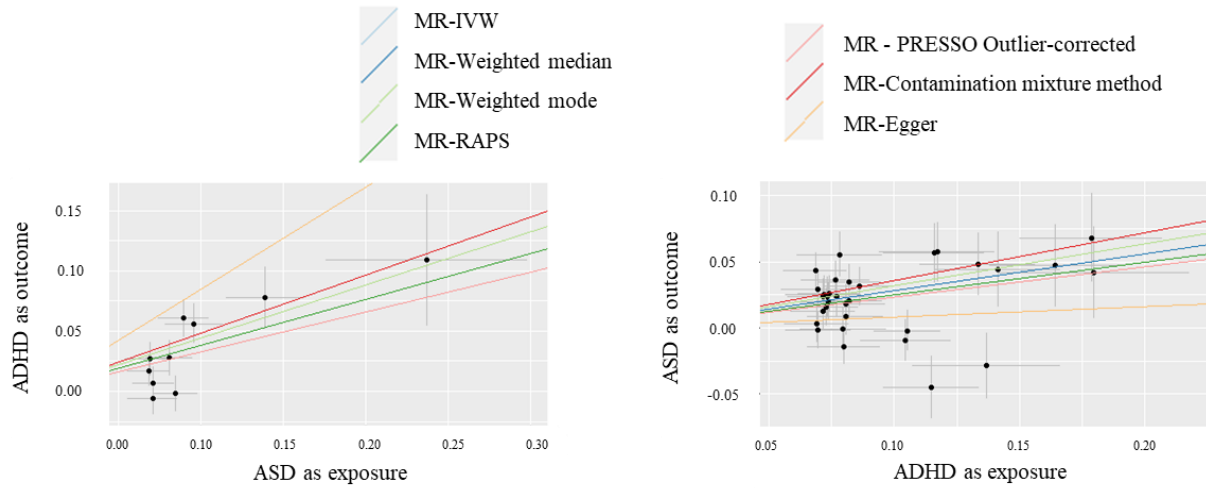
Supp. Table 1. FUMA analysis of SNPs shared by ASD and ADHD.

ensg	symbol	CHR	Positional mapping posMapMaxCADD	EQTL mapping eqtlMapSNPs	Chromatin interaction mapping	SNP	Previsously reported by Genomic SEM studies	Previsously reported by GWAS
ENSG00000117569	PTBP2	1			Adult_Cortex	rs2391769		Grove et al.
ENSG00000188641	DPYD	1			Fetal_Cortex	rs2391769	Lee et al.	
ENSG00000109323	MANBA	4		37		rs227378		Grove et al.
ENSG00000156395	SORCS3	10	13.2		Adult_Cortex	rs6584649	Lee et al.	Demontis et al.
ENSG00000173404	INSM1	20			Adult_Cortex	rs6047310		
ENSG00000088930	XRN2	20	13.49		Adult_Cortex:Fetal_Cortex	rs6047310	Schork et al.	Grove et al.
ENSG00000125816	NKX2-4	20			Fetal_Cortex	rs6047310		Grove et al.
ENSG00000125813	PAX1	20			Fetal_Cortex	rs6047310		

Supp. Table 2. FUMA analysis of SNPs specific to ASD.

ensg	symbol	CHR	Positional mapping posMapMaxCADD	EQTL mapping eqtlMapSNPs	Chromatin interaction mapping	IndSigSNPs	Reported by Grove et al.
ENSG00000088930	XRN2	20	12.87		Fetal_Cortex	rs910805	X
ENSG00000125816	NKX2-4	20			Fetal_Cortex	rs910805	X

Supp. Table 3. FUMA analysis of SNPs specific to ADHD.

