Supplemental Information

Cohort information

In this study, we made use of in-house samples, as well as data gathered through collaborations and data sharing platforms. In total, 16 cohorts contributed data, which are listed in Table S1 together with demographic information. Table S2 lists the number of subjects with brain disorder diagnoses per cohort. Table S3 lists additional information on each of the cohorts: their source, comments (including funding acknowledgements), and references that can be consulted for detailed descriptions of data gathering characteristics.

Table S1. Demographic information and total hippocampal volume per cohort included in the analyses

Cohort	Sample size	Sex, % male	Age in years (SD)	Hippocampal volume in cubic millimeter (SD)
PING	413	51.8	12.1 (4.9)	7054 (724)
PNC	514	50.6	15.4 (3.6)	7223 (667)
NIMAGE	223	58.7	17.7 (3.6)	6875 (607)
UBA	1024	34.9	22.5 (3.3)	7094 (652)
BIG	2318	47.8	25.5 (10.1)	7398 (738)
UNIBA	361	56.5	28.4 (8.3)	6879 (643)
TOP	1130	53.1	32.4 (10.2)	7289 (733)
HUBIN	174	69.0	42.1 (8.1)	7321 (712)
DEMGEN	40	40.0	44.9 (22.1)	7222 (735)
NCNG	361	32.4	52.2 (17.1)	6822 (766)
UKBB	12634	48.1	55.9 (7.5)	6941 (728)
STROKEMRI	117	41.0	57.9 (15.5)	6760 (745)
HUNT	783	46.5	58.9 (4.2)	6674 (677)
BETULA	328	47.9	62.6 (13.3)	6675 (752)
ADNI2	253	56.9	72.9 (7.1)	6169 (916)
ADNI1	624	57.9	75.5 (6.7)	5583 (1004)
All	21297	48.3	47.8 (17.5)	6961 (798)

SD=standard deviation

Table S2. Brain disorder diagnoses per cohort

Cohort	ADHD	BD	Dementia	HC	MCI	MDD	Prodr.	Subthr. ADHD	SZ	SZ-SIB	SZ BD mix
ADNI1	0	0	137	179	308	0	0	0	0	0	0
ADNI2	0	0	20	106	127	0	0	0	0	0	0
BETULA	0	0	0	328	0	0	0	0	0	0	0
BIG	0	0	0	2318	0	0	0	0	0	0	0
DEMGEN	0	0	0	40	0	0	0	0	0	0	0
HUBIN	0	0	0	94	0	0	0	0	80	0	0
HUNT	0	0	0	783	0	0	0	0	0	0	0
NCNG	0	0	0	361	0	0	0	0	0	0	0
NIMAGE	100	0	0	89	0	0	0	34	0	0	0
PING	0	0	0	413	0	0	0	0	0	0	0
PNC	0	0	0	514	0	0	0	0	0	0	0
STROKEMRI	0	0	0	117	0	0	0	0	0	0	0
TOP	0	211	0	563	0	0	18	0	233	0	105
UBA	0	0	0	1024	0	0	0	0	0	0	0
UKBB	0	0	0	12634	0	0	0	0	0	0	0
UNIBA	0	0	0	270	0	2	0	0	72	17	0

ADHD=attention-deficit/hyperactivity disorder, BD=bipolar disorder, HC=healthy controls, MCI=mild cognitive impairment, MDD=major depressive disorder, Prodr.=prodromal psychosis, subtrh.ADHD= subthreshold ADHD, SZ=schizophrenia, SZ-SIB=SZ siblings

Table S3. Cohorts included in the current study

Cohort	Source	Comment	Reference
ADNI1 ADNI2	http://adni.loni.usc.edu/ http://adni.loni.usc.edu/	Data collection and sharing for this project was funded by the Alzheimer's Disease Neuroimaging Initiative (ADNI) (National Institutes of Health Grant U01 AG024904) and DOD ADNI (Department of Defense award number W81XWH-12-2-0012). ADNI is funded by the National Institute on Aging, the National Institute of Biomedical Imaging and Bioengineering, and through generous contributions from the following: AbbVie, Alzheimer's Association; Alzheimer's Drug Discovery Foundation; Araclon Biotech; BioClinica, Inc.; Biogen; Bristol-Myers Squibb Company; CereSpir, Inc.; Cogstate; Eisai Inc.; Elan Pharmaceuticals, Inc.; Eli Lilly and Company; EuroImmun; F. Hoffmann-La Roche Ltd and its affiliated company Genentech, Inc.; Fujirebio; GE Healthcare; IXICO Ltd.; Janssen Alzheimer Immunotherapy Research & Development, LLC.; Johnson & Johnson Pharmaceutical Research & Development LLC.; Lumosity; Lundbeck; Merck & Co., Inc.; Meso Scale Diagnostics, LLC.; NeuroRx Research; Neurotrack Technologies; Novartis Pharmaceuticals Corporation; Pfizer Inc.; Piramal Imaging; Servier; Takeda Pharmaceutical Company; and Transition Therapeutics. The Canadian Institutes of Health Research is providing funds to support ADNI clinical sites in Canada. Private sector contributions are facilitated by the Foundation for the National Institutes of Health (www.fnih.org). The grantee organization is the Northern California Institute for Research and Education, and the study is coordinated by the Alzheimer's Therapeutic Research Institute at the University of Southern California. ADNI data are disseminated by the Laboratory for Neuro Imaging at the University of Southern California.	(1,2)
BETULA	Authors	Betula was supported by a Wallenberg Scholar Grant (KAW)	(3)
BIG	Authors	This study used the BIG database, which was established in Nijmegen in 2007. This resource is now part of Cognomics, a joint initiative by researchers of the Donders Centre for Cognitive Neuroimaging, the Human Genetics and Cognitive Neuroscience departments of the Radboud University Medical Centre, and the Max Planck Institute for Psycholinguistics. The Cognomics Initiative is supported by the participating departments and centres and by external grants, that is, the Biobanking and Biomolecular Resources Research Infra-structure (Netherlands) (BBMRI-NL), the Hersenstichting Nederland, and the Netherlands Organisation for Scientific Research (NWO). The research leading to these results also received	(4)

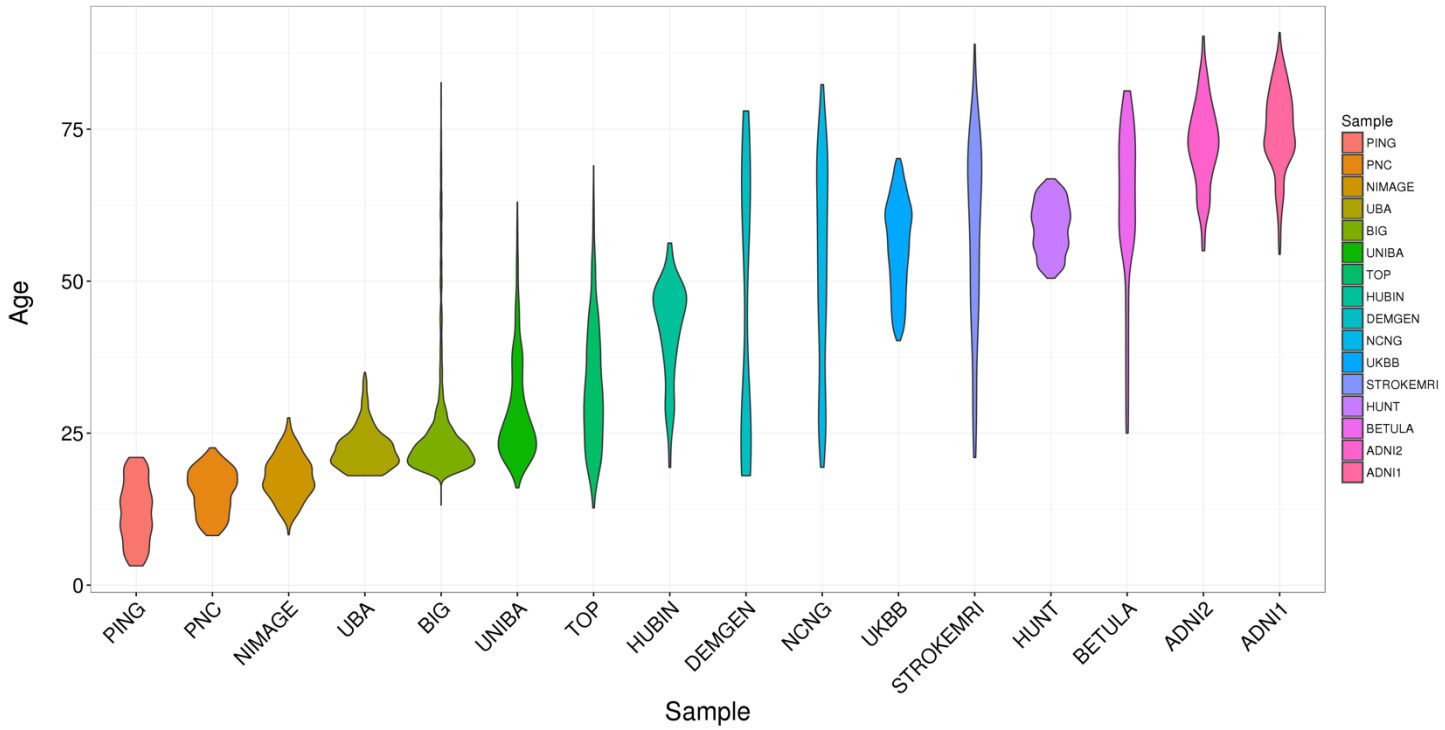
		funding from the European CommunityÕs Seventh Framework Programme (FP7/2007Ð2 013) under grant agreements nû 602805 (Aggresso-type), nû 278948 (TACTICS), and nû 602450 (IMAGEMEND), and from the European CommunityÕs Horizon 2020 Programme (H2020/2014Ð2020) under grant agreement nû 643051 (MiND).In addition, the work was supported by a grant for the ENIGMA Consortium (grant number U54 EB020403) from the BD2K Initiative of a cross-NIH partnership. Barbara Franke is supported by a Vici grant from NWO (grant 016-130-669). The Cognomics Initiative Resource, the Brain Imaging Genetics (BIG) sample (http://www.cognomics.nl), stems from an ongoing study, which started in 2007. The BIG sample is a collection of healthy volunteers aged 18–40 years, who participated in studies at the Donders Centre for Cognitive Neuroimaging (DCCN) of the Radboud University in Nijmegen. Subjects were of Caucasian descent with no self-reported neurological or psychiatric history, and mainly high level of education (80% with bachelor student level or higher). All participants gave written informed consent and the study was approved by the local ethics committee (CMO Region Arnhem-Nijmegen, the Netherlands). The self-reported healthy individuals underwent anatomical MRI scans, usually as part of their involvement in diverse smaller-scale studies at the DCCN. Structural T1-weighted images were acquired using MPRAGE sequence (1.0x1.0 x1.0 mm3 voxel size) with a 1.5T scanner (Sonata and Avanto, Siemens, Erlangen, Germany) or a 3T scanner (Trio and TrioTim, Siemens, Erlangen, Germany).	
DEMGEN	Authors		(5)
HUBIN	Authors	This study was supported by the Swedish Research Council (2006-2992, 2006-986, K2007-62X-15077-04-1, 2008-2167, K2008-62P-20597-01-3. K2010-62X-15078-07-2, K2012-61X-15078-09-3, 2017-00949), the regional agreement on medical training and clinical research between Stockholm County Council and the Karolinska Institutet, the Knut and Alice Wallenberg Foundation, and the HUBIN project	(6)
HUNT	https://www.ntnu.edu/hunt	The HUNT Study is a collaboration between HUNT Research Centre, Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology (NTNU), Nord-Trøndelag County Council, Central Norway Regional Health Authority, and the Norwegian Institute of Public Health. HUNT-MRI and the genetic analysis were funded by grants from the Liaison Committee between the Central Norway Regional Health Authority and NTNU to principal investigator Asta Håberg, and the Norwegian National Advisory Unit for functional MRI. We thank the HUNT MRI participants, MRI	(7,8)

		technicians and the Department of Diagnostic Imaging at Levanger Hospital, Professor Lars Jacob Stovner (NTNU) and the administrative staff at HUNT.	
NCNG	Authors	The sample collection was supported by grants from the Bergen Research Foundation and the University of Bergen, the Dr Einar Martens Fund, the K.G. Jebsen Foundation, the Research Council of Norway, to SLH, VMS, AJL, and TE. The authors thank Dr. Eike Wehling for recruiting participants in Bergen, and Professor Jonn-Terje Geitung and Haraldplass Deaconess Hospital for access to the MRI facility. Additional support by RCN grants 177458/V50 and 231286/F20	(9)
NIMAGE	Authors	This project was supported by grants from National Institutes of Health (grant R01MH62873 to SV Faraone) for initial sample recruitment, and from NWO Large Investment (grant 1750102007010 to JK Buitelaar), NWO Brain & Cognition (grant 433-09-242 to JK Buitelaar), ZonMW Grant 60-60600-97-193, and grants from Radboud University Medical Center, University Medical Center Groningen, Accare, and VU University Amsterdam for subsequent assessment waves. NeuroIMAGE also receives funding from the European Community's Seventh Framework Programme (FP7/2007 – 2013) under grant agreements n° 602805 (Aggressotype), n° 278948 (TACTICS), and n° 602450 (IMAGEMEND), and from the European Community's Horizon 2020 Programme (H2020/2014 – 2020) under grant agreements n° 643051 (MiND) and n° 667302 (CoCA).	(10)
PING	http://pingstudy.ucsd.edu/	Data used in the preparation of this article were obtained from the Pediatric Imaging, Neurocognition and Genetics (PING) Study database (http://ping.chd.ucsd.edu/). PING was launched in 2009 by the National Institute on Drug Abuse (NIDA) and the Eunice Kennedy Shriver National Institute Of Child Health & Human Development (NICHD) as a 2-year project of the American Recovery and Reinvestment Act. The primary goal of PING has been to create a data resource of highly standardized and carefully curated magnetic resonance imaging (MRI) data, comprehensive genotyping data, and developmental and neuropsychological assessments for a large cohort of developing children aged 3 to 20 years. The scientific aim of the project is, by openly sharing these data, to amplify the power and productivity of investigations of healthy and disordered development in children, and to increase understanding of the origins of variation in neurobehavioral phenotypes. For up-to-date information, see http://ping.chd.ucsd.edu/." Data collection and sharing for this project was funded by the Pediatric Imaging, Neurocognition and Genetics Study (PING) (National Institutes of	(11)

