Bone & Joint Research

Supplementary Material

10.1302/2046-3758.111.BJR-2021-0277.R1

Dataset description and subject details

Major depressive disorder | Wray et al, 2018

The major depressive disorder (MDD) dataset includes 135,458 cases and 344,901 controls from seven case-control cohorts. A total of 44 loci were identified as associated with major depression. The first cohort included 29 case-control samples of European descent where lifetime diagnosis of MDD was ascertained using structured clinical interviews (DSM-V, ICD-9, or ICD-10), clinician-administered checklists, or review of medical records. Six additional cohorts of European ancestry, including the Hyde et al. study (23andMe Inc.), determined case status using other methods including national or hospital treatment registers, self-reported symptoms or treatment by a medical professional, or direct interviews.

Osteoarthritis | Tachmazidou et al., 2019

Tachmazidou et al leveraged the UK Biobank and arcOGEN resources to perform the largest genome-wide meta-analysis for osteoarthritis (OA) to date across ~17.5 million

single nucleotide variants in up to 455,221 individuals. In UKBB, Tachmazidou et al. performed sample and variant-based QC to produce a set of approximately 450,000 related Europeans and 17 million variants. Tachmazidou et al derived four OA definitions from self-report and hospital records. In arcOGEN, Tachmazidou et al imputed the data into HRC panel and performed sample and variant-based QC to produce a set of approximately 14,000 unrelated Europeans and 11 million variants. Tachmazidou et al derived three OA definitions from total joint replacement records or radiological evidence of disease.

LD score regression

LD score regression (LDSC) software v1.0.1 was used to analyze the genetic correlation of MDD with osteoarthritis. The 1000 Genome project phase 3[1] was used to estimate the LD structure for European populations, which was obtained from the LD score regression website.[2-4] Single nucleotide polymorphisms (SNPs) were filtered by 1.1 million variants, subset of 1000 Genomes and HapMap3,[5] with MAF above 0.05, MHC, and other long-range LD regions excluded.

Polygenic overlap analysis

Frei et al[6] introduced a novel statistical framework (MiXeR) to quantify polygenic overlap irrespective of genetic correlation between traits. In the MiXeR analysis, an effective sample size of Neff = 4/(1/Ncase + 1/Ncontrol) was used to account for

imbalanced numbers of cases and controls. The python_convert (v0.9.2) pipeline was used to harmonize GWAS summary statistics (https://github.com/precimed/python_convert). Calculation of the LD structure, LD scores l_i and shape parameter η_j are based on 9,997,231 SNPs from 1000 Genomes Phase 3 data, downloaded from LD score regression website.[2-4]

Cross-trait meta-analysis

ASSET meta-analysis is an agnostic approach that generalizes standard fixed-effects meta-analysis by allowing a subset of the input GWASs to have no effect on a given SNP. The method exhaustively explores all possible subsets of "non-null" GWAS inputs within a fixed-effect framework to identify the strongest association signal in both positive and negative directions. Only SNPs that were present for both the traits were retained as inputs to the ASSET meta-analysis, resulting in 11,070,634 SNPs for subsequent analysis. We carried out one-sided analysis by exploring models in which all non-null studies have effects in the same direction. Default parameters were applied with the "h.traits" function in ASSET.

FUMA was used to map SNPs to genes and identify LD-independent genomic regions.[7] Firstly, independent significant SNPs (IndSigSNPs) were identified on the basis of their p-value being genome-wide significant ($p \leq 5.0 \times 10^{-8}$) and being independent from each other ($r^2 < 0.6$). Secondly, Lead SNPs were identified as a subset of the independent significant SNPs that were in LD with each other at $r^2 < 0.1$ within a

1 Mb window. Genomic risk loci were identified by merging lead SNPs if they were closer than 250 kb apart. Clumping procedures were carried out on the basis of the European 1000 Genomes Project phase 3 reference panel. Due to extensive LD, the MHC region was merged into one region (chr6:25-35Mb). Genes within 100 kb of each variant were mapped.

