

**Table S1. Subject demographics**

Union of subjects across xQTL types, <i>N</i> = 494	Mean or percentage	Standard deviation or [count]
Age at death (years)	88.43	6.63
Age at enrollment (years)	81.39	7.09
Years of education	16.47	3.47
Male	37.90%	[187]
Pathological AD	58.30%	[288]
Clinical AD	38.30%	[189]

Intersection of subjects across xQTL types, <i>N</i> = 411	Mean or percentage	Standard deviation or [count]
Age at death (years)	88.83	6.55
Age at enrollment (years)	81.66	6.94
Years of education	16.58	3.41
Male	36.50%	[150]
Pathological AD	58.90%	[242]
Clinical AD	37.20%	[153]

**Table S2. Provenance of omic datasets**

<b>Data type</b>	<b>Initial report of genome-wide data</b>	<b>Theme of original manuscript</b>	<b>Prior QTL analysis</b>
Genotypes	De Jager <i>et al Neurobiol Aging</i> 2012	GWAS of cognitive decline	none
DNA methylation	De Jager <i>et al Nat Neurosci</i> 2014	Methylome-wide association study for amyloid plaques	none
RNA sequence	Lim <i>et al. Nat Comm</i> 2017	Assessment of circadian and seasonal rhythms in brain RNAseq data	none
H3K9Ac profiles	Lim <i>et al. Nat Comm</i> 2017	Assessment of circadian and seasonal rhythms in brain RNAseq and epigenomic data	none

**Table S3. Replication based on  $\pi_1$** 

$\pi_1$  estimated as the proportion of reported eQTLs and mQTLs in previous studies that appear significant in our estimated xQTL associations.  
 mQTL and haQTL associations were also converted to eQTL associations to examine their replication rates on reported eQTLs in previous studies.

eQTL studies		Braineac											CommonMind	DGN	ImmVar	
xQTL type	window	aveALL	CRBL	FCTX	HIPP	MEDU	OCTX	PUTH	SNIG	TCTX	THAL	WHMT	DLPFC	Blood	CD4	Monocyte
eQTL	1MB	0.5986	0.5376	0.5585	0.5479	0.7056	0.7432	0.6799	0.4291	0.5697	0.5617	0.5834	0.9114	0.6347	0.6679	0.6053
eQTL	100KB	0.7123	0.7519	0.8821	0.7494	0.8566	0.8202	0.7658	0.7061	0.7476	0.8158	0.7418	0.9224	0.6660	0.7623	0.6739
mQTL	5KB	0.4030	0.3784	0.4764	0.3390	0.3715	0.5567	0.4666	0.3074	0.4075	0.3462	0.4252	0.4439	0.3113	0.3693	0.4384
mQTL	100KB	0.2096	0.2436	0.2251	0.2412	0.2471	0.2521	0.2826	0.3449	0.2035	0.2471	0.2385	0.2133	0.2064	0.2089	0.2333
haQTL	1MB	0.1607	0.1798	0.1911	0.2394	0.3498	0.2251	0.2579	0.1215	0.1231	0.0744	0.2347	0.1927	0.1248	0.1728	0.2240
haQTL	100KB	0.3175	0.3789	0.3813	0.4920	0.5743	0.5247	0.4403	0.3744	0.3571	0.2200	0.4664	0.3408	0.2768	0.3747	0.4571

mQTL studies		Hannon
xQTL type	window	Brain
mQTL	5KB	0.8720
mQTL	100KB	0.8710

**Table S4. Sharing of xQTL SNPs based on  $\pi_1$** 

$\pi_1$  estimated as the proportion of xQTL associations for a “test” (column) phenotype with the same xQTL SNPs as a “discovery” (row) phenotype that appear significant. Only the closest molecular feature to each xQTL SNP was used in the  $\pi_1$  estimation.

Window xQTL	1Mb window	5Kb eQTL	1Mb mQTL	1Mb haQTL	1Mb window	5Kb eQTL	40Kb mQTL	40Kb haQTL
eQTL	1Mb	NA	0.4430	0.4138	1Mb	NA	0.4430	0.4074
mQTL	5Kb	0.4947	NA	0.4129	5Kb	0.4947	NA	0.4469
haQTL	1Mb	0.4545	0.6250	NA	40Kb	0.5200	0.5882	NA