		Health Grant RC2DA029475). PING is funded by the National Institute on Drug Abuse and the Eunice Kennedy Shriver National Institute of Child Health & Human Development. PING data are disseminated by the PING Coordinating Center at the Center for Human Development, University of California, San Diego.	
PNC	https://www.med.upenn.edu	Support for the collection of the data sets was provided by grant RC2MH089983 awarded to R. Gur and RC2MH089924 awarded to H. Hakonarson. Subjects were recruited through the Center for Applied Genomics at The Children's Hospital in Philadelphia.	(12,13)
STROKEMRI/ MOT	Authors	Supported by the Research Council of Norway (249795, 248238), the South-Eastern Norway Regional Health Authority (2014097, 2015044, 2015073, 2016083), and the Norwegian ExtraFoundation for Health and Rehabilitation (2015/FO5146).	(14)
TOP	Authors	The work was funded by the Research Council of Norway (213837, 223273, 204966/F20, 213694, 229129, 249795/F20, 248778), the South-Eastern Norway Regional Health Authority (2013-123, 2014-097, 2015-073, #2017-112) and Stiftelsen Kristian Gerhard Jebsen.	(15–18)
UBA	Authors	European Community's Seventh Framework Programme (FP7/2007–2013) grant agreement #602450 (IMAGEMEND); Swiss National Science Foundation (grants 163434, 147570 and 159740)	(19)
UKBB	https://www.ukbiobank.ac.uk/	All subjects with a primary or secondary ICD-10 diagnosis with a mental or neurological disorder were excluded prior to analysis and the remaining subjects included as healthy controls. The used UK Biobank project ID number is #27412.	(20)
UNIBA	Authors	This work was supported by a "Capitale Umano ad Alta Qualificazione" grant by Fondazione Con Il Sud awarded to Alessandro Bertolino and by a Hoffmann-La Roche Collaboration Grant awarded to Giulio Pergola. This project has received funding from the European Union Seventh Framework Programme for research, technological development and demonstration under grant agreement no. 602450 (IMAGEMEND). This paper reflects only the author's views and the European Union is not liable for any use that may be made of the information contained therein.	(21)

Figure S1. Demographics distributions per sample. Figure S1A shows the distribution of age in years (on the y-axis) per cohort (indicated on the x-axis), sorted by increasing mean age. Figure S1B visualizes the mean hippocampal volume in cubic millimeter (on the y-axis) per cohort (on the x-axis).

A



B

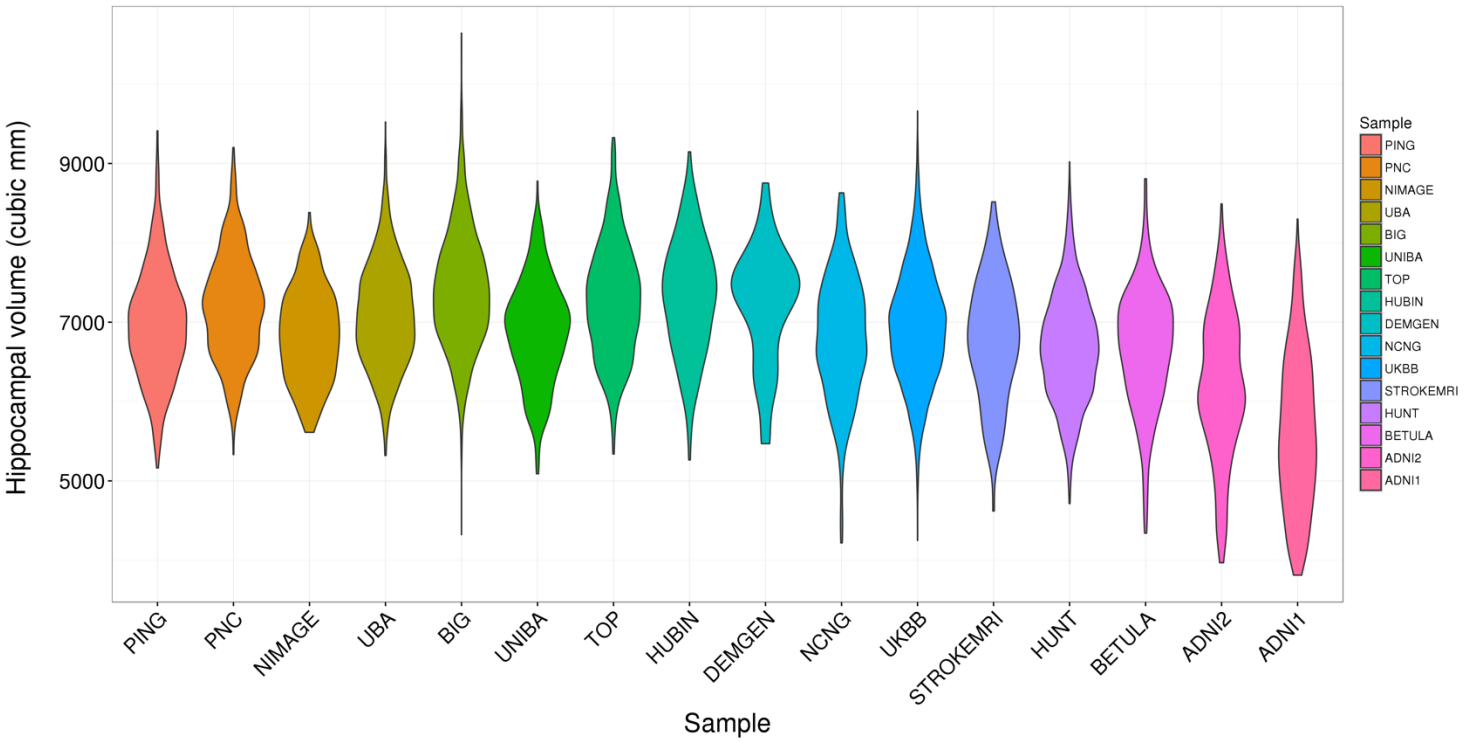


Figure S2. Volume per hippocampal subfield. The y-axis shows the volume in cubic millimeter per subfield, indicated on the x-axis. The lower, middle and upper lines of the boxes indicate the 25th, 50th (i.e. median) and 75th percentile, respectively. The whiskers indicate +/- 1.5 times interquartile range above/below the quartiles.

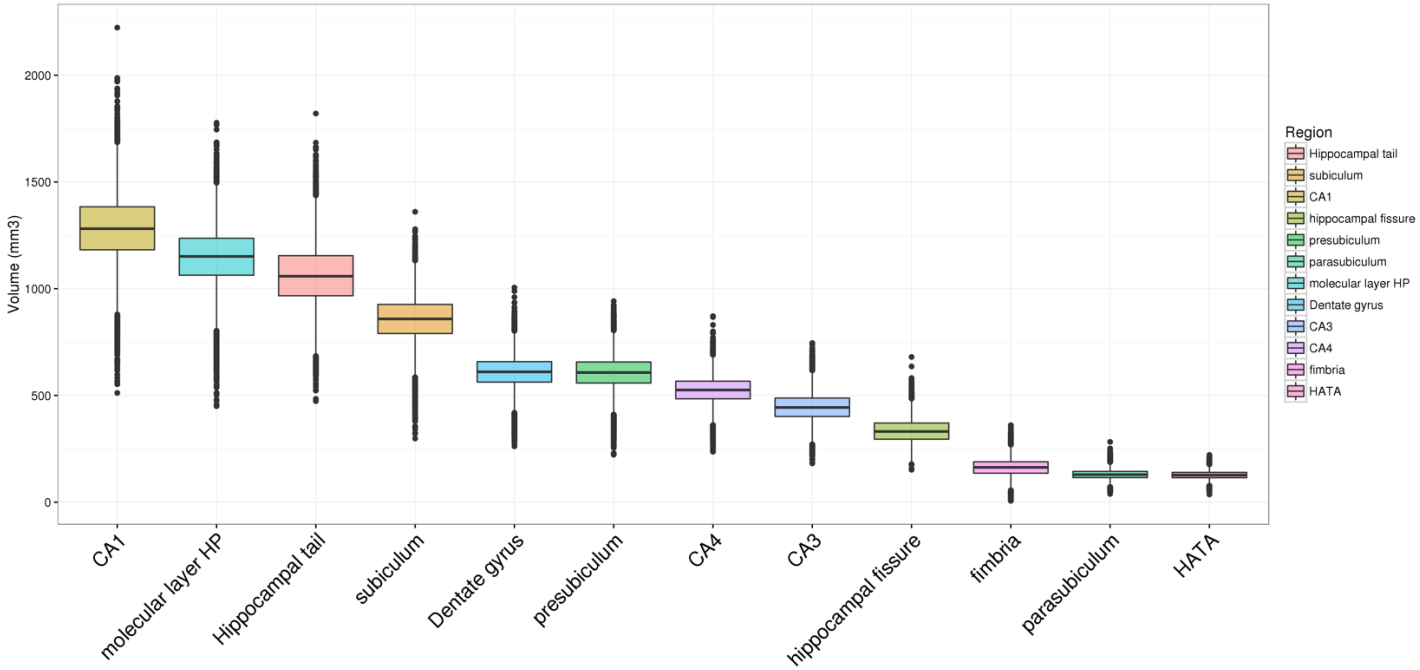


Image preprocessing and quality control

Raw data for all individuals was stored and analysed locally at the University of Oslo, where we deployed a harmonized analysis protocol applied to each individual subject raw data. We performed automated surface-based morphometry and subcortical segmentation using Freesurfer v5.3. Several of the samples were carefully screened by trained research personnel to identify segmentation errors, assess the quality of each subject's brain images manually, edit segmentation where possible and to exclude bad data. However, due to the vast number of subjects it was not feasible to manually check the segmentation of all images. We therefore deployed an automated quality control protocol that excluded potential outliers based on global data quality measures (in addition to the described manual exclusions). In brief, we regressed age, age^2, sex and scanning site from mean cortical thickness, cortex volume, subcortical gray matter volume and from estimated total intracranial volume. Next, we z-standardized the resulting absolute of the residuals and excluded those subjects that exceeded pre-defined standard deviation (SD) thresholds. Before the analyses, we excluded individuals identified by manual QC as well as those exceeding a threshold of 4 SD on any of the regions of interest or ICV.

Freesurfer v5.3 vs v6.0

The vast majority of structural MRI scans available for this study had already been preprocessed with FreeSurfer v5.3. Given the large computational cost of re-processing these scans with FreeSurfer v6.0, we decided to stick with this version and run the v6.0 hippocampal subfield segmentation on top. We did perform a sanity check: First, we ran the recon-all –all stream from v6.0, followed by the v6.0 hippocampal subfield segmentation for fifty participants. We then correlated the resulting hippocampal subfield estimates with those obtained through the combination of v5.3 for the main segmentation with v6.0 for the subfield segmentation for these same fifty subjects. The resulting correlation per subfield is shown below.

Subfield	Correlation
Hippocampal tail	0.96
Subiculum	0.95
CA1	0.93
Hippocampal fissure	0.94
Presubiculum	0.94
Parasubiculum	0.87
Molecular layer	0.93
Dentate gyrus	0.91
CA3	0.92
CA4	0.89
Fimbria	0.89
HATA	0.93
Whole hippocampus	0.95

Genotyping and quality control

Genetic data were obtained at each site using commercially available genotyping platforms. For all cohorts except BIG and UK Biobank (UKBB), we carried out phasing and imputation in-house according to protocols in line with those applied by the ENIGMA consortium (http://enigma.ini.usc.edu). This consisted of standard pre-imputation quality controls, excluding markers exhibiting high rates of genotyping missingness (above 5%), minor allele frequency (MAF) below 1% or deviating from Hardy Weinberg equilibrium ($p<1*10^{-6}$). Individuals exhibiting high rates of genotyping missingness (above 5%), cryptic relatedness (pi-hat above 18.5%) or genome-wide heterozygosity (outside mean ±4 SD of the sample) were removed from the analyses. We restricted our analyses to those with European ancestry as determined through multidimensional scaling (MDS). MACH (http://www.sph.umich.edu/csg/abecasis/MACH) was used to impute the genotypes onto the reference haplotypes from the 1000 Genomes Project (build 37, assembly hg19). After imputation, genetic data were further quality checked to remove poorly imputed SNPs (estimated $R^2<0.3$) and those with low MAF (<5%) or failing HWE at $1x10^{-6}$. For UKBB and BIG, we used the provided imputed data, which were processed with established protocols.[24,25] We further carried out the same post-imputation QC steps as described for the other samples.

Table S3. Genome-wide complex trait analysis heritability estimates, with full test statistics.