MR analysis

To infer credible causal associations between MDD and OA, we performed Mendelian randomization analysis using GSMR V1.0.9.[8] This method uses summary-level data to test for putative causal associations between a risk factor (exposure) and an outcome by using independent genomewide significant SNPs as instrumental variables as an index of the exposure. HEIDI outlier detection was used to filter genetic instruments that showed clear pleiotropic effects on the exposure phenotype and the outcome phenotype. We used a threshold p-value of 0.01 for the outlier detection analysis in HEIDI, which removes 1% of SNPs by chance if there is no pleiotropic effect. We tested for bidirectional causation by repeating the analyses while switching the role of each correlated phenotype as an exposure and intelligence as the outcome. For each trait, we selected independent ($r^2 = 0.01$), genome-wide significant lead SNPs as instrumental variables in the analyses.

The method estimates a putative causal effect of the exposure on the outcome (b_{xy}) as a function of the relationship between the SNP's effects on the exposure (b_{zx}) and the

SNP's effects on the outcome (b_{zy}), given the assumption that the effect of non-pleiotropic SNPs on an exposure (x) should be related to their effect on the outcome (y) in an independent sample only via mediation through the phenotypic causal pathway (b_{xy}). The estimated causal effect coefficients (b_{xy}) are approximately equal to the natural log odds ratio for a case-control trait. An odds ratio of 2 can be interpreted as a doubled risk compared with the population prevalence of a binary trait for every standard deviation increase in the exposure trait.

Fine-mapping of transcriptome-wide associations

FOCUS (Fine-mapping Of CaUsal gene Sets)[9] is software to fine-map transcriptome-wide association study (TWAS) statistics at genomic risk regions. The software takes as input summary GWAS data along with eQTL weights and outputs a credible set of genes to explain observed genomic risk. FOCUS v0.6.10 was used to identify potential causal genes from the meta-analysis result of MDD and OA.[9] A multiple tissue, multiple eQTL reference panel weight database from the software (https://github.com/bogdanlab/focus/) was used. This combines GTEx v7 weights from PrediXcan[10] with METSIM, NTR, YFS, and CMC weights from FUSION software[11] into a single usable database for FOCUS. By integrating the GWAS summary result, expression weights, and LD among SNPs, it identifies causal gene to be included in a 90%-credible set and give a posterior inclusion probability (PIP) to estimate the causality in relevant tissues.

We applied FOCUS analysis on the meta-analysis result of MDD and OA in three relevant tissues, including brain, blood, and heart. The results from the three tissues were merged and irrelevant tissues other than the four tissues were removed.

Table i. Independent significant single-nucleotide polymorphisms of the meta-analysis shared by major depressive disorder and osteoarthritis. Protein-coding genes are in bold.