Window xQTL	1Mb window	5Kb eQTL	2Kb mQTL	2Kb haQTL	100Kb window	100Kb eQTL	100Kb mQTL	100Kb haQTL
eQTL	1Mb	NA	0.4430	0.4167	100Kb	NA	0.3982	0.4519
mQTL	5Kb	0.4947	NA	0.5276	100Kb	0.6168	NA	0.3946
haQTL	2Kb	0.4815	0.5238	NA	100Kb	0.5319	0.5814	NA

**Table S5. Mediation analysis based on causal inference test**

Notation                           Methy & Acety = represent epigenome with first PC of histone acetylation peaks  
   and methylation probes associated with a given shared xQTL SNP  
 Methy Only = represent epigenome with first PC of  
   methylation probes associated with a given shared xQTL SNP  
 Acety Only = represent epigenome with first PC of  
   histone acetylation peaks associated with a given shared xQTL SNP  
*m* = 20,916 tested association sets  
 Model determination        pCausal < 0.05/*m* & pReact > 0.05/*m* => Causal  
   pCausal > 0.05/*m* & pReact < 0.05/*m* => Reactive  
   pCausal > 0.05/*m* & pReact > 0.05/*m* => Independent  
   Otherwise => Unclassified

Methy & Acety	Causal	Reactive	Indep	Unclassified	Total
#Association sets	1893	726	17699	598	20916
Percentage (%)	9.05	3.47	84.62	2.86	100.00

Methy Only	Causal	Reactive	Indep	Unclear	Total
#Association sets	685	586	19342	303	20916
Percentage (%)	3.28	2.80	92.47	1.45	100.00

Acety Only	Causal	Reactive	Indep	Unclear	Total
#Association sets	1230	1204	17992	490	20916
Percentage (%)	5.88	5.76	86.02	2.34	100.00

**Table S6A. Partitioned heritability of all xQTL SNPs**

Stratified LD score regression applied to estimate partitioned heritability with all xQTL SNPs as one category and all SNPs as background.

Window sizes for eQTL, mQTL, and haQTL analysis were 1Mb, 5Kb, and 1Mb, respectively

Prop.\_SNPs = 0.10

Prop.\_h2 denotes proportion of heritability

GWAS dataset	#Subjects		All xQTL SNPs					
	Cases	Controls	Prop._h2	Prop._h2_std_error	Enrichment	Enrichment_std_error	Enrichment_p	
ADHD PGC	2960	6583	-1.62E-01	2.39E-01	-1.55E+00	2.28E+00	1.54E-01	
Alzheimer IGAP (stage 1)	17008	37154	5.42E-01	1.33E-01	5.19E+00	1.27E+00	2.48E-06	
Anxiety ANGST (case-control)	17130		9.14E-02	1.20E-01	8.75E-01	1.15E+00	9.13E-01	
Anxiety ANGST (factor score)	18186		1.68E-01	1.57E-01	1.60E+00	1.50E+00	6.61E-01	
Autism PGC	5305	5305	1.37E-01	5.71E-02	1.31E+00	5.46E-01	5.69E-01	
Bipolar PGC	11974	51792	3.04E-01	4.75E-02	2.91E+00	4.55E-01	6.17E-06	
BipolarVsSchizo PGC (bipolar only)	10410	19423	3.36E-01	5.43E-02	3.21E+00	5.20E-01	7.70E-06	
MDD CONVERGE	5303	5337	2.25E-01	1.13E-01	2.16E+00	1.08E+00	1.75E-01	
Schizophrenia2 PGC	36989	113075	2.43E-01	1.97E-02	2.32E+00	1.88E-01	5.76E-11	
BipolarVsSchizo PGC (schizo only)	9369	19423	2.41E-01	3.38E-02	2.31E+00	3.24E-01	2.19E-05	
BMI GIANT (BMI) 2010	NA	249796	2.49E-01	2.96E-02	2.38E+00	2.83E-01	1.52E-06	
BMI GIANT (Height) 2010	NA	183727	4.51E-01	3.61E-02	4.31E+00	3.45E-01	3.77E-19	
Bowel Disease IBD (Europe Crohn's Disease)	5956	21770	6.07E-01	1.04E-01	5.81E+00	9.94E-01	2.95E-10	
Bowel Disease IBD (Europe Ulcerative Colitis)	6968	21770	7.82E-01	1.35E-01	7.48E+00	1.29E+00	4.46E-09	
Bowel Disease IBD (Europe IBD)	12924	21770	6.66E-01	9.94E-02	6.38E+00	9.51E-01	9.44E-14	
Diabetes DIAGRAM Trans-ethnic T2D GWAS	27206	57574	4.42E-01	6.33E-02	4.23E+00	6.05E-01	9.89E-12	

**Table S6B. Partitioned heritability of all xQTL SNPs**

Stratified LD score regression applied to estimate partitioned heritability with all xQTL SNPs as one category and LDSC baseline with all 53 categories as background.