ROI	*H2*	*SE*	*Pval*
Hippocampal tail	0.27	0.02	1.00e-16
Subiculum	0.22	0.02	1.00e-16
CA1	0.22	0.02	1.00e-16
Hippocampal fissure	0.20	0.02	1.00e-16
Presubiculum	0.21	0.02	1.00e-16
Parasubiculum	0.14	0.02	1.00e-16
Molecular layer HP	0.21	0.02	1.00e-16
Dentate gyrus	0.22	0.02	1.00e-16
CA3	0.24	0.02	1.00e-16
CA4	0.22	0.02	1.00e-16
Fimbria	0.17	0.02	1.00e-16
HATA	0.17	0.02	1.00e-16
Whole hippocampus	0.23	0.02	1.00e-16
Lateral ventricle	0.16	0.02	1.00e-16
Cerebellum	0.25	0.02	1.00e-16
Thalamus	0.20	0.02	1.00e-16
Caudate	0.25	0.02	1.00e-16
Putamen	0.22	0.02	1.00e-16
Pallidum	0.16	0.02	1.00e-16
Brain stem	0.27	0.02	1.00e-16
Amygdala	0.17	0.02	1.00e-16
Accumbens	0.17	0.02	1.00e-16
Frontal	0.18	0.02	1.00e-16
Parietal	0.18	0.02	1.00e-16
Temporal	0.20	0.02	1.00e-16
Occipital	0.25	0.02	1.00e-16
Cingulate	0.15	0.02	1.00e-16
Insular	0.22	0.02	1.00e-16

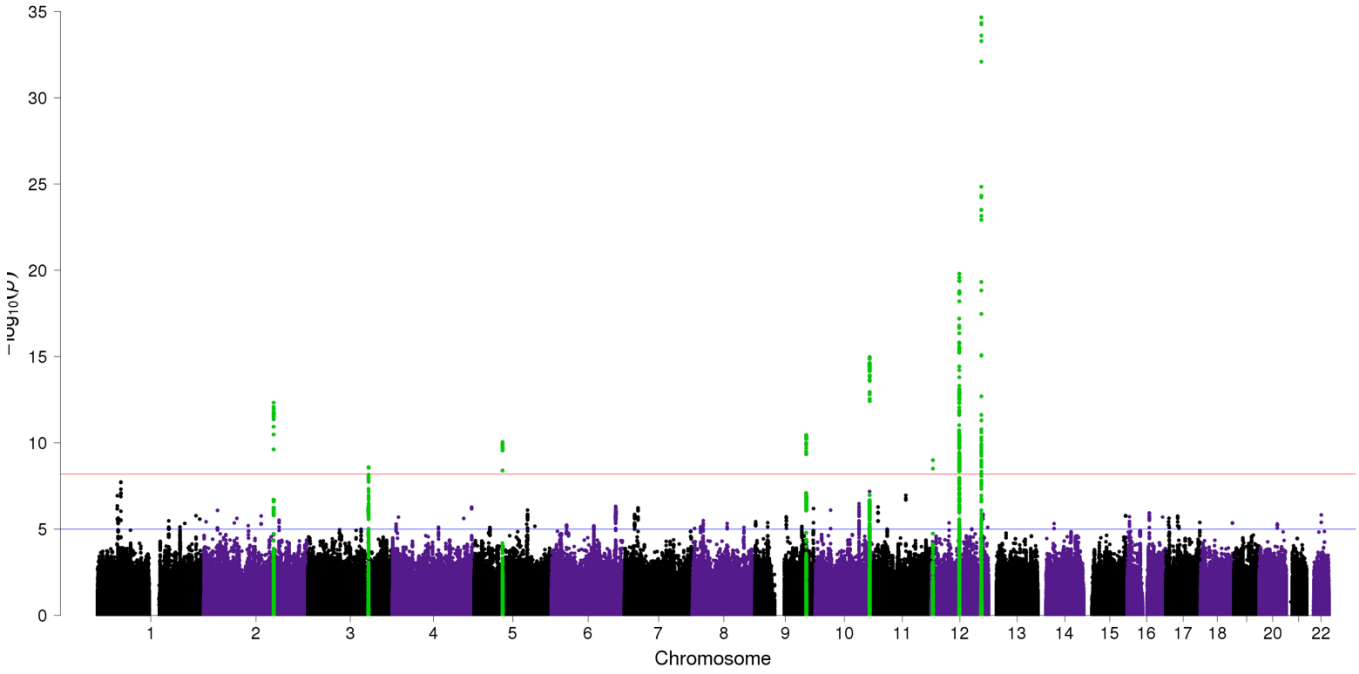
ROI=Region of interest, H2=Heritability, SE=Standard error, Pval=P-value

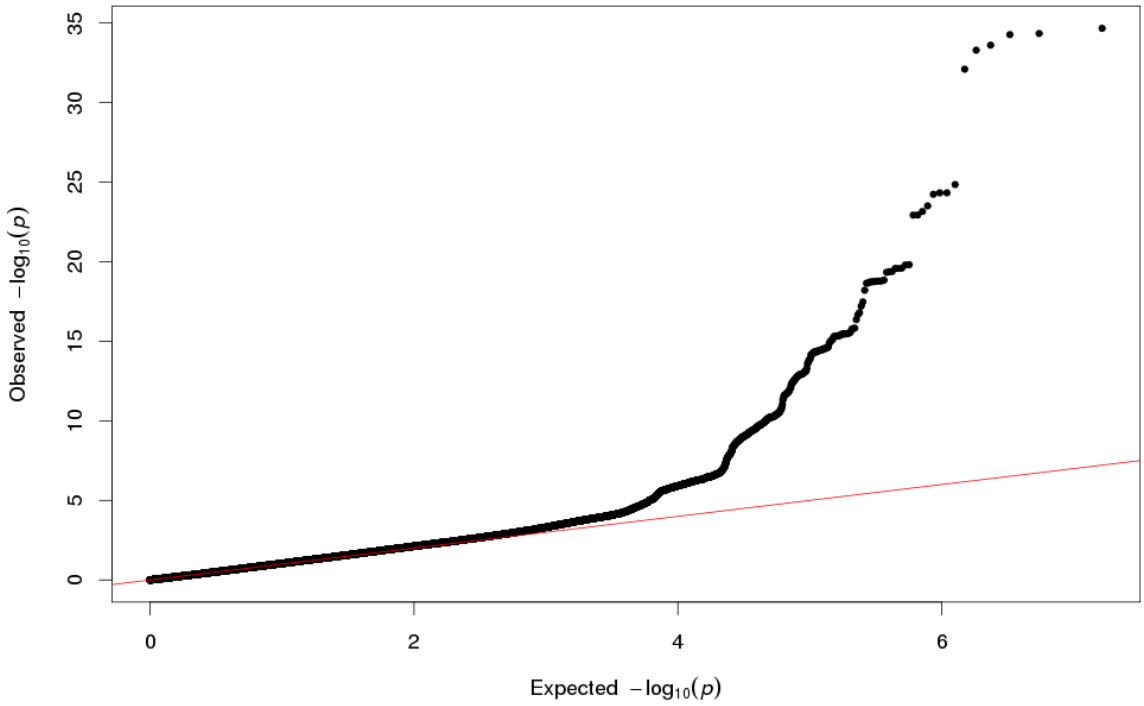
Table S4. Genetic correlation, calculated through linkage disequilibrum score regression (LDSC), of Alzheimer's disease and schizophrenia diagnosis with each of the subfields, corrected for total hippocampal volume.

Structure	Alzheimer's disease			Schizophrenia		
	Rg	SE	P-value	Rg	SE	P-value
Whole hippocampus	-0.056	0.103	0.585	-0.032	0.04	0.429
Parasubiculum	0.177	0.102	0.083	-0.007	0.046	0.878
Presubiculum	0.143	0.098	0.145	-0.001	0.042	0.977
Subiculum	0.071	0.111	0.519	0.063	0.048	0.187
CA1	-0.088	0.106	0.403	0.02	0.05	0.693
CA3	-0.081	0.084	0.334	-0.054	0.038	0.153
CA4	-0.12	0.097	0.216	-0.06	0.045	0.184
Granule cell layer DG	-0.117	0.096	0.219	-0.064	0.045	0.153
HATA	-0.188	0.107	0.079	-0.067	0.047	0.152
Fimbria	-0.246	0.13	0.058	-0.055	0.052	0.295
Molecular layer DG	-0.086	0.107	0.421	0.011	0.052	0.829
Hippocampal fissure	-0.149	0.105	0.153	0.081	0.052	0.118
Hippocampal tail	0.108	0.092	0.241	0.037	0.045	0.405

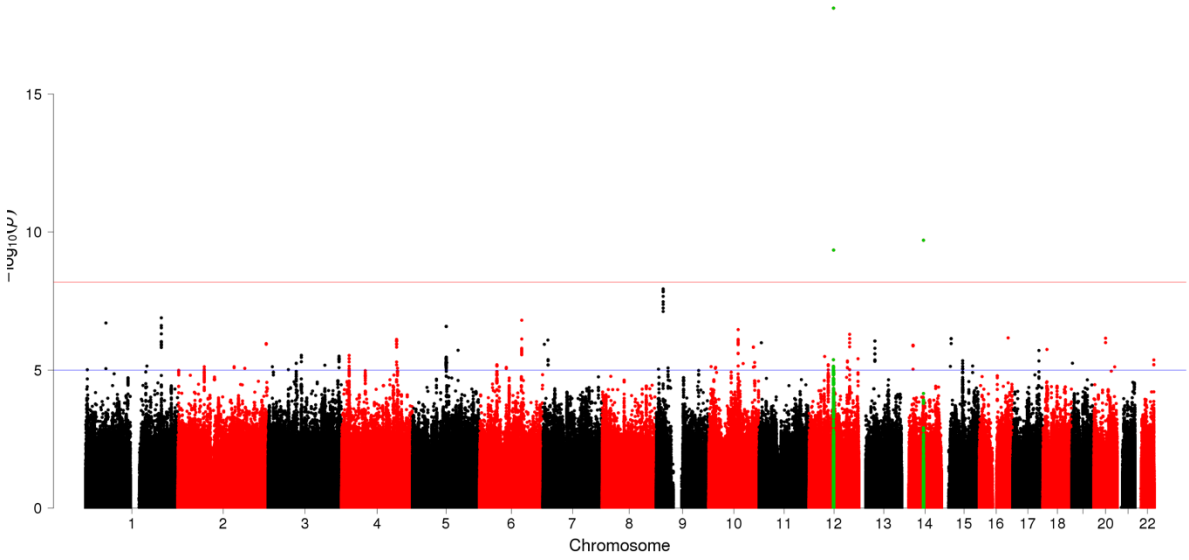
Figure S3. Manhattan and QQ plots for whole hippocampus and per subfield. For the manhattan plots, the red line indicates the adjusted whole-genome significance threshold (6.5x10-9 p-value), the blue line the suggestive threshold (1x10-5).