Locus	rsID	Chr	BP	p-value	OR (95% CI)	Gene
1	rs11209909	1	72553122	3.57×10^{-8}	0.98 (0.98-0.99)	**NEGR1**
1	rs12128707	1	72588119	3.92×10^{-10}	0.98 (0.97-0.99)	**NEGR1**
1	rs34124399	1	72603500	2.22×10^{-8}	0.98 (0.97-0.98)	**NEGR1**
1	rs12134600	1	72635996	2.32×10^{-9}	1.0 (1.0-1.0)	**NEGR1**
1	rs12740789	1	72752073	2.59×10^{-11}	0.97 (0.97-0.98)	**NEGR1**; RPL31P12
1	rs10789340	1	72940273	1.29×10^{-14}	0.98 (0.97-0.98)	
1	rs782212	1	72945666	3.43×10^{-10}	0.98 (0.97-0.99)	
1	rs61771930	1	73231490	4.56×10^{-9}	1.0 (1.0-1.0)	RP4-660H19.1; RP11-262K1.1
8	rs9678810	2	33398399	5.14×10^{-9}	0.97 (0.96-0.98)	**LTBP1**
11	rs6720885	2	99971289	1.30×10^{-8}	0.98 (0.98-0.99)	**EIF5B**
14	rs12471530	2	215433178	1.75×10^{-8}	0.98 (0.97-0.99)	AC107218.3
15	rs13084037	3	49214066	4.22×10^{-9}	0.98 (0.97-0.99)	**KLHDC8B**; C3orf84
15	rs1532204	3	49609477	2.31×10^{-8}	1.0 (1.0-1.0)	**BSN**
15	rs199956414	3	50022089	5.51×10^{-11}	0.97 (0.96-0.98)	**RBM6**
22	rs13143036	4	121623038	3.99×10^{-10}	0.98 (0.97-0.99)	**PRDM5**
22	rs71600495	4	121628028	2.01×10^{-8}	0.98 (0.97-0.99)	**PRDM5**
23	rs45510091	4	123186393	3.26×10^{-9}	1.0 (1.0-1.1)	**KIAA1109**
25	rs1363104	5	103917797	1.46×10^{-12}	1.0 (1.0-1.0)	RP11-6N13.1

27	rs1549212	5	166996722	4.77×10^{-9}	0.98 (0.98-0.99)	**TENM2**
29	rs9479138	6	152215199	1.42×10^{-8}	1.0 (1.0-1.0)	**ESR1**
30	rs62442913	7	1970649	3.94×10^{-8}	0.98 (0.97-0.99)	**MAD1L1**
30	rs3823624	7	2110346	1.55×10^{-9}	1.0 (1.0-1.0)	**MAD1L1**
31	rs10950398	7	12264871	6.82×10^{-9}	1.0 (1.0-1.0)	**TMEM106B**
34	rs13246482	7	109794839	1.51×10^{-8}	0.97 (0.96-0.98)	
39	rs3793577	9	23737627	4.73×10^{-8}	0.98 (0.98-0.99)	**ELAVL2**
40	rs7044244	9	96397689	1.52×10^{-8}	0.98 (0.98-0.99)	**PHF2**
43	rs10818400	9	122664468	1.23×10^{-8}	0.98 (0.98-0.99)	RP11-360A18.2
44	rs11596214	10	106453832	4.24×10^{-8}	0.98 (0.98-0.99)	**SORCS3**
44	rs1021363	10	106610839	4.15×10^{-9}	1.0 (1.0-1.0)	**SORCS3**
45	rs10488798	11	30825179	7.37×10^{-11}	0.98 (0.97-0.99)	**DCDC1**
45	rs10835766	11	31374329	6.35×10^{-12}	0.98 (0.97-0.98)	**DCDC1**
45	rs1806153	11	31850105	1.07×10^{-9}	1.0 (1.0-1.0)	**RCN1**
46	rs644740	11	65561468	2.10×10^{-8}	0.98 (0.98-0.99)	**OVOL1**
47	rs7942337	11	76465272	2.02×10^{-9}	0.98 (0.97-0.99)	RP11-672A2.1; RP11-21L23.4
48	rs11608185	11	113294976	5.82×10^{-11}	1.0 (1.0-1.0)	**DRD2**
48	rs7940164	11	113451765	4.85×10^{-9}	0.98 (0.98-0.99)	
49	rs7305875	12	23971243	3.00×10^{-10}	1.0 (1.0-1.0)	**SOX5**
49	rs78337797	12	23987925	5.80×10^{-9}	1.0 (1.0-1.0)	**SOX5**
51	rs2193743	12	108885446	5.30×10^{-9}	0.98 (0.98-0.99)	RP11-13G14.4