Window sizes for eQTL, mQTL, and haQTL analysis were 1Mb, 5Kb, and 1Mb, respectively

Prop.\_SNPs = 0.10

Prop.\_h2 denotes proportion of heritability

GWAS dataset	#Subjects		All xQTL SNPs					
	Cases	Controls	Prop._h2	Prop._h2_std_error	Enrichment	Enrichment_std_error	Enrichment_p	
ADHD PGC	2960	6583	-3.32E-02	1.38E-01	-3.17E-01	1.32E+00	2.74E-01	
Alzheimer IGAP (stage 1)	17008	37154	1.72E-01	6.40E-02	1.65E+00	6.12E-01	2.82E-01	
Anxiety ANGST (case-control)	17130		1.25E-01	1.29E-01	1.20E+00	1.24E+00	8.69E-01	
Anxiety ANGST (factor score)	18186		2.22E-01	1.98E-01	2.12E+00	1.89E+00	4.51E-01	
Autism PGC	5305	5305	1.08E-01	4.69E-02	1.03E+00	4.49E-01	9.49E-01	
Bipolar PGC	11974	51792	2.19E-01	4.44E-02	2.09E+00	4.25E-01	5.91E-03	
BipolarVsSchizo PGC (bipolar only)	10410	19423	2.03E-01	4.23E-02	1.94E+00	4.04E-01	1.56E-02	
MDD CONVERGE	5303	5337	1.93E-01	1.34E-01	1.85E+00	1.28E+00	4.34E-01	
Schizophrenia2 PGC	36989	113075	1.89E-01	1.90E-02	1.80E+00	1.82E-01	1.38E-05	
BipolarVsSchizo PGC (schizo only)	9369	19423	1.67E-01	2.62E-02	1.60E+00	2.51E-01	1.16E-02	
BMI GIANT (BMI) 2010	NA	249796	2.07E-01	2.59E-02	1.98E+00	2.47E-01	1.21E-04	
BMI GIANT (Height) 2010	NA	183727	2.16E-01	2.26E-02	2.07E+00	2.16E-01	4.20E-06	
Bowel Disease IBD (Europe Crohn's Disease)	5956	21770	2.09E-01	4.50E-02	2.00E+00	4.31E-01	1.40E-02	
Bowel Disease IBD (Europe Ulcerative Colitis)	6968	21770	2.91E-01	6.91E-02	2.79E+00	6.61E-01	5.35E-03	
Bowel Disease IBD (Europe IBD)	12924	21770	2.34E-01	4.77E-02	2.24E+00	4.56E-01	2.47E-03	
Diabetes DIAGRAM Trans-ethnic T2D GWAS	27206	57574	2.21E-01	3.92E-02	2.11E+00	3.75E-01	9.33E-04	

**Table S6C. Partitioned heritability of all xQTL SNPs shared between any xQTL types and all other xQTL SNPs**

Stratified LD score regression applied to estimate partitioned heritability with all shared xQTL SNPs as one category, all other xQTL SNPs as another category, and all SNPs as background

Window sizes for eQTL, mQTL, and haQTL analysis were 1Mb, 5Kb, and 1Mb, respectively

Prop.\_SNPs = 0.02 and 0.09 for shared xQTL SNPs and all other xQTL SNPs, respectively