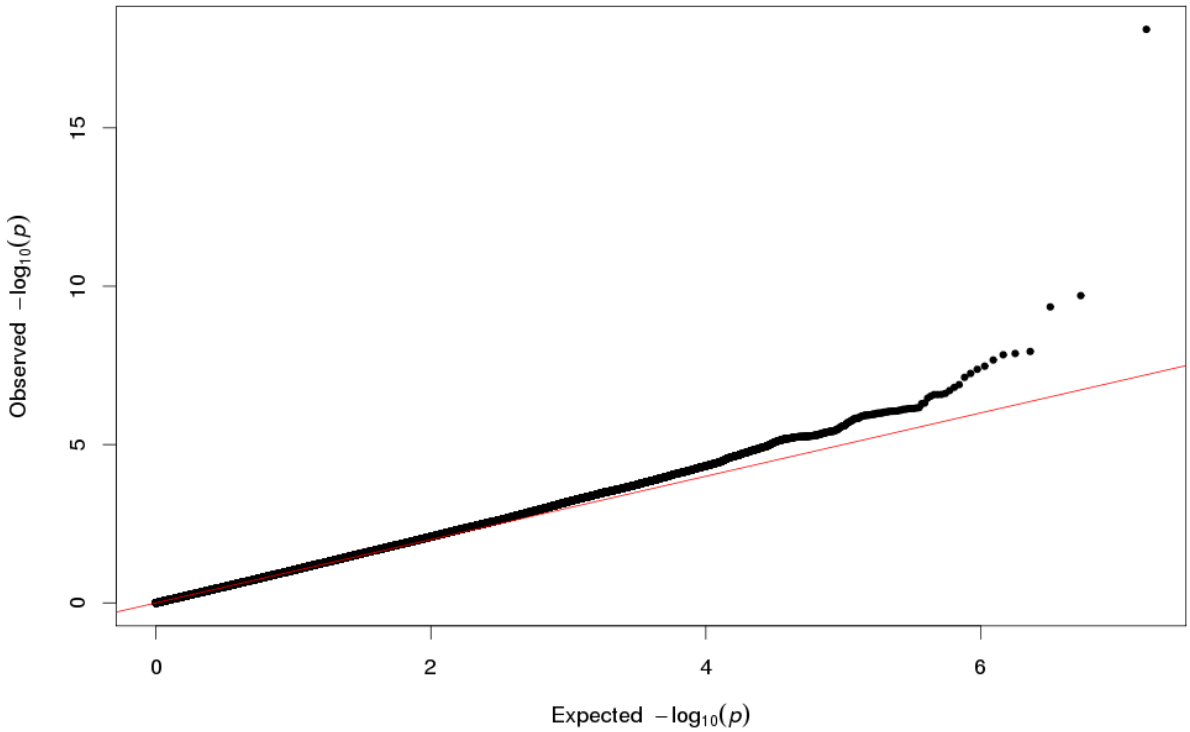
Whole hippocampus



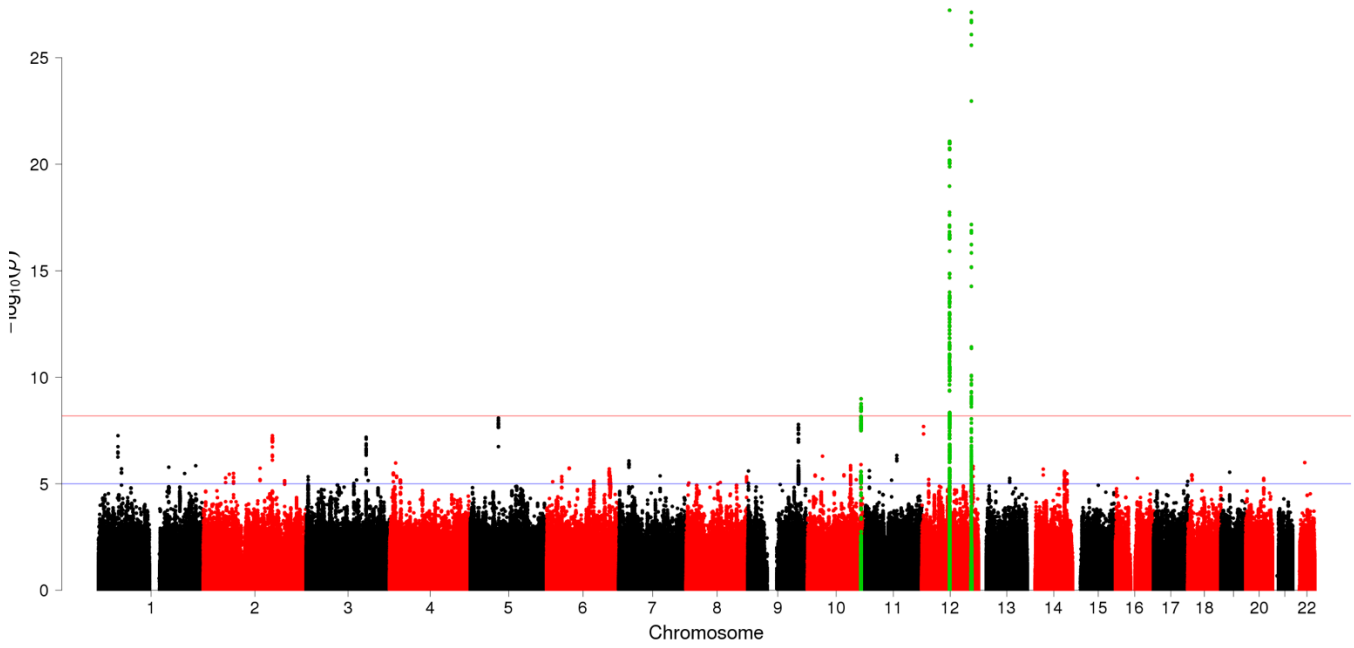


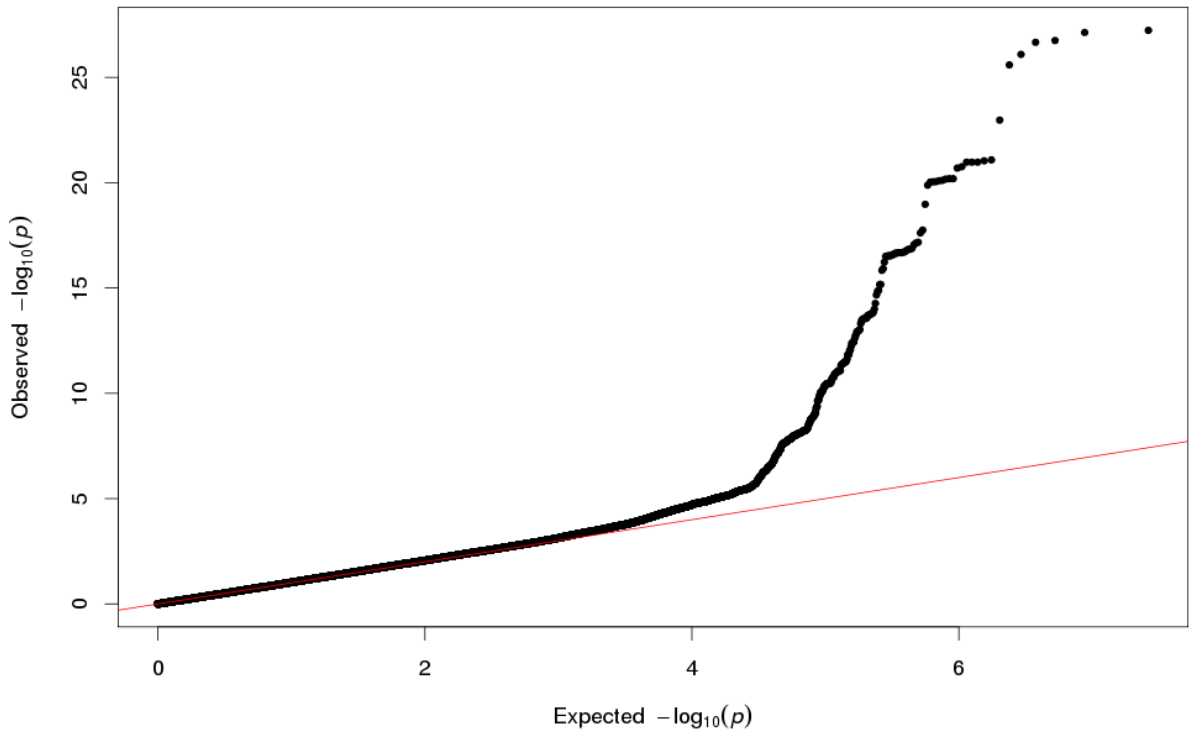
CA1 corrected for total hippocampal volume



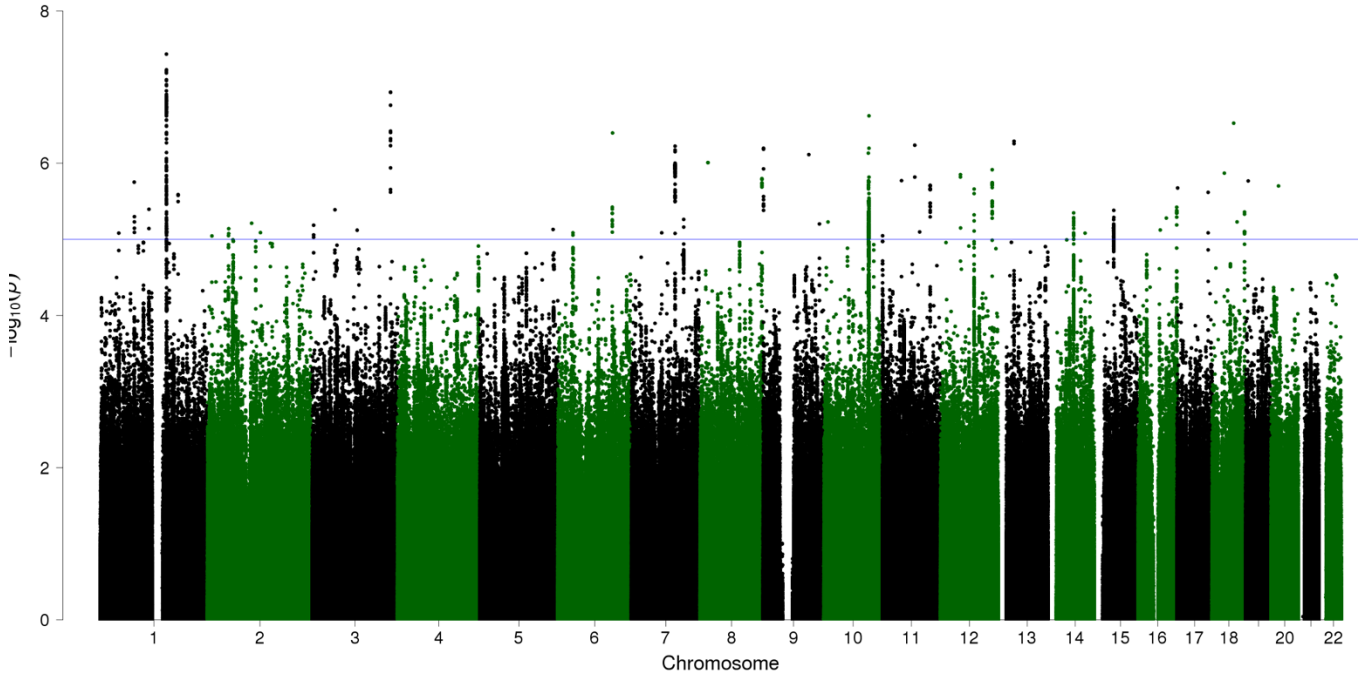


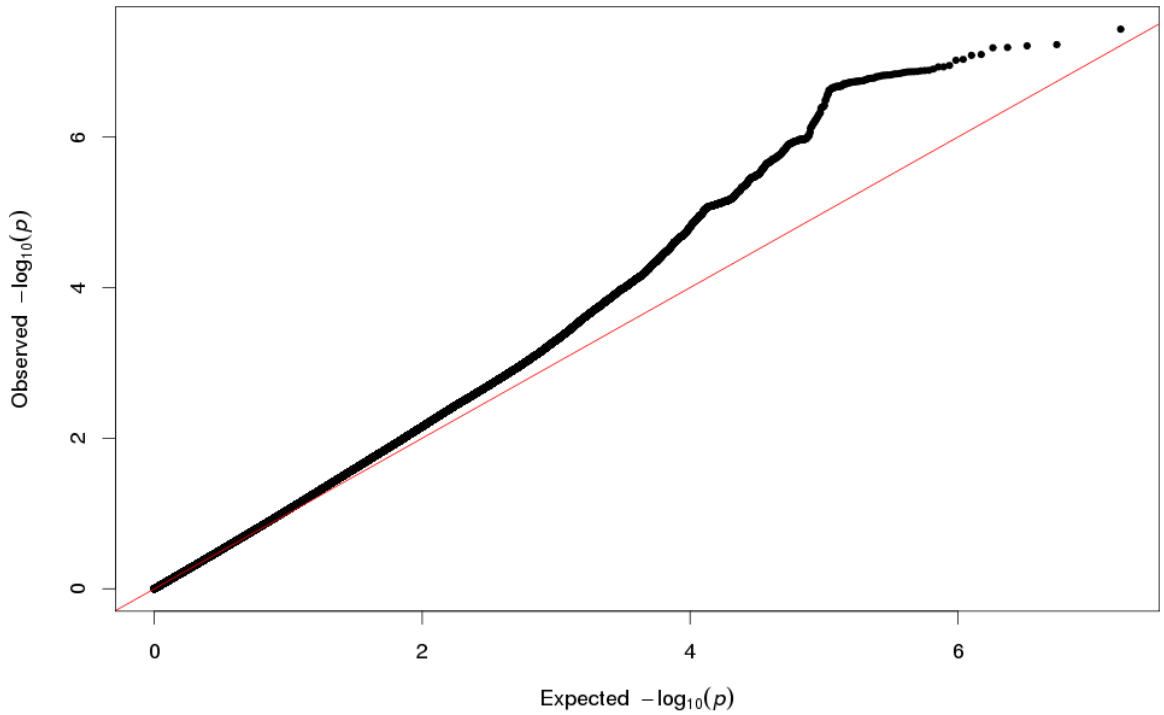
CA1 uncorrected for total hippocampal volume



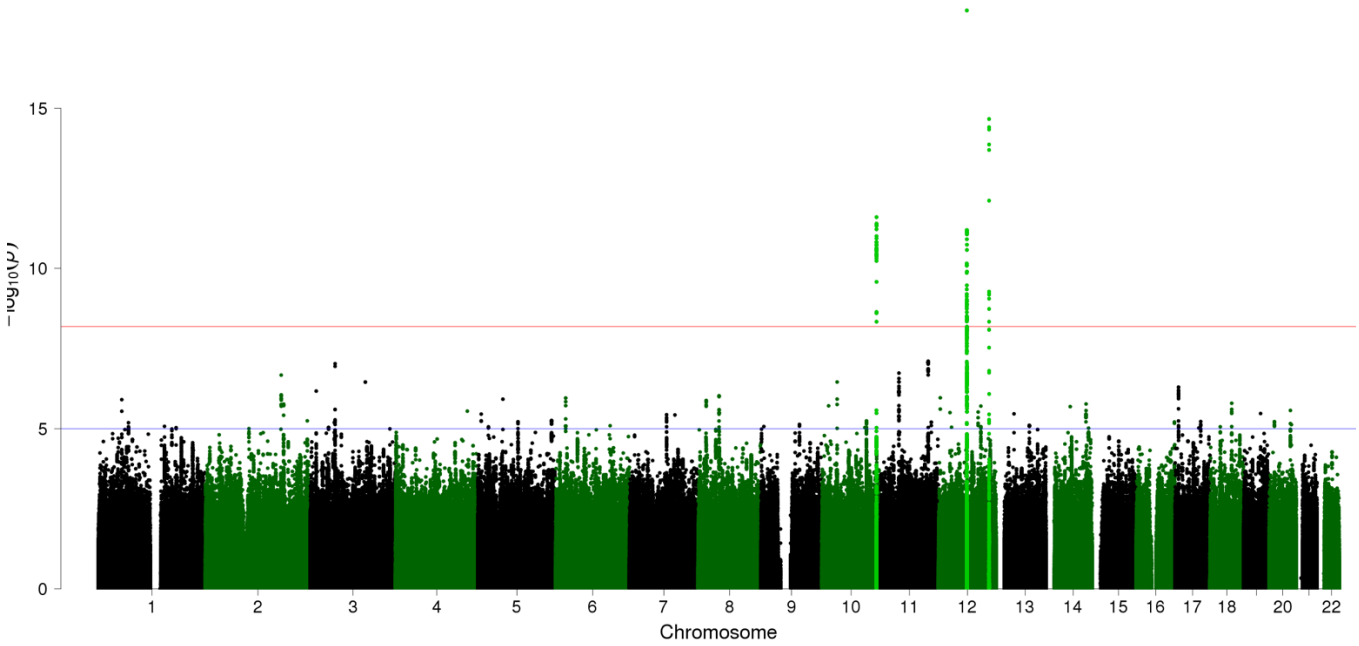


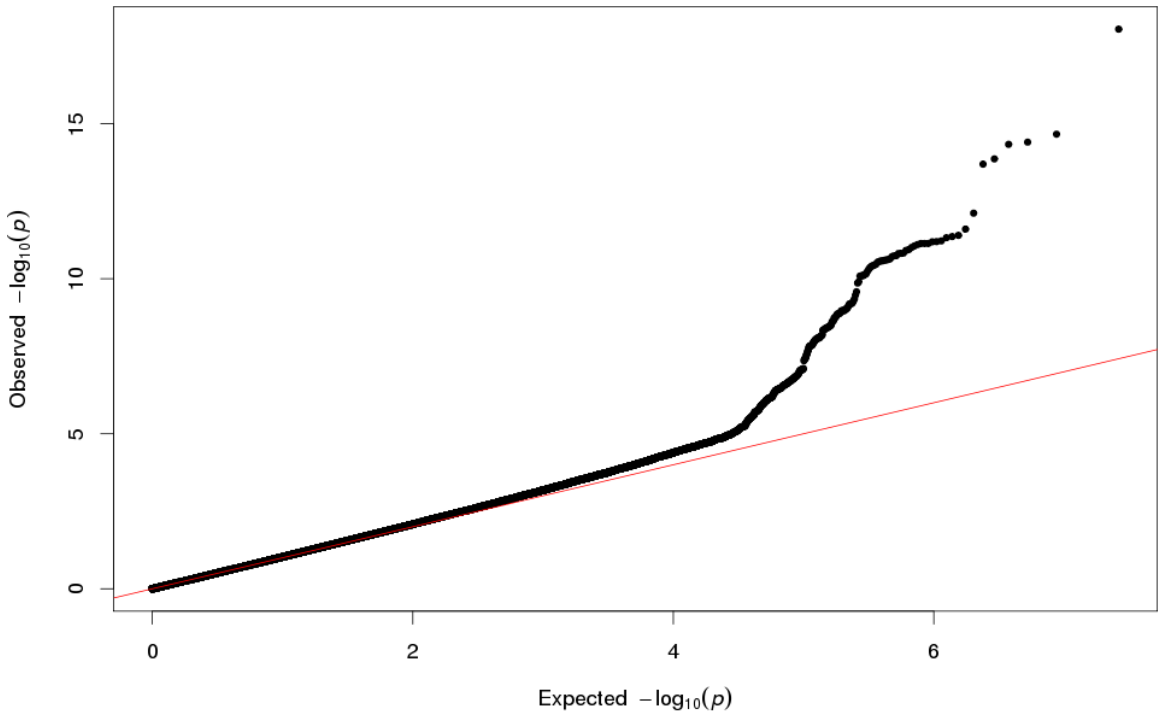
CA3 corrected for total hippocampal volume