52	rs73224311	12	121344656	3.68×10^{-8}	1.0 (1.0-1.1)	**SPPL3**; CLIC1P1
53	rs1891945	13	53607340	4.39×10^{-8}	0.98 (0.98-0.99)	**OLFM4**
53	rs9536347	13	53644011	5.83×10^{-9}	1.0 (1.0-1.0)	**OLFM4**; LINC01065
53	rs2759694	13	53695378	1.04×10^{-15}	1.0 (1.0-1.0)	**OLFM4**; LINC01065
53	rs7323372	13	53857542	1.31×10^{-12}	0.98 (0.97-0.98)	RN7SL618P; AL450423.1
53	rs9536386	13	53879428	5.37×10^{-12}	1.0 (1.0-1.0)	RN7SL618P; AL450423.1
54	rs1950829	14	42097937	8.10×10^{-10}	1.0 (1.0-1.0)	**LRFN5**
58	rs12102100	15	37587461	4.75×10^{-10}	1.0 (1.0-1.0)	
58	rs8037355	15	37643831	6.57×10^{-13}	0.98 (0.97-0.98)	
58	rs4924163	15	37772709	7.97×10^{-9}	1.0 (1.0-1.0)	RP11-720L8.1
60	rs191117454	16	1249053	2.06×10^{-8}	1.0 (1.0-1.0)	**CACNA1H**
63	rs555334082	16	89857415	4.94×10^{-8}	0.97 (0.96-0.98)	**FANCA**

BP, base protein; Chr, chromosome; CI, confidence interval; OR, odds ratio.

Table ii. Protein-coding genes within clumping range of independent significant single nucleotide polymorphisms of the meta-analysis shared by major depressive disorder and osteoarthritis.

Gene	Chr:start-end	Minimum p-value	Ind Sig SNPs
NEGR1	1:71861623-72748417	5.53E-14	rs12128707;rs2630400;rs11209909;rs12134600;rs34124399;rs1870676;rs12740789;rs10789340;rs7531118
LTBP1	2:33172039-33624576	8.05E-13	rs17566944;rs62133340;rs2061027;rs9678810
TSGA10	2:99613724-99771427	8.15E-05	rs6720885
C2orf15	2:99757948-99939204	1.56E-08	rs6720885
LYG2	2:99858709-99871745	5.93E-06	rs6720885
LYG1	2:99900701-99921205	1.56E-08	rs6720885
TXNDC9	2:99935445-99957165	1.56E-08	rs6720885
EIF5B	2:99953816-100017789	1.30E-08	rs6720885
REV1	2:100016938-100106497	1.74E-08	rs6720885
VWC2L	2:215275789-215443683	1.75E-08	rs12471530
QRICH1	3:49067140-49131796	2.56E-05	rs13084037
QARS	3:49133365-49142553	2.26E-05	rs13084037
USP19	3:49145479-49158371	2.26E-05	rs13084037
LAMB2	3:49158547-49170551	2.51E-05	rs13084037
CCDC71	3:49199968-49203754	5.07E-09	rs13084037
KLHDC8B	3:49209044-49213917	4.22E-09	rs13084037
C3orf84	3:49215065-49229291	4.22E-09	rs13084037
CCDC36	3:49235861-49295537	1.22E-08	rs13084037