Prop.\_h2 denotes proportion of heritability

Disease Study	#Subjects		All xQTL SNPs that are shared across any xQTL types					Enrichment_p
	Cases	Controls	Prop._h2	Prop._h2_std_error	Enrichment	Enrichment_std_error	Enrichment_p	
ADHD PGC	2960	6583	-1.02E-02	5.87E-02	-6.48E-01	3.73E+00	6.39E-01	
Alzheimer IGAP (stage 1)	17008	37154	2.99E-02	3.47E-02	1.90E+00	2.20E+00	6.81E-01	
Anxiety ANGST (case-control)	17130	18186	-8.04E-02	4.85E-02	-5.11E+00	3.08E+00	1.17E-02	
Anxiety ANGST (factor score)	18186	18186	4.87E-03	4.74E-02	3.09E-01	3.01E+00	8.16E-01	
Autism PGC	5305	5305	9.78E-03	1.99E-02	6.21E-01	1.26E+00	7.65E-01	
Bipolar PGC	11974	51792	6.16E-02	2.13E-02	3.91E+00	1.35E+00	2.31E-02	
BipolarVsSchizo PGC (bipolar only)	10410	19423	6.42E-02	2.28E-02	4.08E+00	1.45E+00	3.10E-02	
MDD CONVERGE	5303	5337	2.42E-02	2.95E-02	1.53E+00	1.88E+00	7.71E-01	
Schizophrenia2 PGC	36989	113075	4.02E-02	9.67E-03	2.56E+00	6.15E-01	1.32E-02	
BipolarVsSchizo PGC (schizo only)	9369	19423	4.82E-02	1.42E-02	3.06E+00	9.00E-01	2.16E-02	
BMI GIANT (BMI) 2010	NA	249796	4.07E-02	1.23E-02	2.58E+00	7.80E-01	4.29E-02	
BMI GIANT (Height) 2010	NA	183727	5.34E-02	1.51E-02	3.39E+00	9.59E-01	1.18E-02	
Bowel Disease IBD (Europe Crohn's Disease)	5956	21770	5.83E-02	2.46E-02	3.71E+00	1.56E+00	6.21E-02	
Bowel Disease IBD (Europe Ulcerative Colitis)	6968	21770	9.29E-02	4.40E-02	5.90E+00	2.79E+00	7.97E-02	
Bowel Disease IBD (Europe IBD)	12924	21770	7.53E-02	3.00E-02	4.79E+00	1.91E+00	3.74E-02	
Diabetes DIAGRAM Trans-ethnic T2D GWAS	27206	57574	4.70E-02	2.14E-02	2.99E+00	1.36E+00	1.40E-01	



**Table S6C. Partitioned heritability of all xQTL SNPs shared between any xQTL types and all other xQTL SNPs**

Stratified LD score regression applied to estimate partitioned heritability with all shared xQTL SNPs as one category, all other xQTL SNPs as another category, and all SNPs as background  
 Window sizes for eQTL, mQTL, and haQTL analysis were 1Mb, 5Kb, and 1Mb, respectively  
 Prop.\_SNPs = 0.02 and 0.09 for shared xQTL SNPs and all other xQTL SNPs, respectively  
 Prop.\_h2 denotes proportion of heritability

Disease Study	#Subjects		All other xQTL SNPs					Enrichment_p
	Cases	Controls	Prop._h2	Prop._h2_std_error	Enrichment	Enrichment_std_error	Enrichment_p	
ADHD PGC	2960	6583	-1.68E-01	2.24E-01	-1.89E+00	2.52E+00	1.52E-01	
Alzheimer IGAP (stage 1)	17008	37154	5.51E-01	1.40E-01	6.20E+00	1.58E+00	9.94E-07	
Anxiety ANGST (case-control)	17130	17130	2.72E-01	1.56E-01	3.06E+00	1.76E+00	1.53E-01	
Anxiety ANGST (factor score)	18186	18186	1.84E-01	1.80E-01	2.07E+00	2.02E+00	5.49E-01	
Autism PGC	5305	5305	1.38E-01	6.30E-02	1.55E+00	7.09E-01	4.36E-01	
Bipolar PGC	11974	51792	2.30E-01	4.72E-02	2.60E+00	5.32E-01	2.51E-03	
BipolarVsSchizo PGC (bipolar only)	10410	19423	2.62E-01	5.15E-02	2.95E+00	5.80E-01	5.11E-04	
MDD CONVERGE	5303	5337	2.10E-01	1.21E-01	2.37E+00	1.36E+00	2.28E-01	
Schizophrenia2 PGC	36989	113075	2.01E-01	2.23E-02	2.26E+00	2.52E-01	9.36E-07	
BipolarVsSchizo PGC (schizo only)	9369	19423	1.84E-01	3.93E-02	2.08E+00	4.42E-01	1.25E-02	
BMI GIANT (BMI) 2010	NA	249796	2.06E-01	2.78E-02	2.32E+00	3.13E-01	2.70E-05	
BMI GIANT (Height) 2010	NA	183727	4.06E-01	3.76E-02	4.57E+00	4.23E-01	5.20E-15	
Bowel Disease IBD (Europe Crohn's Disease)	5956	21770	5.70E-01	9.65E-02	6.42E+00	1.09E+00	1.67E-09	
Bowel Disease IBD (Europe Ulcerative Colitis)	6968	21770	7.04E-01	1.35E-01	7.93E+00	1.52E+00	6.43E-08	
Bowel Disease IBD (Europe IBD)	12924	21770	6.05E-01	9.58E-02	6.82E+00	1.08E+00	3.98E-11	
Diabetes DIAGRAM Trans-ethnic T2D GWAS	27206	57574	4.09E-01	6.53E-02	4.60E+00	7.35E-01	1.38E-09	

**Table S7A. Partitioned heritability of all xQTL SNPs**

Stratified LD score regression applied to estimate partitioned heritability with all xQTL SNPs as one category and all SNPs as background.