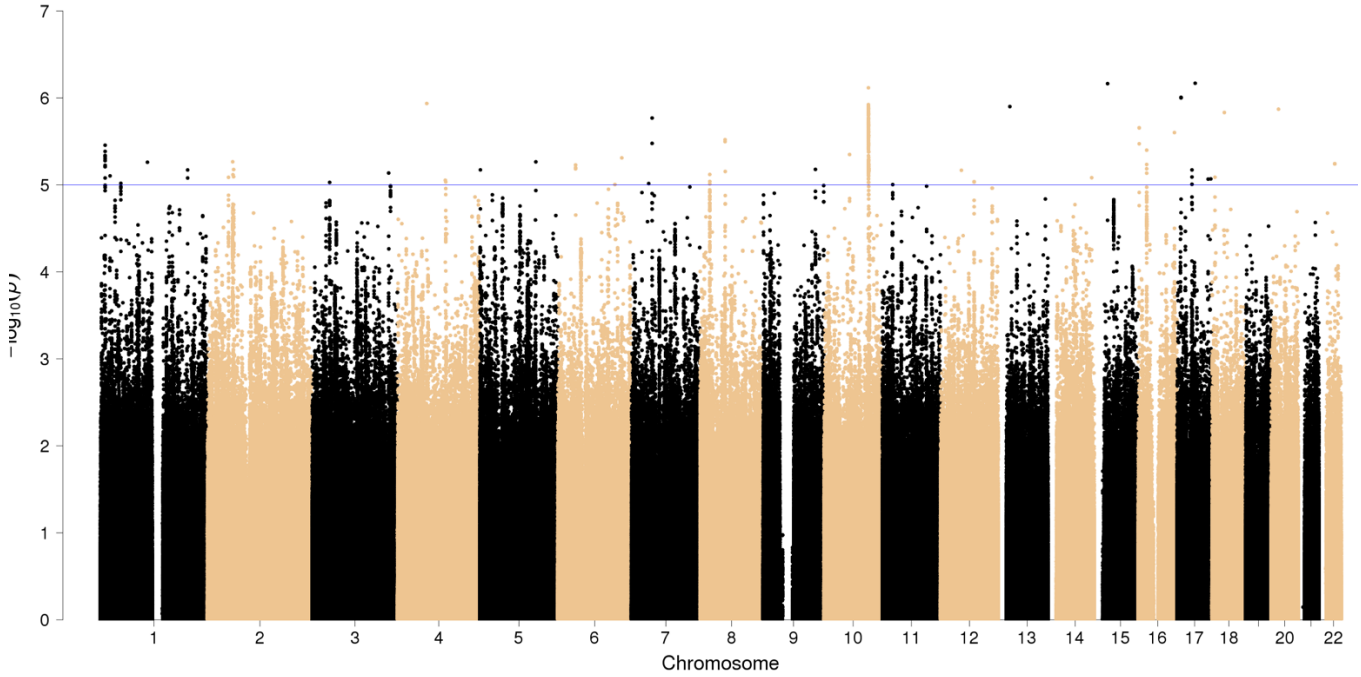


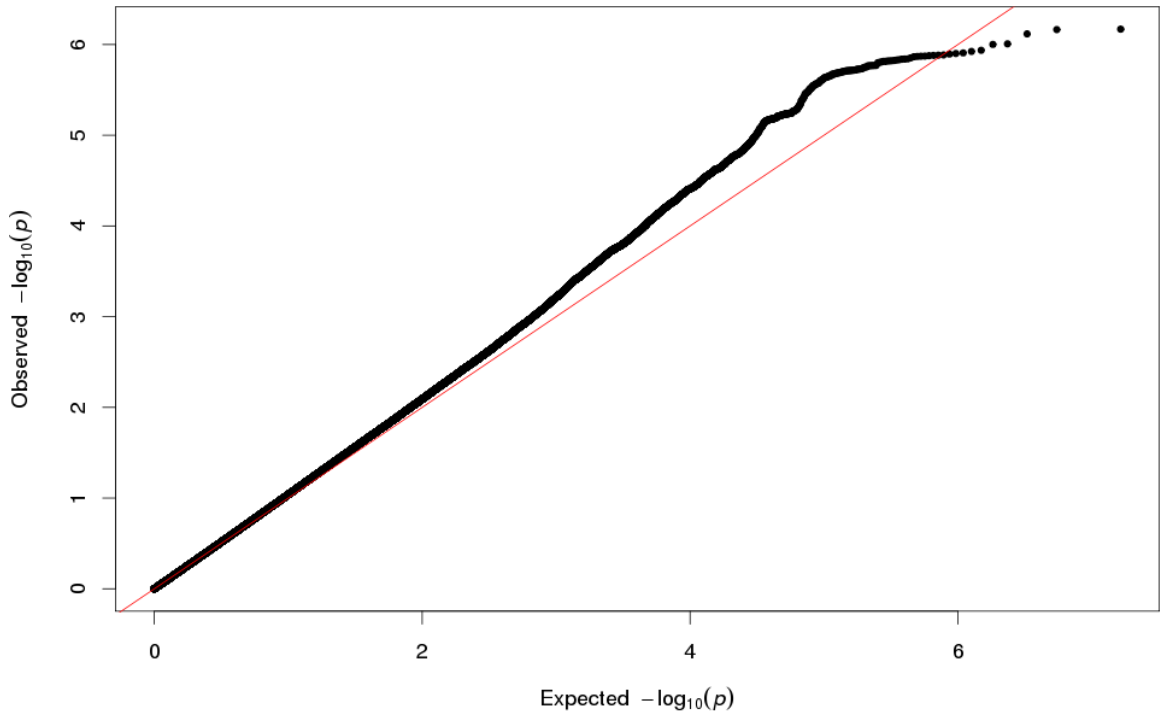
CA3 uncorrected for total hippocampal volume



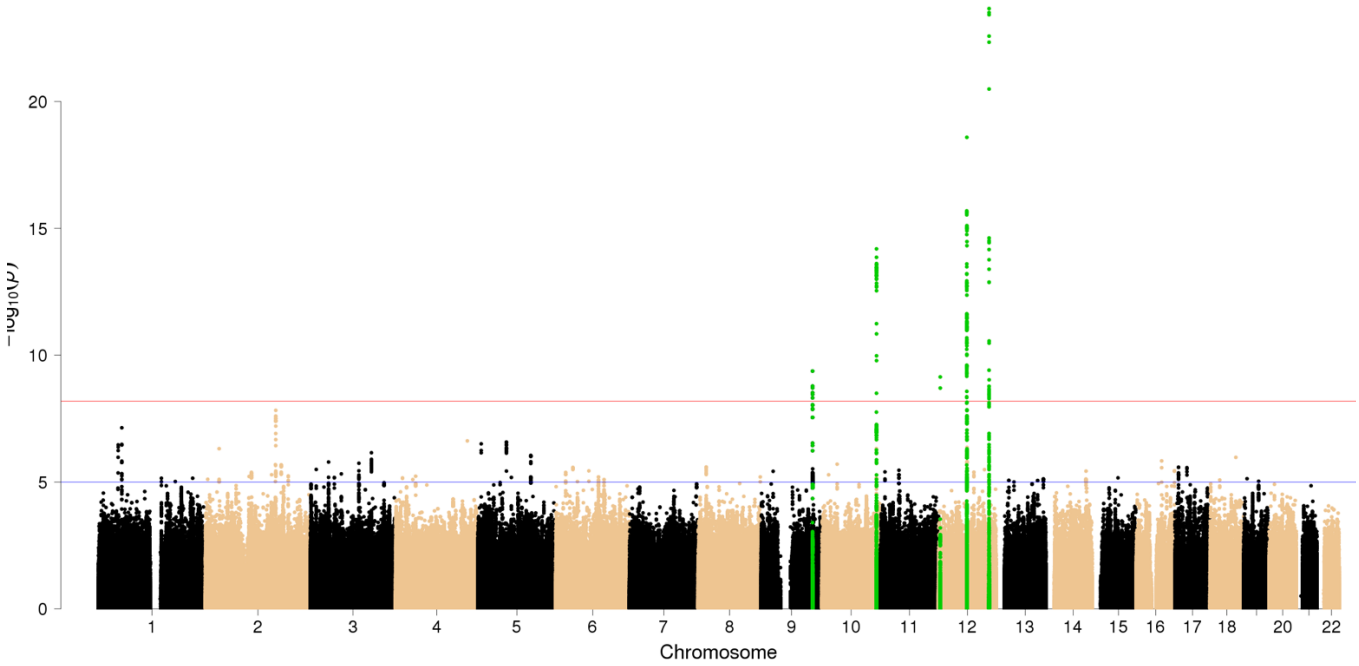


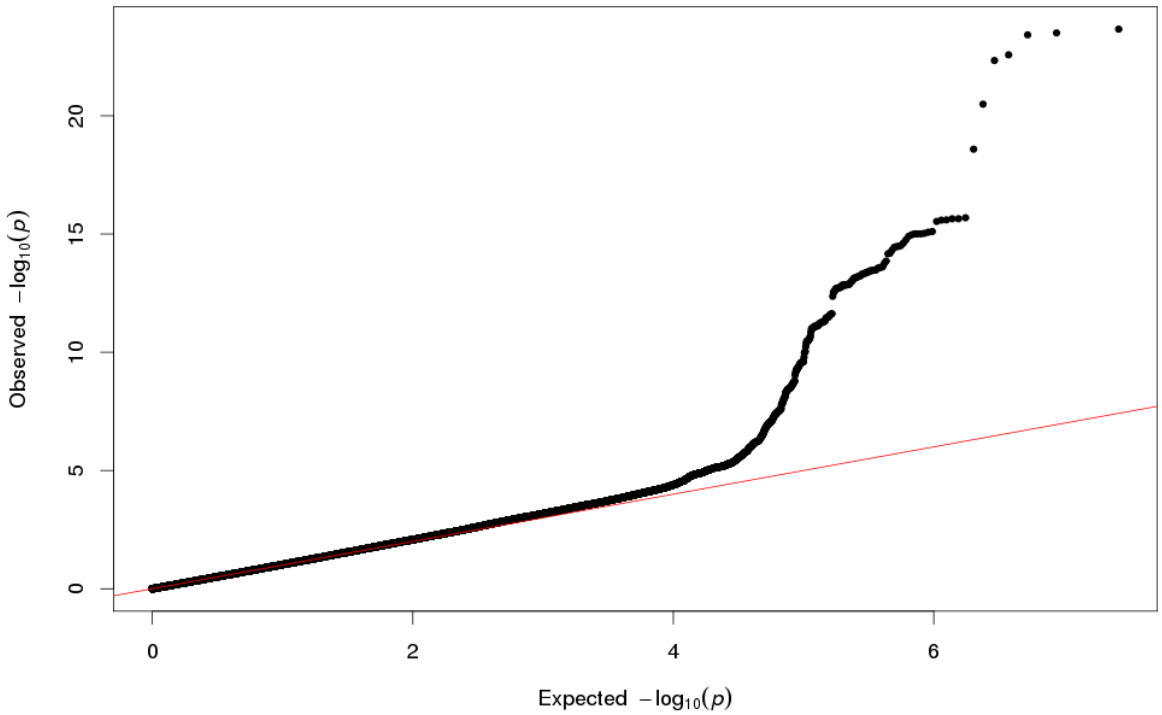
CA4 corrected for total hippocampal volume