C3orf62	3:49306035-49315342	1.92E-08	rs13084037
USP4	3:49315264-49378145	1.92E-08	rs13084037
GPX1	3:49394609-49396033	2.44E-07	rs13084037;rs1532204
RHOA	3:49396578-49450431	2.44E-07	rs13084037;rs1532204
TCTA	3:49449639-49453908	2.94E-07	rs13084037
AMT	3:49454211-49460186	2.94E-07	rs13084037
NICN1	3:49460379-49466759	3.20E-07	rs13084037
DAG1	3:49506146-49573048	1.97E-07	rs13084037
BSN	3:49591922-49708978	2.31E-08	rs13084037;rs1532204
APEH	3:49711435-49721396	1.94E-06	rs1532204
MST1	3:49721380-49726934	7.80E-08	rs1532204;rs2271960
RNF123	3:49726932-49758962	7.04E-08	rs1532204;rs2271960
AMIGO3	3:49754267-49761349	7.04E-08	rs2271960;rs1532204
GMPPB	3:49754277-49761384	7.04E-08	rs2271960;rs1532204
IP6K1	3:49761727-49823975	7.81E-08	rs1532204;rs2271960
CDHR4	3:49828165-49837268	8.65E-08	rs2271960;rs1532204
FAM212A	3:49840687-49842463	8.65E-08	rs2271960;rs1532204
UBA7	3:49842640-49851379	8.65E-08	rs1532204;rs2271960
TRAIP	3:49866034-49894007	4.18E-09	rs2271960;rs1532204;rs199956414
CAMKV	3:49895421-49907655	2.98E-09	rs1532204;rs2271960;rs199956414;rs9831967
MST1R	3:49924435-49941299	3.59E-10	rs199956414;rs2271960;rs9831967

MON1A	3:49946302-49967606	1.33E-09	rs199956414;rs2271960;rs9831967
RBM6	3:49977440-50137478	5.51E-11	rs199956414;rs9831967;rs2271960
RBM5	3:50126341-50156454	9.16E-10	rs199956414;rs9831967;rs2271960
SEMA3F	3:50192478-50226508	1.92E-09	rs9831967;rs1046953;rs199956414
PRDM5	4:121606074-121844025	3.99E-10	rs13143036;rs71600495
KIAA1109	4:123073488-123283913	3.26E-09	rs45510091
ADAD1	4:123300121-123350957	NA	rs45510091
IL2	4:123372625-123377880	4.44E-09	rs45510091
IL21	4:123533783-123542224	1.23E-07	rs45510091
TENM2	5:166711804-167691162	4.77E-09	rs1549212
ESR1	6:151977826-152450754	1.42E-08	rs9479138
MAD1L1	7:1855429-2272878	1.55E-09	rs62442913;rs3823624
TMEM106B	7:12250867-12282993	6.82E-09	rs10950398
ELAVL2	9:23690102-23826335	4.73E-08	rs3793577
PHF2	9:96338689-96441869	1.52E-08	rs7044244
SORCS3	10:106400859-107024993	2.59E-09	rs11596214;rs61867293;rs1021363
DCDC1	11:30851916-31391357	6.35E-12	rs10488798;rs10835766
DNAJC24	11:31391387-31453396	3.69E-11	rs10835766
ELP4	11:31531297-31805546	1.51E-07	rs1806153
PAX6	11:31806340-31839509	1.40E-07	rs1806153
RCN1	11:31833939-32127301	1.07E-09	rs1806153

OVOL1	11:65554493-65564690	2.10E-08	rs644740
TSKU	11:76493295-76509198	1.92E-09	rs7942337;rs1149620
TTC12	11:113185251-113254266	8.47E-07	rs11608185
ANKK1	11:113258513-113271140	7.76E-08	rs11608185
DRD2	11:113280318-113346413	5.82E-11	rs11608185
SOX5	12:23682440-24103966	3.00E-10	rs7305875;rs78337797
CABP1	12:121078355-121105127	4.56E-07	rs73224311
MLEC	12:121124672-121139667	1.78E-06	rs73224311
UNC119B	12:121148238-121161443	9.09E-07	rs73224311
ACADS	12:121163538-121177811	1.39E-07	rs73224311
SPPL3	12:121200313-121342174	3.68E-08	rs73224311
HNF1A	12:121416346-121440315	5.98E-05	rs73224311
OLFM4	13:53602894-53626192	1.20E-18	rs1891945;rs2799339;rs12552;rs2759694
LRFN5	14:42076773-42373752	8.10E-10	rs1950829
CACNA1H	16:1203241-1271771	2.06E-08	rs191117454
FANCA	16:89803957-89883065	4.94E-08	rs555334082

SNP, single nucleotide polymorphism.