ensg	symbol	CHR	Positional mapping posMapMaxCADD	EQTL mapping eqtlMapSNPs	Chromatin interaction mapping	IndSigSNPs	Reported by Demontis at al.
ENSG00000066056	ARTN	1		114	Adult_Cortex:Fetal_Cortex	rs2527776;rs549845;rs17531412;rs113551349;rs17531412:rs2527776:rs549845	X
ENSG00000066185	B4GALT2	1	16			rs2527776	X
ENSG00000066322	C1orf210	1			Adult_Cortex	rs2842198:rs549845:rs17531412:rs2527776	
ENSG00000117394	C1orf228	1			Fetal_Cortex	rs2842198:rs17531412:rs2527776	
ENSG00000117395	CCDC23	1			Fetal_Cortex	rs2842198	
ENSG00000117399	CCDC24	1	16		Adult_Cortex:Fetal_Cortex	rs2527776;rs17531412	X
ENSG00000117400	CCDC30	1			Adult_Cortex:Fetal_Cortex	rs2842198	
ENSG00000117407	CDC20	1	22.4		Adult_Cortex:Fetal_Cortex	rs2842198	
ENSG00000117408	DHODH	16		8		rs212178	
ENSG00000117410	DUSP6	12	23.2			rs1427829	X
ENSG00000117411	EBNA1BP2	1			Adult_Cortex	rs2842198	X
ENSG00000126091	ELOVL1	1	22.4		Adult_Cortex:Fetal_Cortex	rs2842198;rs2842198:rs549845:rs17531412	X
ENSG00000126106	ERMAP	1			Fetal_Cortex	rs2842198	
ENSG00000127125	FOXJ3	1			Adult_Cortex:Fetal_Cortex	rs2842198:rs17531412	
ENSG00000128573	FOXP2	7	18.18		Adult_Cortex:Fetal_Cortex	rs10262192	X
ENSG00000261701	HPR	16		18		rs212178	X
ENSG00000132768	HYI	1	18.87			rs2842198	X
ENSG00000135272	IPO13	1	13.6		Adult_Cortex:Fetal_Cortex	rs2527776;rs17531412	
ENSG00000137872	KDM4A	1	17.97			rs17531412	X
ENSG00000139318	MDFIC	7			Fetal_Cortex	rs10262192	
ENSG00000142949	MED8	1	18.26	57	Adult_Cortex:Fetal_Cortex	rs2842198;rs2842198:rs549845:rs17531412:rs2527776	X
ENSG00000156687	MPL	1	22.4			rs2842198	
ENSG00000159214	PCDH7	4	18.34			rs28411770	X
ENSG00000159479	PPCS	1			Adult_Cortex:Fetal_Cortex	rs2842198	
ENSG00000164010	PTPRF	1	18.13		Adult_Cortex:Fetal_Cortex	rs17531412;rs549845;rs2842198:rs549845:rs17531412:rs2527776	X
ENSG00000164011	SEMA6D	15	17.68			rs8039398	X
ENSG00000169851	SLC2A1	1			Adult_Cortex	rs2842198:rs17531412	
ENSG00000177868	SLC6A9	1	16			rs2527776	X
ENSG00000178922	ST3GAL3	1	17.97	53	Adult_Cortex:Fetal_Cortex	rs17531412;rs113551349;rs2527776;rs2842198:rs17531412:rs549845:rs2527776	X
ENSG00000179178	SZT2	1	18.87		Adult_Cortex:Fetal_Cortex	rs2842198;rs2842198:rs549845:rs17531412:rs2527776	X
ENSG00000186409	TIE1	1		61	Adult_Cortex	rs2842198;rs2842198:rs17531412	
ENSG00000196517	TMEM125	1			Adult_Cortex	rs2842198	
ENSG00000198198	TMEM53	1			Fetal_Cortex	rs2842198:rs17531412:rs2527776	
ENSG00000198815	WDR65	1			Adult_Cortex	rs2842198	X
ENSG00000243710	ZMYND12	1			Adult_Cortex:Fetal_Cortex	rs2842198	X
ENSG00000253313	ZNF691	1			Adult_Cortex	rs2842198	

Supp. Table 4. Bidirectional Mendelian randomization (MR). Causal relationship between ASD as exposure (*p*-value at 1e-6) and ADHD as outcome (left). Causal relationship between ADHD as exposure (*p*-value at 1e-6) and ASD as outcome (right).