Window sizes for eQTL, mQTL, and haQTL analysis were 100Kb, 100Kb, and 100Kb, respectively

Prop.\_SNPs = 0.23

Prop.\_h2 denotes proportion of heritability

GWAS dataset	#Subjects		All xQTL SNPs					
	Cases	Controls	Prop._h2	Prop._h2_std_error	Enrichment	Enrichment_std_error	Enrichment_p	
ADHD PGC	2960	6583	6.95E-02	2.98E-01	3.04E-01	1.30E+00	5.57E-01	
Alzheimer IGAP (stage 1)	17008	37154	8.80E-01	1.86E-01	3.86E+00	8.13E-01	7.06E-08	
Anxiety ANGST (case-control)	17130		3.60E-01	2.14E-01	1.58E+00	9.38E-01	4.84E-01	
Anxiety ANGST (factor score)	18186		2.49E-01	2.02E-01	1.09E+00	8.85E-01	9.17E-01	
Autism PGC	5305	5305	3.82E-01	7.50E-02	1.67E+00	3.29E-01	3.45E-02	
Bipolar PGC	11974	51792	4.90E-01	5.48E-02	2.15E+00	2.40E-01	1.85E-07	
BipolarVsSchizo PGC (bipolar only)	10410	19423	5.40E-01	6.87E-02	2.37E+00	3.01E-01	4.45E-07	
MDD CONVERGE	5303	5337	3.23E-01	1.37E-01	1.41E+00	5.98E-01	4.16E-01	
Schizophrenia2 PGC	36989	113075	4.10E-01	2.19E-02	1.79E+00	9.59E-02	1.72E-14	
BipolarVsSchizo PGC (schizo only)	9369	19423	4.37E-01	4.35E-02	1.91E+00	1.91E-01	3.55E-07	
BMI GIANT (BMI) 2010	NA	249796	3.98E-01	3.69E-02	1.74E+00	1.62E-01	2.44E-06	
BMI GIANT (Height) 2010	NA	183727	6.91E-01	3.87E-02	3.03E+00	1.69E-01	8.70E-25	
Bowel Disease IBD (Europe Crohn's Disease)	5956	21770	9.34E-01	1.14E-01	4.09E+00	4.99E-01	7.63E-17	
Bowel Disease IBD (Europe Ulcerative Colitis)	6968	21770	1.11E+00	1.45E-01	4.85E+00	6.35E-01	3.23E-14	
Bowel Disease IBD (Europe IBD)	12924	21770	1.04E+00	1.09E-01	4.55E+00	4.76E-01	4.99E-20	
Diabetes DIAGRAM Trans-ethnic T2D GWAS	27206	57574	6.57E-01	7.74E-02	2.88E+00	3.39E-01	1.01E-11	

**Table S7B. Partitioned heritability of all xQTL SNPs**

Stratified LD score regression applied to estimate partitioned heritability with all xQTL SNPs as one category and LDSC baseline with all 53 categories as background.

Window sizes for eQTL, mQTL, and haQTL analysis were 100Kb, 100Kb, and 100Kb, respectively