Table iii. Gene-trait associations identified in published genome-wide association studies. Depression includes major depressive disorder and depressive symptoms.

Gene	Trait	PMID
DCDC1	depression	27479909; 30718901
DRD2	depression	29942085; 29662059; 30718901
ELAVL2	depression	29942085; 30718901
KIAA1109	depression	29942085; 30718901
KLHDC8B	depression	29942085; 30718901
LRFN5	depression	29662059; 30718901; 29700475
MAD1L1	depression	29942085; 29662059; 30718901
NEGR1	depression	29942085
OLFM4	depression	27479909; 29942085; 30718901; 29700475
PHF2	depression	29942085
SORCS3	depression	27479909; 29942085; 29662059; 30718901; 27089181; 29700475
SOX5	depression	29942085; 30718901; 29700475
SPPL3	depression	27479909; 29942085; 30718901
TENM2	depression	29942085; 29662059; 29700475
TMEM106B	depression	29942085; 29662059; 30718901; 29700475
LTBP1	osteoarthritis	30664745; 30374069
RBM6	osteoarthritis	30664745

PMID, PubMed ID.

Table iv. Fine-mapping of transcriptome-wide association signals.

Gene	Tissue	TWAS_Z	PIP	Region
RPL31P12	brain_cerebellum	-7.61	1	1:71684831-1:74326484
UQCC	brain_dorsolateral_prefrontal_cortex	6.75	1	20:32813689-20:34960446
AXIN1	brain_cerebellar_hemisphere	-5.74	0.999	16:1207833-16:2763816
ZNF184	brain_hypothalamus	-5.13	0.997	6:25684587-6:26789628
DNAJC24	brain_dorsolateral_prefrontal_cortex	5.33	0.994	11:30141357-11:32276662
FAM86B3P	brain_cerebellar_hemisphere	-5.28	0.991	8:7153384-8:9154694
GPX1	brain_frontal_cortex_ba9	5.99	0.949	3:47727379-3:49316164
PRSS16	brain_cerebellum	-5.33	0.925	6:28018353-6:28917091
HIST1H4H	brain_dorsolateral_prefrontal_cortex	3.98	0.911	6:25684587-6:26789628
TRMT61A	brain_dorsolateral_prefrontal_cortex	4.63	0.885	14:103012102-14:105001691
CDT1	brain_cortex	4.7	0.789	16:89041165-16:90292788
FANCL	brain_dorsolateral_prefrontal_cortex	-4.54	0.782	2:57429100-2:58296890
SETD8	brain_dorsolateral_prefrontal_cortex	4.88	0.763	12:122009763-12:124976982
RBM6	brain_cerebellum	-5.97	0.74	3:49317338-3:51830565
SLC30A9	brain_hypothalamus	-5.31	0.729	4:40203025-4:42213058
MRPS14	brain_dorsolateral_prefrontal_cortex	-4.53	0.692	1:173097989-1:175089768
BDH2	brain_spinal_cord_cervical_c-1	-3.6	0.68	4:100678551-4:103220401
TMED2	brain_caudate_basal_ganglia	-3.4	0.653	12:122009763-12:124976982
NF1	brain_amygdala	4.44	0.642	17:27334244-17:29786491
ZNF204P	brain_cerebellum	2.83	0.595	6:28018353-6:28917091
ATP1A3	brain_cerebellum	5.82	0.586	19:40985003-19:42131442
LFNG	brain_putamen_basal_ganglia	2.9	0.565	7:1353968-7:2061783
PAX6	brain_dorsolateral_prefrontal_cortex	2.16	0.503	11:30141357-11:32276662
CHURC1	brain_frontal_cortex_ba9	4.25	0.499	14:63790015-14:65219505
SPTBN2	brain_substantia_nigra	-4.36	0.494	11:63805335-11:65898631
FAM167A	brain_dorsolateral_prefrontal_cortex	-4.85	0.45	8:10463197-8:11278541
RP11-481A20.10	brain_cerebellar_hemisphere	5.27	0.415	8:11279221-8:13491594
AC005795.1	brain_frontal_cortex_ba9	-5.73	0.414	19:40985003-19:42131442
ZSCAN23	brain_dorsolateral_prefrontal_cortex	-5.27	0.409	6:26791421-6:28017250
ZNF391	brain_caudate_basal_ganglia	2.68	0.375	6:28018353-6:28917091
TMEM129	brain_cerebellum	-0.59	0.359	4:1478711-4:2841772
OVOL1	brain_cortex	4.34	0.354	11:63805335-11:65898631
AC110781.3	brain_nucleus_accumbens_basal_ganglia	4.94	0.342	7:1353968-7:2061783
ZC3H7B	brain_frontal_cortex_ba9	4.07	0.28	22:40545828-22:42690262