	ASD on ADHD			ADHD on ASD		
	n(SNPs)=15			n(SNPs)=40		
	β	SE	*p*-value	β	SE	*p*-value
MR-IVW	0.51	0.09	2.34e-08	0.33	0.05	1.54e-11
MR-Weighted median	0.46	0.09	1.09e-07	0.31	0.05	1.09e-10
MR-Weighted mode	0.56	0.19	1.09e-02	0.33	0.11	5.23e-03
MR-RAPS	0.56	0.08	1.12e-11	0.34	0.05	4.90e-11
MR-PRESSO Outlier-corrected	0.51	0.08	3.85e-05	0.34	0.05	1.46e-08
MR-Contamination mixture method	0.66	0.09	1.77e-05	0.41	0.05	5.90e-10
MR-Egger intercept	-0.02	0.03	4.52e-01	0.03	0.02	1.74e-01
MR-Egger	0.76	0.34	2.50e-02	0.04	0.22	8.47e-01

MR: Mendelian randomization. SNPs: Single-Nucleotide Polymorphisms. ASD: Autism Spectrum Disorder. ADHD: Attention Deficit Hyperactivity Disorder.
MR-IVW: Mendelian Randomization Inverse Weighted Variance; MR-RAPS: Mendelian Randomization Robust Adjusted Profile Score; MR-PRESSO: Pleiotropy RESidual Sum and Outlier.

Supp. Table 5. Bidirectional MR after excluding SNPs shared by ASD and ADHD. Causal relationship between ASD as exposure (*p*-value at 1e-6) and ADHD as outcome (left). Causal relationship between ADHD as exposure (*p*-value at 1e-6) and ASD as outcome (right).

	ASD on ADHD			ADHD on ASD		
	n(SNPs)=10			n(SNPs)=32		
	β	SE	*p*-value	β	SE	*p*-value
MR-IVW	0.33	0.08	9.16e-05	0.23	0.04	1.51e-06
MR-Weighted median	0.33	0.10	4.38e-04	0.28	0.05	1.99e-06
MR-Weighted mode	0.44	0.20	5.19e-02	0.32	0.12	9.69e-03
MR-RAPS	0.38	0.09	8.78e-06	0.25	0.05	8.00e-07
MR-PRESSO Outlier-corrected	0.33	0.08	3.55e-03	0.23	0.04	4.30e-05
MR-Contamination mixture method	0.48	0.08	7.05e-04	0.36	0.04	5.21e-08
MR-Egger intercept	-0.05	0.03	8.60e-02	0.01	0.02	4.64e-01
MR-Egger	0.85	0.31	6.00e-03	0.08	0.18	6.57e-01

MR: Mendelian randomization. SNPs: Single-Nucleotide Polymorphisms. ASD: Autism Spectrum Disorder. ADHD: Attention Deficit Hyperactivity Disorder.
MR-IVW: Mendelian Randomization Inverse Weighted Variance; MR-RAPS: Mendelian Randomization Robust Adjusted Profile Score; MR-PRESSO: Pleiotropy RESidual Sum and Outlier.

For more information regarding SNPs included in our functional analyses, please refer to **Supplementary Data 1 to 4**.

Supp. Data 1. Data on SNPs shared by ASD and ADHD reported in GWAScatalog.

Supp. Data 2. Data on SNPs specific to ASD reported in GWAScatalog.

Supp. Data 3. Data on SNPs specific to ADHD reported in GWAScatalog.

Supp. Data 4. Data on SNPs that both (*i*) colocalized between ASD and ADHD and (*ii*) were associated with the general factor at $p<5e\text{-}8$ (i.e., Functional genomic analyses of SNPs shared by ASD and ADHD).