Prop.\_SNPs = 0.23

Prop.\_h2 denotes proportion of heritability

GWAS dataset	#Subjects		All xQTL SNPs					
	Cases	Controls	Prop._h2	Prop._h2_std_error	Enrichment	Enrichment_std_error	Enrichment_p	
ADHD PGC	2960	6583	2.41E-01	2.32E-01	1.06E+00	1.02E+00	9.54E-01	
Alzheimer IGAP (stage 1)	17008	37154	4.41E-01	8.83E-02	1.93E+00	3.87E-01	5.25E-03	
Anxiety ANGST (case-control)	17130		8.36E-01	7.59E-01	3.66E+00	3.32E+00	6.21E-02	
Anxiety ANGST (factor score)	18186		3.54E-01	3.17E-01	1.55E+00	1.39E+00	6.33E-01	
Autism PGC	5305	5305	3.40E-01	6.44E-02	1.49E+00	2.82E-01	5.47E-02	
Bipolar PGC	11974	51792	4.32E-01	5.86E-02	1.89E+00	2.57E-01	5.70E-05	
BipolarVsSchizo PGC (bipolar only)	10410	19423	4.84E-01	7.25E-02	2.12E+00	3.17E-01	3.32E-05	
MDD CONVERGE	5303	5337	2.51E-01	1.65E-01	1.10E+00	7.23E-01	8.87E-01	
Schizophrenia2 PGC	36989	113075	3.81E-01	2.62E-02	1.67E+00	1.15E-01	6.73E-09	
BipolarVsSchizo PGC (schizo only)	9369	19423	3.79E-01	4.23E-02	1.66E+00	1.85E-01	1.14E-04	
BMI GIANT (BMI) 2010	NA	249796	3.58E-01	3.62E-02	1.57E+00	1.59E-01	3.25E-04	
BMI GIANT (Height) 2010	NA	183727	4.50E-01	3.09E-02	1.97E+00	1.35E-01	2.38E-11	
Bowel Disease IBD (Europe Crohn's Disease)	5956	21770	4.40E-01	4.95E-02	1.93E+00	2.17E-01	7.40E-06	
Bowel Disease IBD (Europe Ulcerative Colitis)	6968	21770	5.55E-01	6.41E-02	2.43E+00	2.81E-01	2.77E-07	
Bowel Disease IBD (Europe IBD)	12924	21770	5.30E-01	5.16E-02	2.32E+00	2.26E-01	4.15E-10	
Diabetes DIAGRAM Trans-ethnic T2D GWAS	27206	57574	3.92E-01	5.80E-02	1.72E+00	2.54E-01	1.55E-03	

**Table S7C. Partitioned heritability of all shared xQTL SNPs vs. all other xQTL SNPs**

Stratified LD score regression applied to estimate partitioned heritability with all shared xQTL SNPs as one category,

all other xQTL SNPs as another category, and all SNPs as background

Window sizes for eQTL, mQTL, and haQTL analysis were 100Kb, 100Kb, and 100Kb, respectively

Prop.\_SNPs = 0.04 and 0.19 for shared xQTL SNPs and all other xQTL SNPs, respectively

Prop.\_h2 denotes proportion of heritability

GWAS dataset	#Subjects		All xQTL SNPs that are shared across any xQTL types					
	Cases	Controls	Prop._h2	Prop._h2_std_error	Enrichment	Enrichment_std_error	Enrichment_p	
ADHD PGC	2960	6583	-6.06E-02	1.17E-01	-1.69E+00	3.24E+00	3.28E-01	
Alzheimer IGAP (stage 1)	17008	37154	2.20E-01	7.26E-02	6.12E+00	2.02E+00	1.33E-03	
Anxiety ANGST (case-control)	17130		-5.14E-02	6.00E-02	-1.43E+00	1.67E+00	1.18E-01	
Anxiety ANGST (factor score)	18186		1.56E-01	1.04E-01	4.35E+00	2.88E+00	1.38E-01	
Autism PGC	5305	5305	5.64E-02	3.07E-02	1.57E+00	8.54E-01	4.97E-01	
Bipolar PGC	11974	51792	1.22E-01	2.59E-02	3.40E+00	7.19E-01	4.61E-04	
BipolarVsSchizo PGC (bipolar only)	10410	19423	1.32E-01	2.83E-02	3.67E+00	7.87E-01	4.51E-04	
MIDD CONVERGE	5303	5337	8.69E-02	5.27E-02	2.42E+00	1.47E+00	2.72E-01	
Schizophrenia2 PGC	36989	113075	8.75E-02	1.17E-02	2.43E+00	3.24E-01	1.72E-05	
BipolarVsSchizo PGC (schizo only)	9369	19423	8.59E-02	1.65E-02	2.39E+00	4.59E-01	1.69E-03	
BMI GIANT (BMI) 2010	NA	249796	9.04E-02	1.60E-02	2.51E+00	4.46E-01	6.04E-04	
BMI GIANT (Height) 2010	NA	183727	1.66E-01	2.06E-02	4.63E+00	5.73E-01	6.78E-10	
Bowel Disease IBD (Europe Crohn's Disease)	5956	21770	2.02E-01	5.67E-02	5.61E+00	1.58E+00	9.33E-04	
Bowel Disease IBD (Europe Ulcerative Colitis)	6968	21770	2.92E-01	8.20E-02	8.11E+00	2.28E+00	5.05E-04	
Bowel Disease IBD (Europe IBD)	12924	21770	2.28E-01	5.67E-02	6.34E+00	1.58E+00	8.05E-05	
Diabetes DIAGRAM Trans-ethnic T2D GWAS	27206	57574	1.76E-01	3.47E-02	4.89E+00	9.65E-01	9.92E-06	