FAM86B1	brain_dorsolateral_prefrontal_cortex	5.16	0.251	8:11279221-8:13491594
APOPT1	brain_caudate_basal_ganglia	-1.49	0.223	14:103012102-14:105001691
MAP1LC3A	brain_cerebellar_hemisphere	2.54	0.171	20:32813689-20:34960446
ALG1L11P	brain_caudate_basal_ganglia	4.63	0.167	8:10463197-8:11278541
RP11-481A20.11	brain_cerebellar_hemisphere	5.09	0.163	8:11279221-8:13491594
RP11-10L12.2	brain_cerebellum	-2.85	0.162	4:100678551-4:103220401
CTD-2349P21.9	brain_cerebellar_hemisphere	-3.75	0.146	17:27334244-17:29786491
DALRD3	brain_cerebellum	-5.09	0.119	3:49317338-3:51830565
ACSS2	brain_caudate_basal_ganglia	4	0.117	20:32813689-20:34960446
BSN	brain_cortex	5.61	0.117	3:49317338-3:51830565
TMA7	brain_cerebellum	5.11	0.117	3:49317338-3:51830565
P2RX7	brain_cerebellum	3.21	0.101	12:122009763-12:124976982
AAR2	brain_caudate_basal_ganglia	-4.26	0.101	20:32813689-20:34960446
ICA1L	brain_dorsolateral_prefrontal_cortex	4.08	0.1	2:202819348-2:205799241
CHADL	brain_frontal_cortex_ba9	3.74	0.0878	22:40545828-22:42690262
PDPK2	brain_frontal_cortex_ba9	-3.6	0.0805	16:1207833-16:2763816
SBNO1	brain_substantia_nigra	4.41	0.0784	12:122009763-12:124976982
PINX1	brain_substantia_nigra	-4.38	0.0783	8:10463197-8:11278541
RNF39	brain_cortex	-3.76	0.0771	6:28917832-6:29737971
RELA	brain_hippocampus	3.48	0.0755	11:63805335-11:65898631
GSS	brain_dorsolateral_prefrontal_cortex	3.43	0.0729	20:32813689-20:34960446
FBXL15	brain_hippocampus	3.65	0.0725	10:104380686-10:106695048
SETD8	brain_cerebellum	4.24	0.0714	12:122009763-12:124976982
HLA-K	brain_putamen_basal_ganglia	-2.71	0.0672	6:28917832-6:29737971
RP11-481A20.4	brain_cerebellar_hemisphere	4.89	0.0663	8:11279221-8:13491594
VPS9D1	brain_cortex	-4.07	0.0627	16:89041165-16:90292788