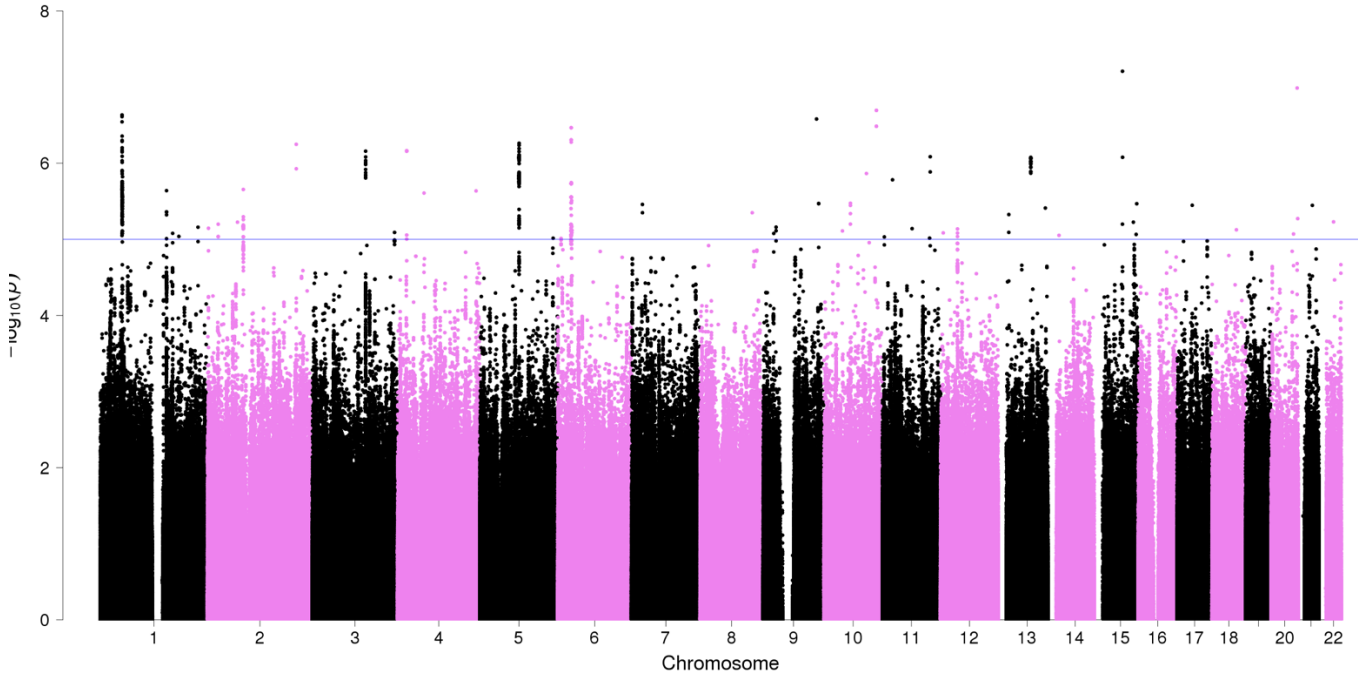


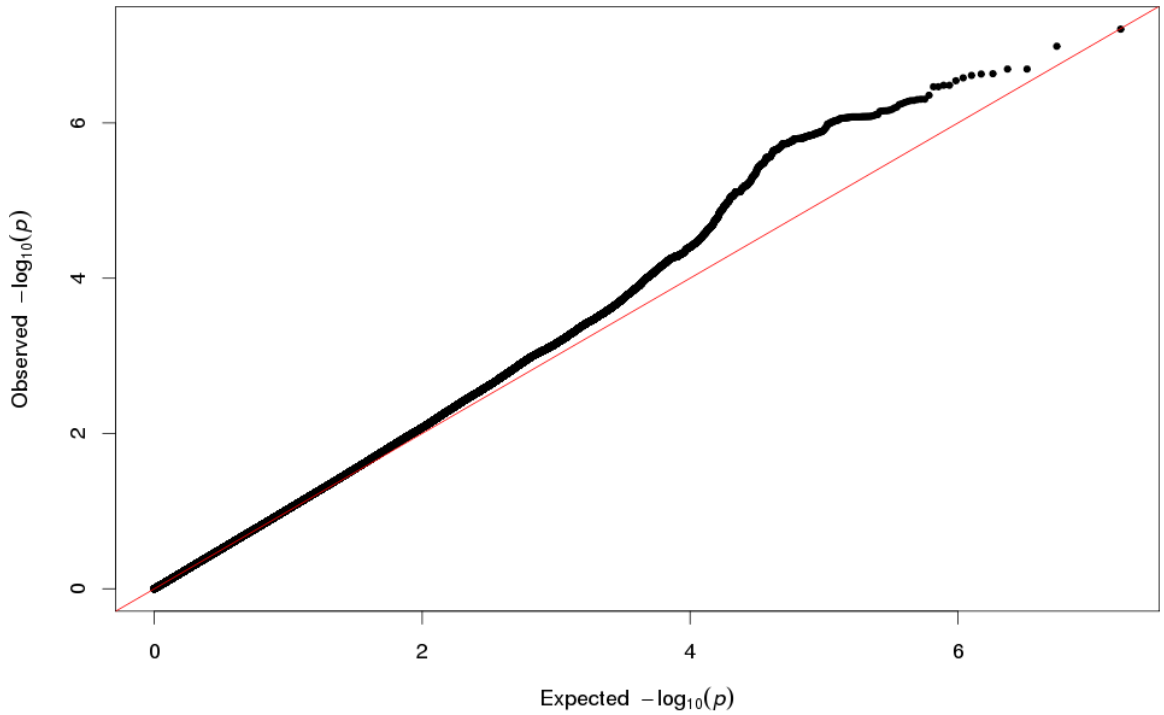
CA4 uncorrected for total hippocampal volume



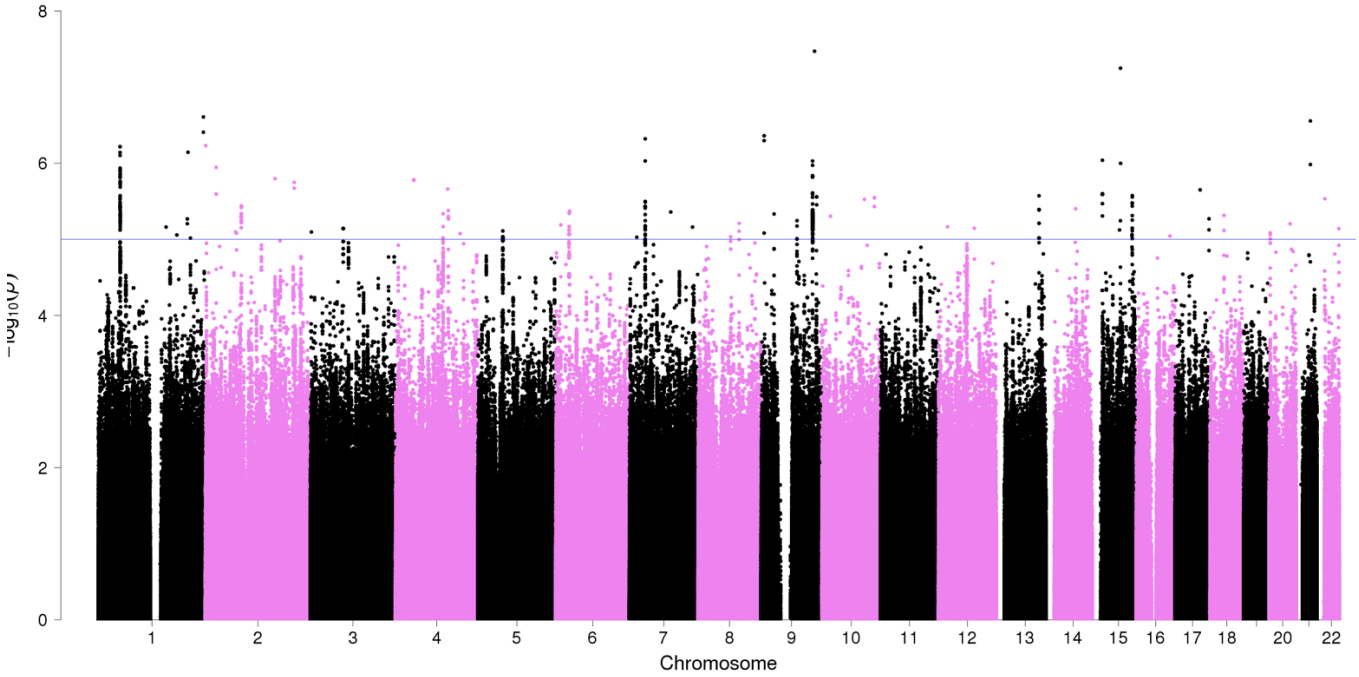


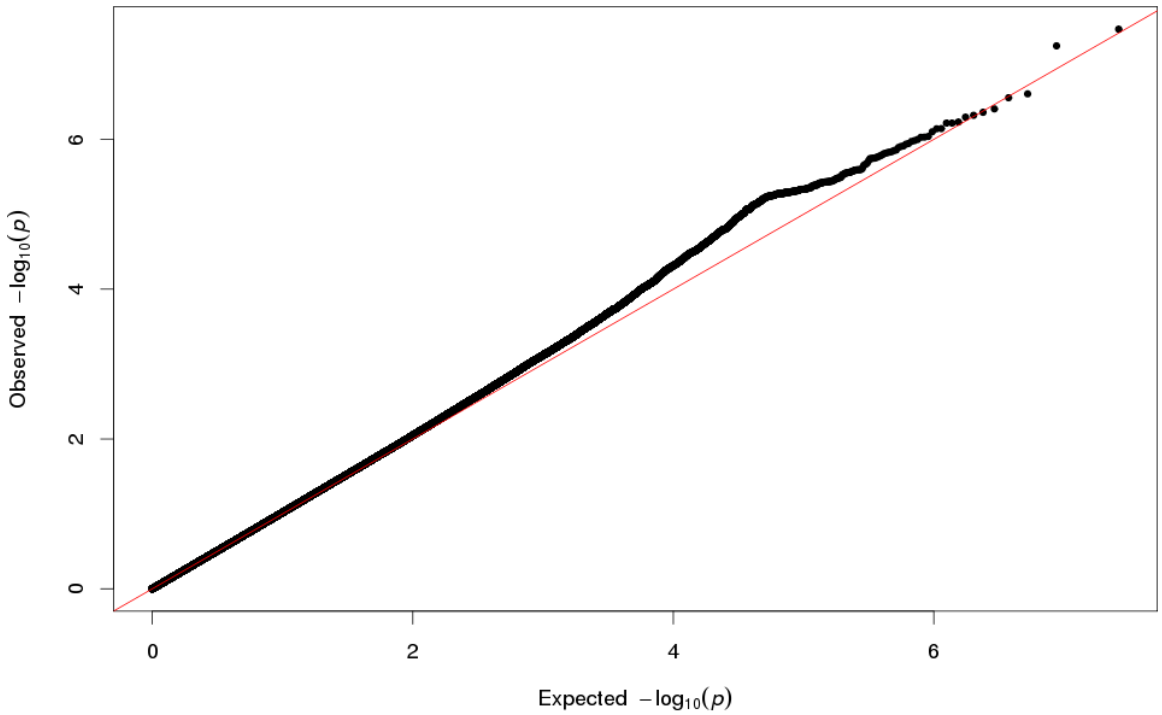
Fimbria corrected for total hippocampal volume



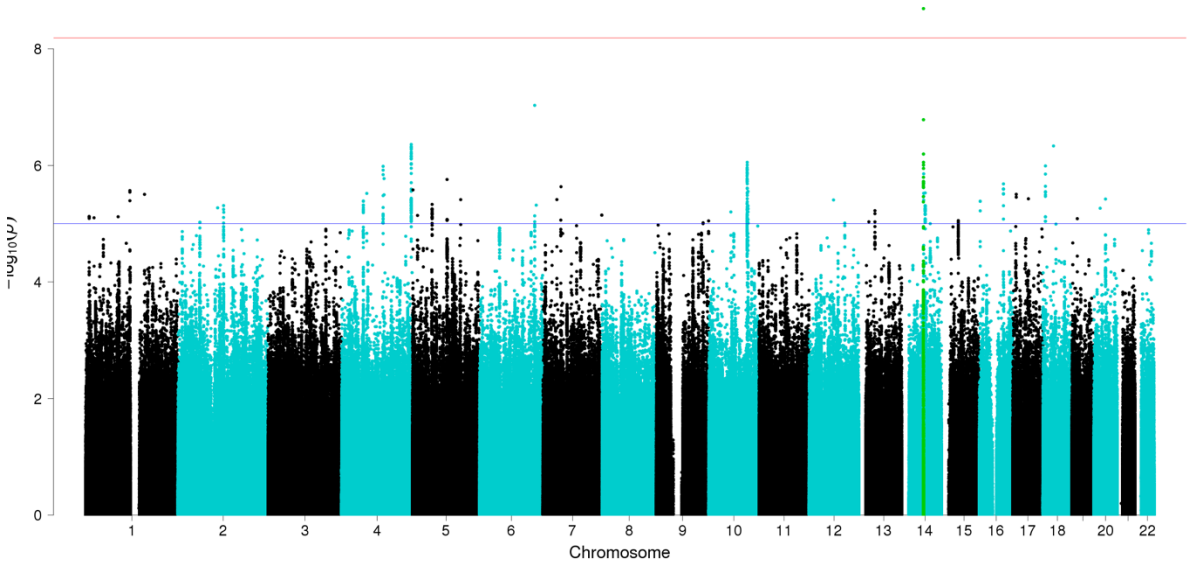


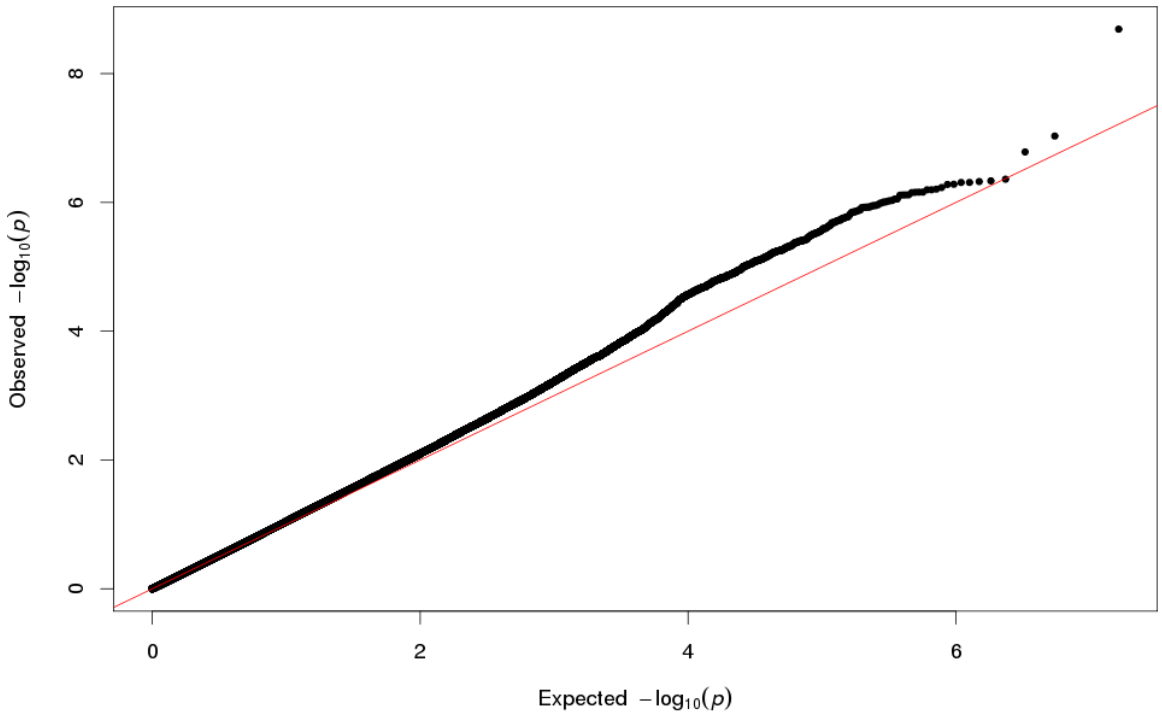
Fimbria uncorrected for total hippocampal volume