**Table S7C. Partitioned heritability of all shared xQTL SNPs vs. all other xQTL SNPs**

Stratified LD score regression applied to estimate partitioned heritability with all shared xQTL SNPs as one category, all other xQTL SNPs as another category, and all SNPs as background

Window sizes for eQTL, mQTL, and haQTL analysis were 100Kb, 100Kb, and 100Kb, respectively

Prop.\_SNPs = 0.04 and 0.19 for shared xQTL SNPs and all other xQTL SNPs, respectively

Prop.\_h2 denotes proportion of heritability

GWAS dataset	#Subjects		All other xQTL SNPs					
	Cases	Controls	Prop._h2	Prop._h2_std_error	Enrichment	Enrichment_std_error	Enrichment_p	
ADHD PGC	2960	6583	1.79E-01	2.39E-01	9.31E-01	1.24E+00	9.55E-01	
Alzheimer IGAP (stage 1)	17008	37154	6.40E-01	1.49E-01	3.33E+00	7.75E-01	7.76E-05	
Anxiety ANGST (case-control)	17130		4.73E-01	2.38E-01	2.46E+00	1.24E+00	1.34E-01	
Anxiety ANGST (factor score)	18186		1.89E-02	2.28E-01	9.83E-02	1.19E+00	4.28E-01	
Autism PGC	5305	5305	3.28E-01	8.07E-02	1.70E+00	4.20E-01	9.43E-02	
Bipolar PGC	11974	51792	3.53E-01	5.14E-02	1.84E+00	2.67E-01	1.12E-03	
BipolarVsSchizo PGC (bipolar only)	10410	19423	3.93E-01	6.17E-02	2.04E+00	3.21E-01	4.31E-04	
MDD CONVERGE	5303	5337	2.17E-01	1.21E-01	1.13E+00	6.30E-01	8.28E-01	
Schizophrenia2 PGC	36989	113075	3.16E-01	2.20E-02	1.64E+00	1.15E-01	5.43E-08	
BipolarVsSchizo PGC (schizo only)	9369	19423	3.45E-01	4.20E-02	1.79E+00	2.18E-01	1.96E-04	
BMI GIANT (BMI) 2010	NA	249796	2.97E-01	3.55E-02	1.54E+00	1.84E-01	2.72E-03	
BMI GIANT (Height) 2010	NA	183727	5.12E-01	3.33E-02	2.66E+00	1.73E-01	8.17E-18	
Bowel Disease IBD (Europe Crohn's Disease)	5956	21770	7.24E-01	1.01E-01	3.76E+00	5.26E-01	1.70E-09	
Bowel Disease IBD (Europe Ulcerative Colitis)	6968	21770	8.03E-01	1.32E-01	4.17E+00	6.86E-01	2.72E-07	
Bowel Disease IBD (Europe IBD)	12924	21770	8.04E-01	9.57E-02	4.18E+00	4.98E-01	7.57E-11	
Diabetes DIAGRAM Trans-ethnic T2D GWAS	27206	57574	4.59E-01	6.93E-02	2.38E+00	3.60E-01	1.97E-05	

**Table S8A.** Number of SNPs detected with xQTL-weighted GWAS

**Notation**

All = non-weighted

Tested = Weighting SNPs proximal to molecular features

LDSC Base = Weighting SNPs that are in the LD score regression baseline model

Union = Weighting SNPs belong to any of the xQTLs

Ovl = Weighting SNPs shared between any of the xQTL types

**Note**

PLINK1.9 was applied to find SNPs in approximate linkage equilibrium ( $r^2 < 0.2$ ).

Some studies used more stringent criterion, e.g.  $r^2 < 0.1$ . Their reported number of independent SNPs would thus be fewer compared to this Table.

Occasionally, SNPs found by wGWAS might not cover all SNPs found by non-weighted GWAS.

Hence, there are studies where new SNPs are found, but a few previously reported SNPs are dropped.