TIAF1	brain_cerebellar_hemisphere	-3.88	0.0583	17:27334244-17:29786491
HCG4	brain_dorsolateral_prefrontal_cortex	-3.06	0.0574	6:28917832-6:29737971
SPINK8	brain_hippocampus	2.96	0.054	3:49317338-3:51830565
RNPS1	brain_cerebellum	-3.09	0.0513	16:1207833-16:2763816
SCARB1	brain_spinal_cord_cervical_c-1	3.27	0.0461	12:122009763-12:124976982
MEI1	brain_cortex	3.55	0.0422	22:40545828-22:42690262
SLC35G5	brain_nucleus_accumbens_basal_ganglia	-4.28	0.0404	8:10463197-8:11278541
C16orf3	brain_dorsolateral_prefrontal_cortex	2.93	0.0393	16:89041165-16:90292788
FAM66D	brain_dorsolateral_prefrontal_cortex	-4.71	0.0292	8:11279221-8:13491594
RP11-753C18.8	brain_cerebellar_hemisphere	3.17	0.0286	10:104380686-10:106695048
HLA-A	brain_cerebellum	-3.39	0.0275	6:28917832-6:29737971
HLA-F	brain_cerebellar_hemisphere	-3.39	0.0275	6:28917832-6:29737971
MICE	brain_cerebellar_hemisphere	-3.39	0.0275	6:28917832-6:29737971
FAM222B	brain_frontal_cortex_ba9	3.5	0.0274	17:27334244-17:29786491
RP11-351I21.7	brain_cerebellar_hemisphere	4.69	0.0258	8:11279221-8:13491594
LRRC37BP1	brain_dorsolateral_prefrontal_cortex	3.52	0.0207	17:27334244-17:29786491
HLA-J	brain_caudate_basal_ganglia	-3.3	0.0199	6:28917832-6:29737971
SUZ12P	brain_putamen_basal_ganglia	3.58	0.0195	17:27334244-17:29786491
MICF	brain_cerebellum	-3.15	0.0159	6:29737971-6:30798168
PGP	brain_substantia_nigra	3	0.0128	16:1207833-16:2763816
RP11-433P17.1	brain_hippocampus	3.08	0.0122	16:1207833-16:2763816

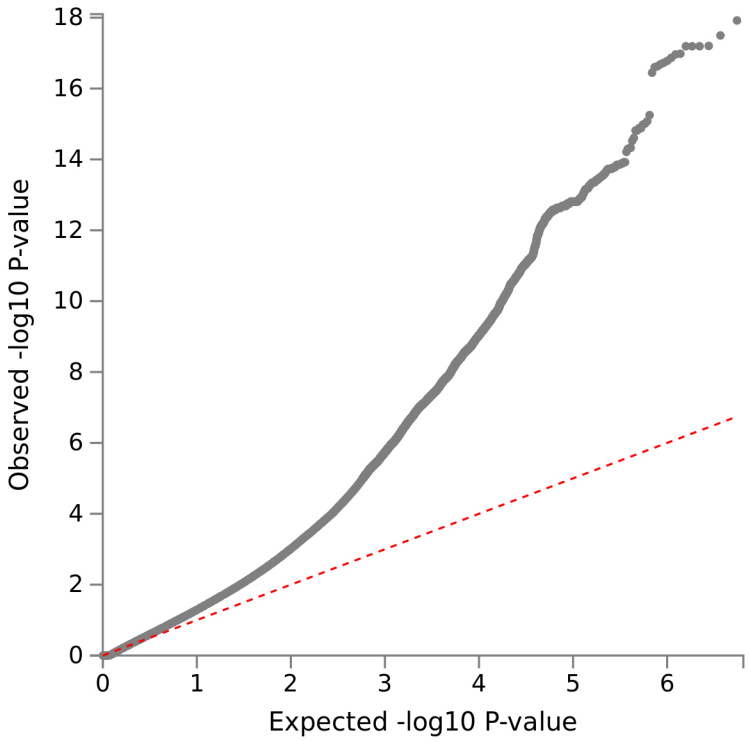

Figure a. Quantile-quantile plots of the observed meta-analysis statistics versus the expected statistics for major depressive disorder and osteoarthritis.

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