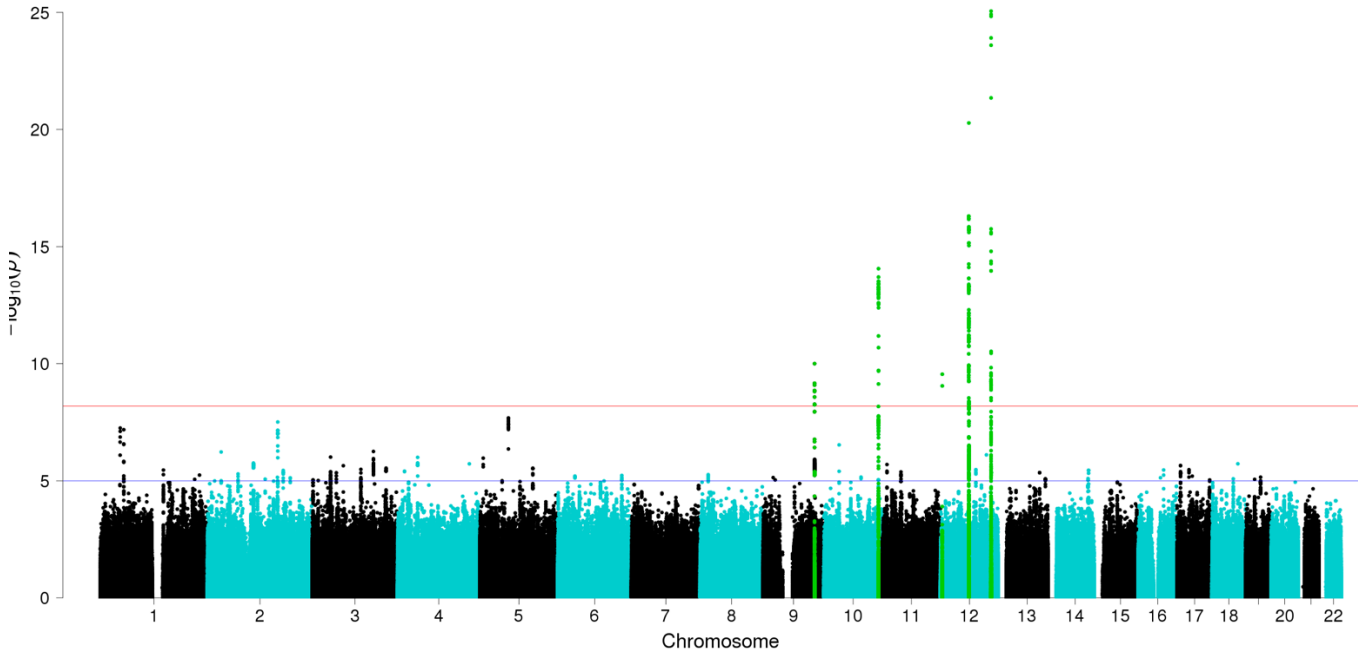


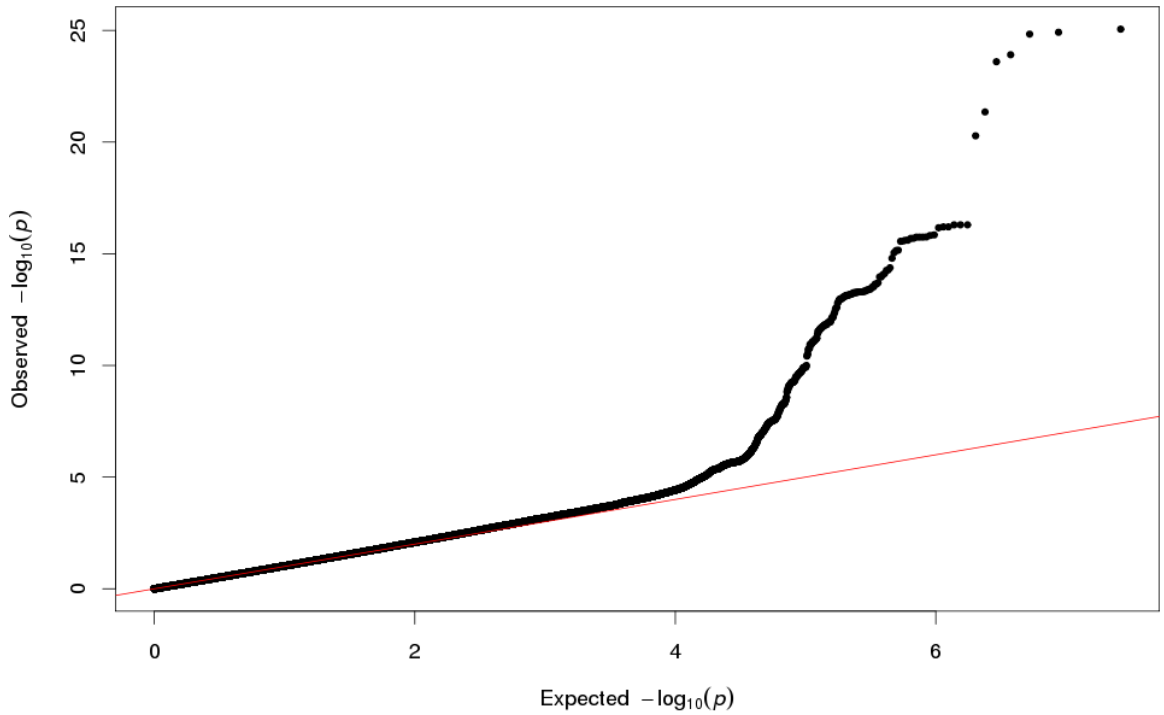
Granule Cell Layer Dentate Gyrus corrected for total hippocampal volume



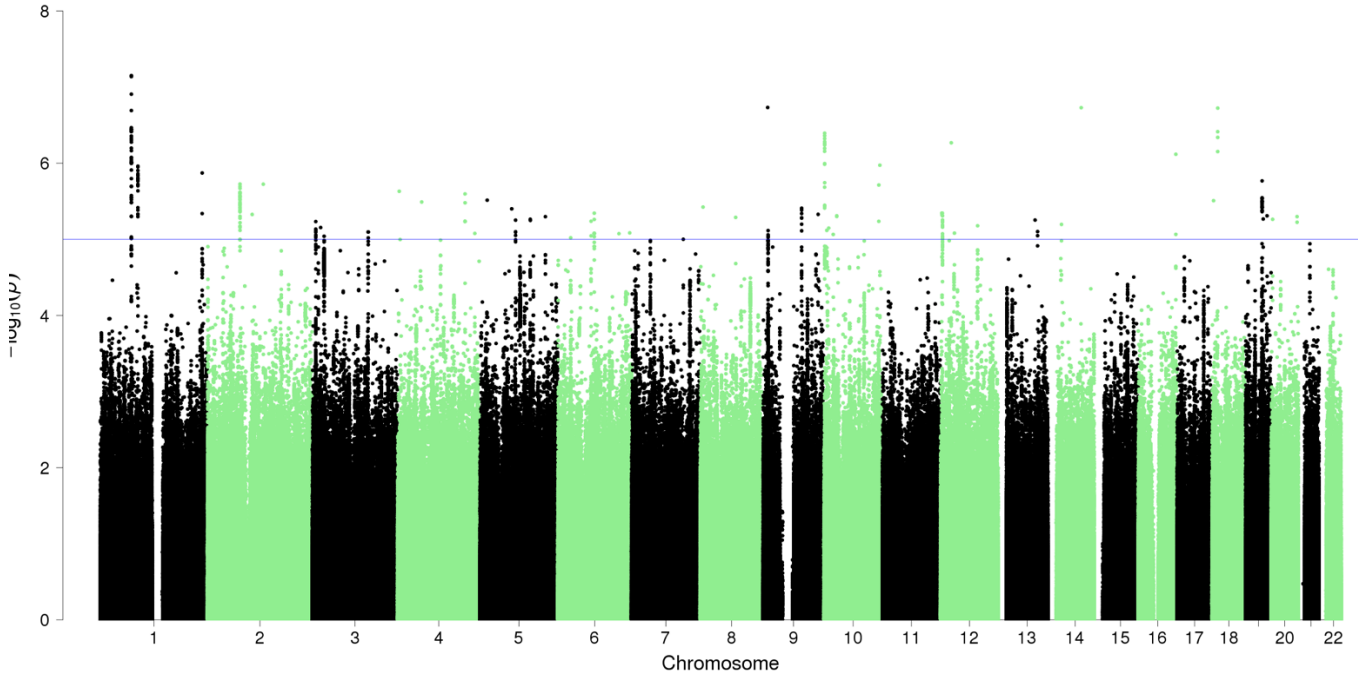


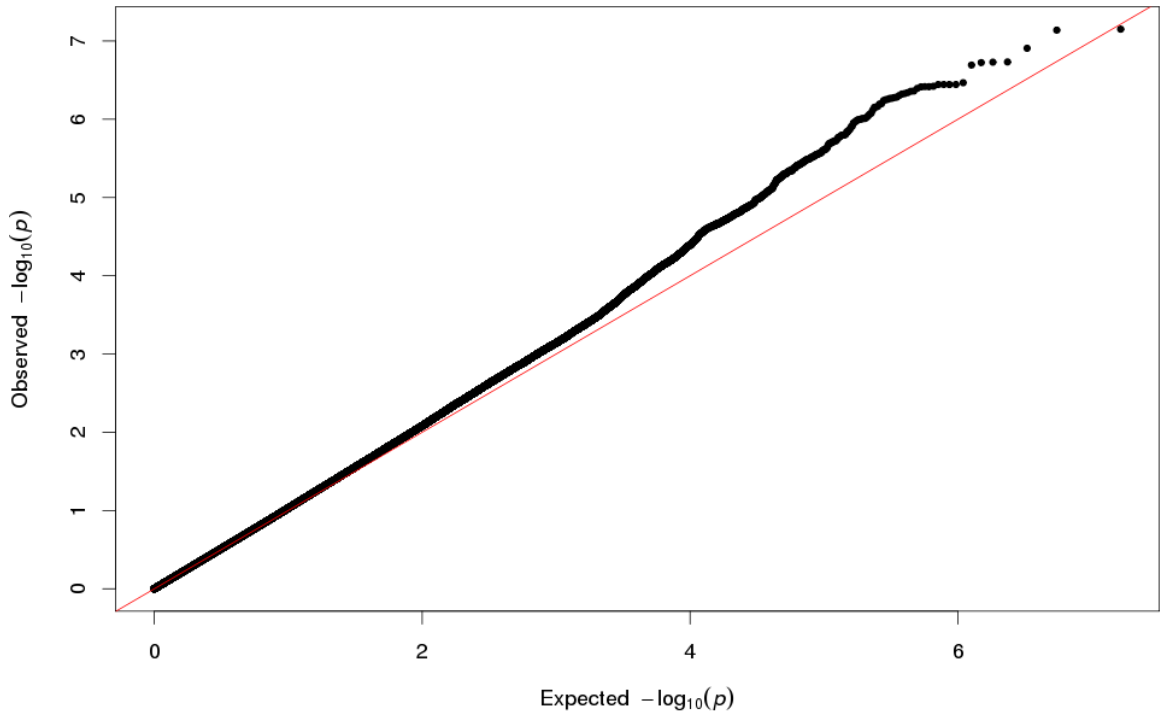
Granule Cell Layer Dentate Gyrus uncorrected for total hippocampal volume