Disease Study	#significant SNPs					#independent significant SNPs					#added indep SNPs wrt All			
	All	Tested	LDSC Base	Union	Ovl	All	Tested	LDSC Base	Union	Ovl	Tested	LDSC Base	Union	Ovl
ADHD PGC	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Alzheimer IGAP (stage 1)	1090	1090	1090	1094	1090	80	80	80	80	80	0	0	1	0
Anxiety ANGST (case-control)	7	7	7	7	7	1	1	1	1	1	0	0	0	0
Anxiety ANGST (factor score)	54	56	55	54	54	1	1	1	1	1	0	0	0	0
Autism PGC	1	1	1	1	1	1	1	1	1	1	0	0	0	0
Bipolar PGC	43	44	44	45	45	4	4	4	4	5	0	0	0	2
BipolarVsSchizo PGC (bipolar only)	2	2	2	5	8	1	1	1	3	1	0	0	2	1
MDD CONVERGE	31	31	31	31	31	2	2	2	2	2	0	0	0	0
Schizophrenia2 PGC	12897	12915	12905	13338	13007	264	262	267	270	273	7	4	22	10
BipolarVsSchizo PGC (schizo only)	48	48	48	78	98	4	4	4	5	6	0	0	1	2
Blood Pressure ICBP (systolic)	111	112	111	113	111	8	9	8	10	10	1	0	2	2
Blood Pressure ICBP (diastolic)	88	89	89	111	94	10	10	10	10	10	0	0	1	0
BMI GIANT (BMI) 2010	772	775	773	842	784	35	34	35	40	35	0	0	5	1
BMI GIANT (Height) 2010	4663	4665	4665	4838	4742	237	236	238	245	243	2	2	18	8
BMI GIANT (WHRadjBMI) 2010	299	302	299	300	301	13	13	13	13	14	0	0	0	1
Bowel Disease IBD (Europe Crohn's Disease)	6024	6155	6070	6200	6101	176	173	178	171	175	4	3	3	0
Bowel Disease IBD (Europe Ulcerative Colitis)	9890	9890	9925	9978	9986	264	264	264	255	263	0	6	8	5
Bowel Disease IBD (Europe IBD)	12950	12975	13022	13189	13096	263	256	263	255	264	5	5	9	5
Diabetes DIAGRAM Trans-ethnic T2D GWAS	548	559	555	552	549	46	47	47	47	46	1	1	1	0

**Table S8B.** Number of SNPs detected with eQTL-weighted GWAS

**Notation**

ROSMAP = Weighting ROSMAP eQTL SNPs

DGN = Weighting DGN eQTL SNPs

**Note**

PLINK1.9 was applied to find SNPs in approximate linkage equilibrium ( $r^2 < 0.2$ ).

Some studies used more stringent criterion, e.g.  $r^2 < 0.1$ . Their reported number of independent SNPs would thus be fewer compared to this Table.

Occasionally, the SNPs found by weighted GWAS might not cover all SNPs found by non-weighted GWAS.

Hence, there are studies where new SNPs are found, but a few previously reported SNPs are dropped.

GWAS dataset	#significant SNPs		#independent significant SNPs		#added indep SNPs wrt All	
	ROSMAP	DGN	ROSMAP	DGN	ROSMAP	DGN
ADHD PGC	0	0	0	0	0	0
Alzheimer IGAP (stage 1)	1090	1091	80	80	0	0
Anxiety ANGST (case-control)	7	7	2	1	1	0
Anxiety ANGST (factor score)	54	54	1	1	0	0
Autism PGC	1	1	1	1	0	0
Bipolar PGC	47	43	4	6	1	2
BipolarVsSchizo PGC (bipolar only)	2	3	1	2	0	1
MDD CONVERGE	31	32	2	3	0	1
Schizophrenia2 PGC	13425	12903	267	274	17	9
BipolarVsSchizo PGC (schizo only)	130	51	7	4	2	1
Blood Pressure ICBP (systolic)	111	112	9	11	1	3
Blood Pressure ICBP (diastolic)	100	93	11	11	2	1
BMI GIANT (BMI) 2010	854	774	36	35	2	0
BMI GIANT (Height) 2010	4813	4685	241	240	12	3
BMI GIANT (WHRadjBMI) 2010	301	301	13	14	0	1
Bowel Disease IBD (Europe Crohn's Disease)	6164	6035	173	180	0	4
Bowel Disease IBD (Europe Ulcerative Colitis)	9981	9896	257	264	5	0
Bowel Disease IBD (Europe IBD)	13265	12955	257	265	8	2
Diabetes DIAGRAM Trans-ethnic T2D GWAS	548	548	46	46	0	0