

**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													GENRED		ImmVar	
xQTL type	window	aveALL	CRBL	FCTX	HIPP	MEDU	OCTX	PUTH	SNIG	TCTX	THAL	WHMT	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	0.6347	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	0.6660	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	0.3113	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	0.2064	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	0.1248	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	0.2768	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” phenotype with the same xQTL SNPs

as a “discovery” phenotype that appear significant

Only the closest molecular feature to each xQTL SNP was used in the  $\pi_1$  estimation

Window xQTL	1Mb eQTL	5Kb mQTL	1Mb haQTL	1Mb eQTL	5Kb mQTL	40Kb haQTL	1Mb eQTL	5Kb mQTL	2Kb haQTL	100Kb eQTL	100Kb mQTL	100Kb haQTL
eQTL	NA	0.4430	0.4138	NA	0.4430	0.4074	NA	0.4430	0.4167	NA	0.3982	0.4519
mQTL	0.4947	NA	0.4129	0.4947	NA	0.4469	0.4947	NA	0.5276	0.6168	NA	0.3946
haQTL	0.4545	0.6250	NA	0.5200	0.5882	NA	0.4815	0.5238	NA	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		-8.04E-02	4.85E-02	-5.11E+00	3.08E+00	1.17E-02	
Anxiety ANGST (factor score)	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**

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

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 comparing to this Table for those settings. 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.

Disease Study	#significant SNPs				
	All	Tested	LDSC Base	Union	Ovl
ADHD PGC	0	0	0	0	0
Alzheimer IGAP (stage 1)	1090	1090	1090	1094	1090
Anxiety ANGST (case-control)	7	7	7	7	7
Anxiety ANGST (factor score)	54	56	55	54	54
Autism PGC	1	1	1	1	1
Bipolar PGC	43	44	44	45	45
BipolarVsSchizo PGC (bipolar only)	2	2	2	5	8
MDD CONVERGE	31	31	31	31	31
Schizophrenia2 PGC	12897	12915	12905	13338	13007
BipolarVsSchizo PGC (schizo only)	48	48	48	78	98
Blood Pressure ICBP (systolic)	111	112	111	113	111
Blood Pressure ICBP (diastolic)	88	89	89	111	94
BMI GIANT (BMI) 2010	772	775	773	842	784
BMI GIANT (Height) 2010	4663	4665	4665	4838	4742
BMI GIANT (WHRadjBMI) 2010	299	302	299	300	301
Bowel Disease IBD (Europe Crohn's Disease)	6024	6155	6070	6200	6101
Bowel Disease IBD (Europe Ulcerative Colitis)	9890	9890	9925	9978	9986
Bowel Disease IBD (Europe IBD)	12950	12975	13022	13189	13096
Diabetes DIAGRAM Trans-ethnic T2D GWAS	548	559	555	552	549

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

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

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 comparing to this Table for those settings. 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.

Disease Study	#independent significant SNPs				
	All	Tested	LDSC Base	Union	Ovl
ADHD PGC	0	0	0	0	0
Alzheimer IGAP (stage 1)	80	80	80	80	80
Anxiety ANGST (case-control)	1	1	1	1	1
Anxiety ANGST (factor score)	1	1	1	1	1
Autism PGC	1	1	1	1	1
Bipolar PGC	4	4	4	4	5
BipolarVsSchizo PGC (bipolar only)	1	1	1	3	1
MDD CONVERGE	2	2	2	2	2
Schizophrenia2 PGC	264	262	267	270	273
BipolarVsSchizo PGC (schizo only)	4	4	4	5	6
Blood Pressure ICBP (systolic)	8	9	8	10	10
Blood Pressure ICBP (diastolic)	10	10	10	10	10
BMI GIANT (BMI) 2010	35	34	35	40	35
BMI GIANT (Height) 2010	237	236	238	245	243
BMI GIANT (WHRadjBMI) 2010	13	13	13	13	14
Bowel Disease IBD (Europe Crohn's Disease)	176	173	178	171	175
Bowel Disease IBD (Europe Ulcerative Colitis)	264	264	264	255	263
Bowel Disease IBD (Europe IBD)	263	256	263	255	264
Diabetes DIAGRAM Trans-ethnic T2D GWAS	46	47	47	47	46

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

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

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 comparing to this Table for those settings.

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.

Disease Study	#added indep SNPs wrt All			
	Tested	LDSC Base	Union	Ovl
ADHD PGC	0	0	0	0
Alzheimer IGAP (stage 1)	0	0	1	0
Anxiety ANGST (case-control)	0	0	0	0
Anxiety ANGST (factor score)	0	0	0	0
Autism PGC	0	0	0	0
Bipolar PGC	0	0	0	2
BipolarVsSchizo PGC (bipolar only)	0	0	2	1
MDD CONVERGE	0	0	0	0
Schizophrenia2 PGC	7	4	22	10
BipolarVsSchizo PGC (schizo only)	0	0	1	2
Blood Pressure ICBP (systolic)	1	0	2	2
Blood Pressure ICBP (diastolic)	0	0	1	0
BMI GIANT (BMI) 2010	0	0	5	1
BMI GIANT (Height) 2010	2	2	18	8
BMI GIANT (WHRadjBMI) 2010	0	0	0	1
Bowel Disease IBD (Europe Crohn's Disease)	4	3	3	0
Bowel Disease IBD (Europe Ulcerative Colitis)	0	6	8	5
Bowel Disease IBD (Europe IBD)	5	5	9	5
Diabetes DIAGRAM Trans-ethnic T2D GWAS	1	1	1	0



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

ROSMAP = Weighting ROSMAP eQTL SNPs

DGN = Weighting DGN eQTL SNPs

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 comparing to this Table for those settings. 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
MIDD 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