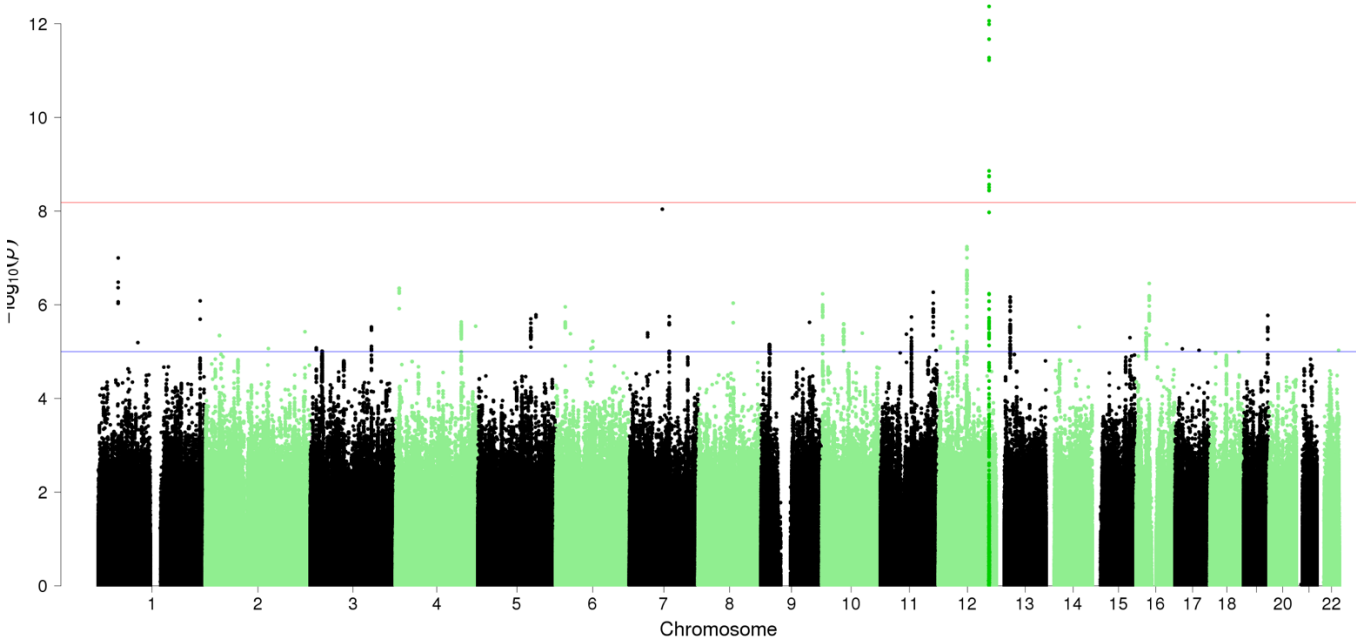


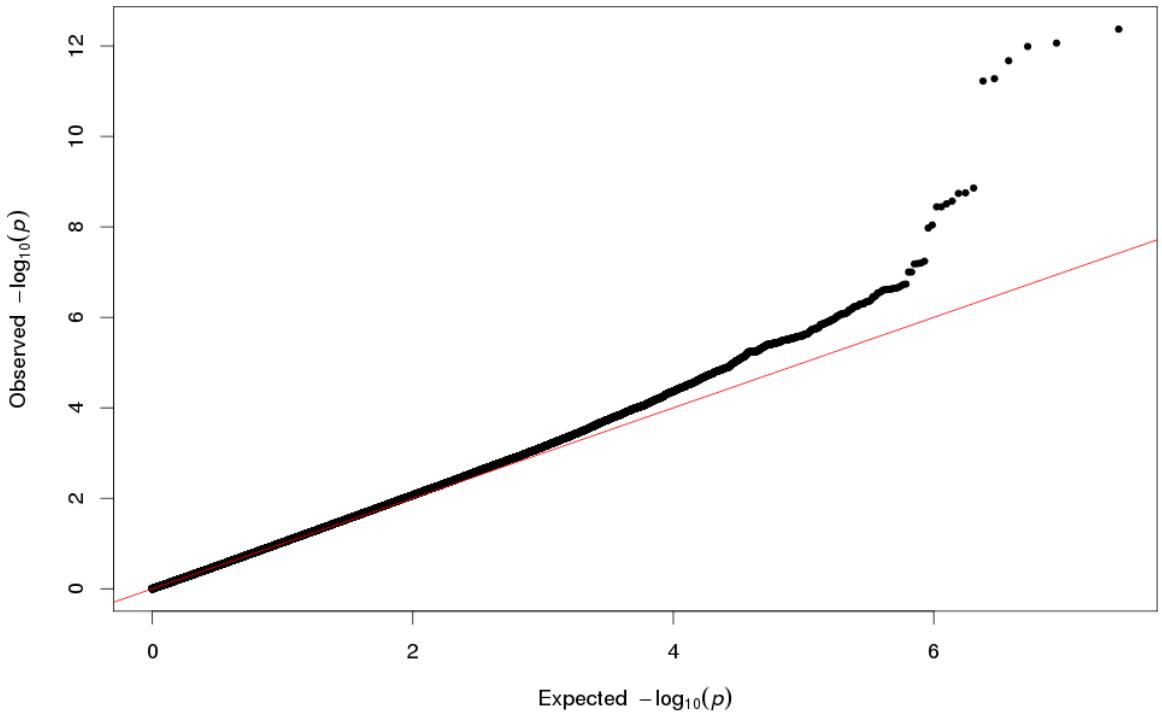
HATA corrected for total hippocampal volume



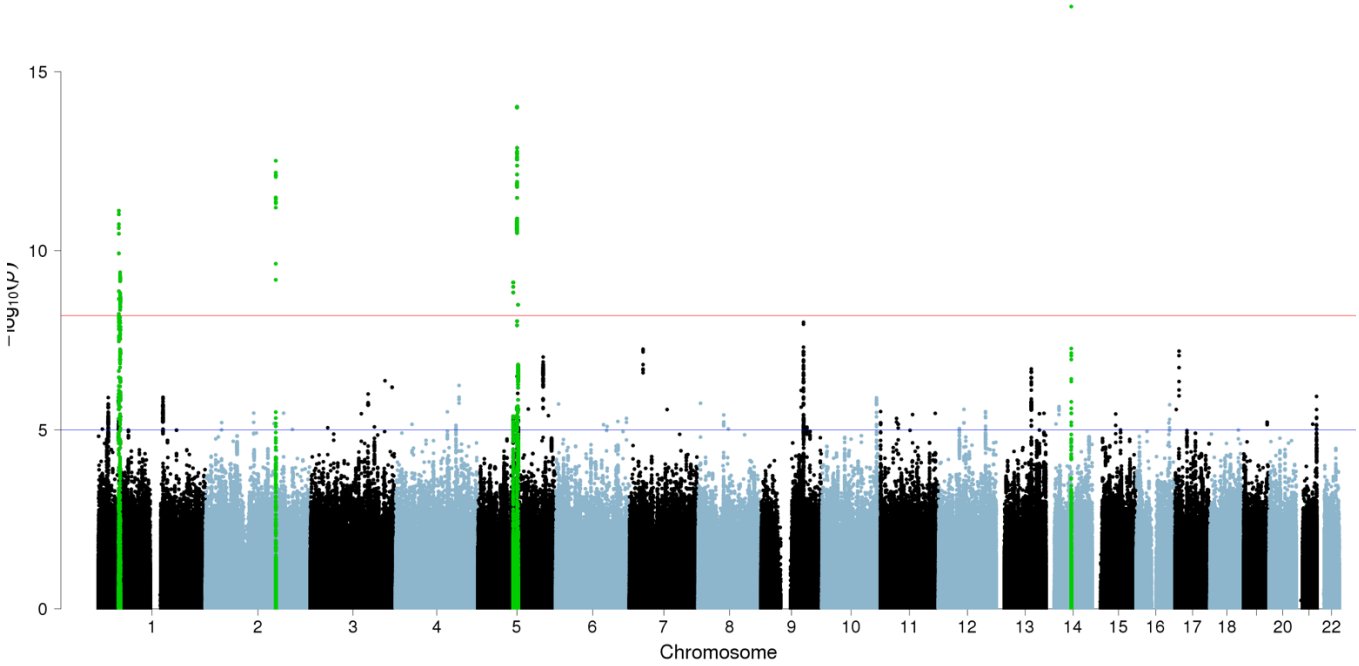


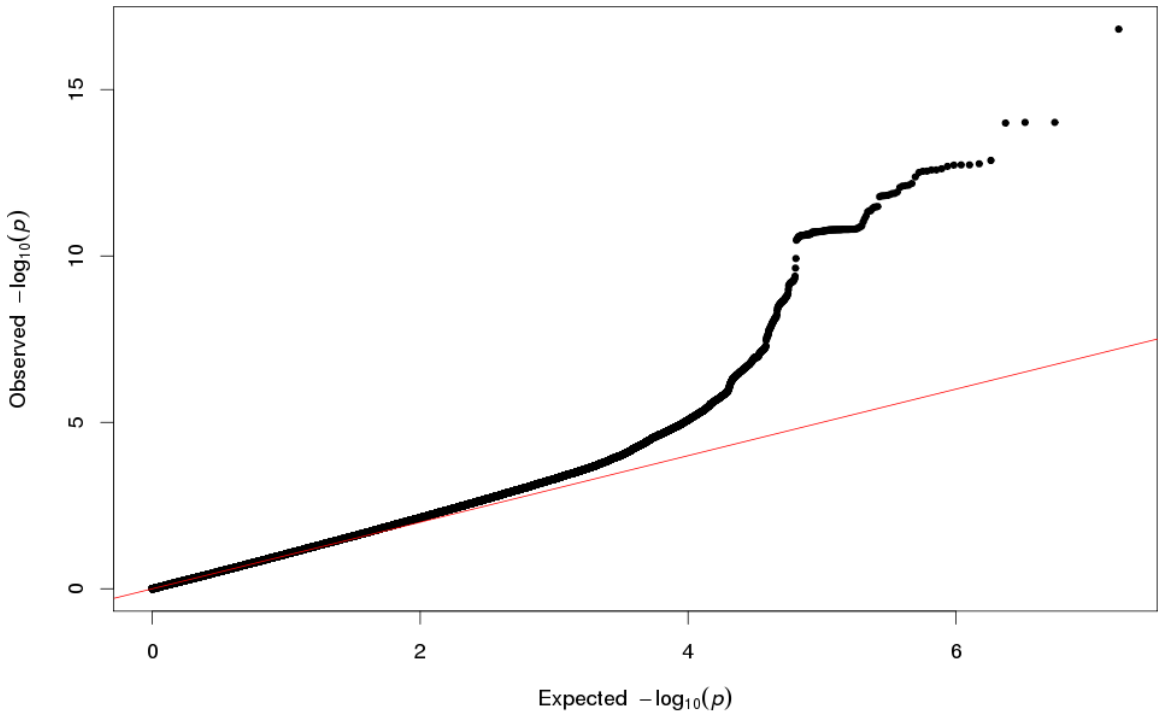
HATA uncorrected for total hippocampal volume



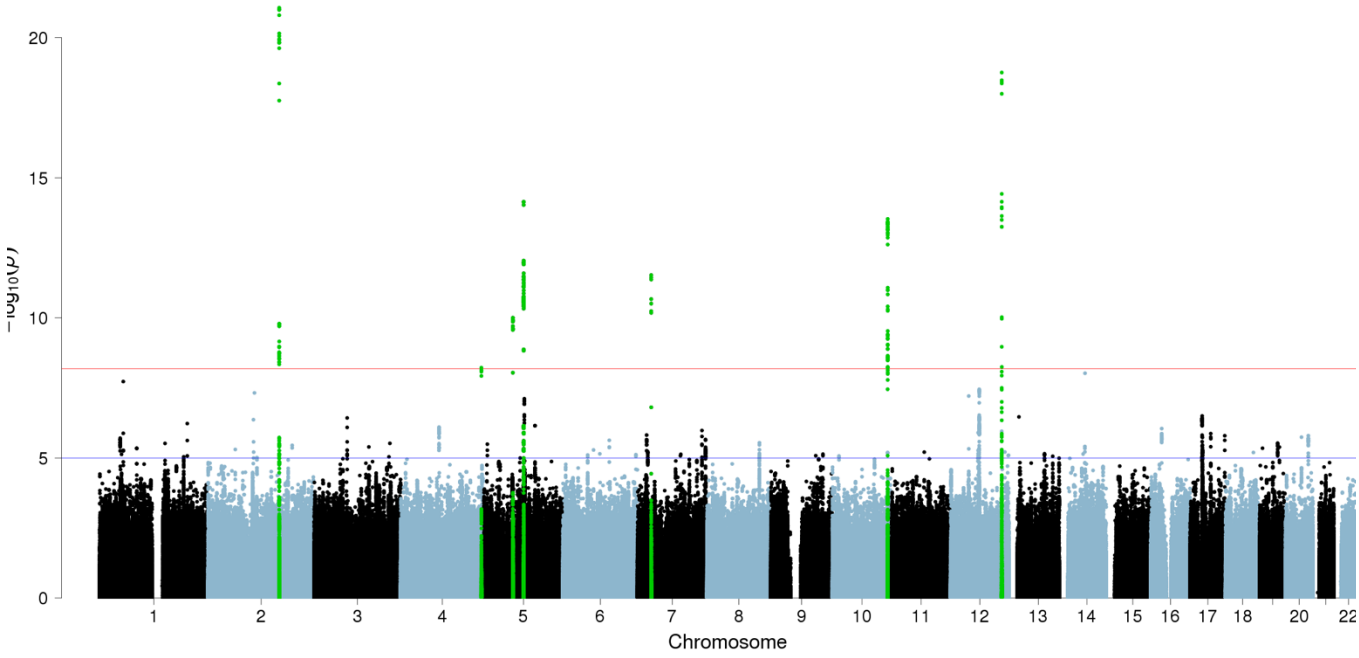


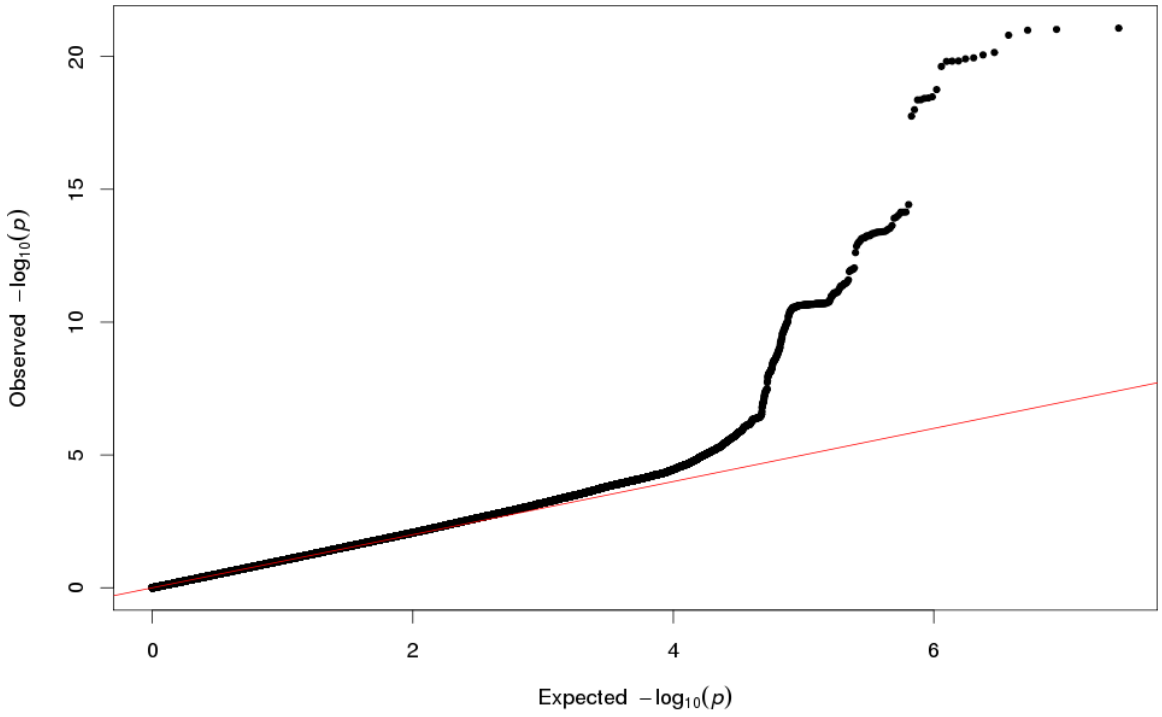
Tail corrected for total hippocampal volume



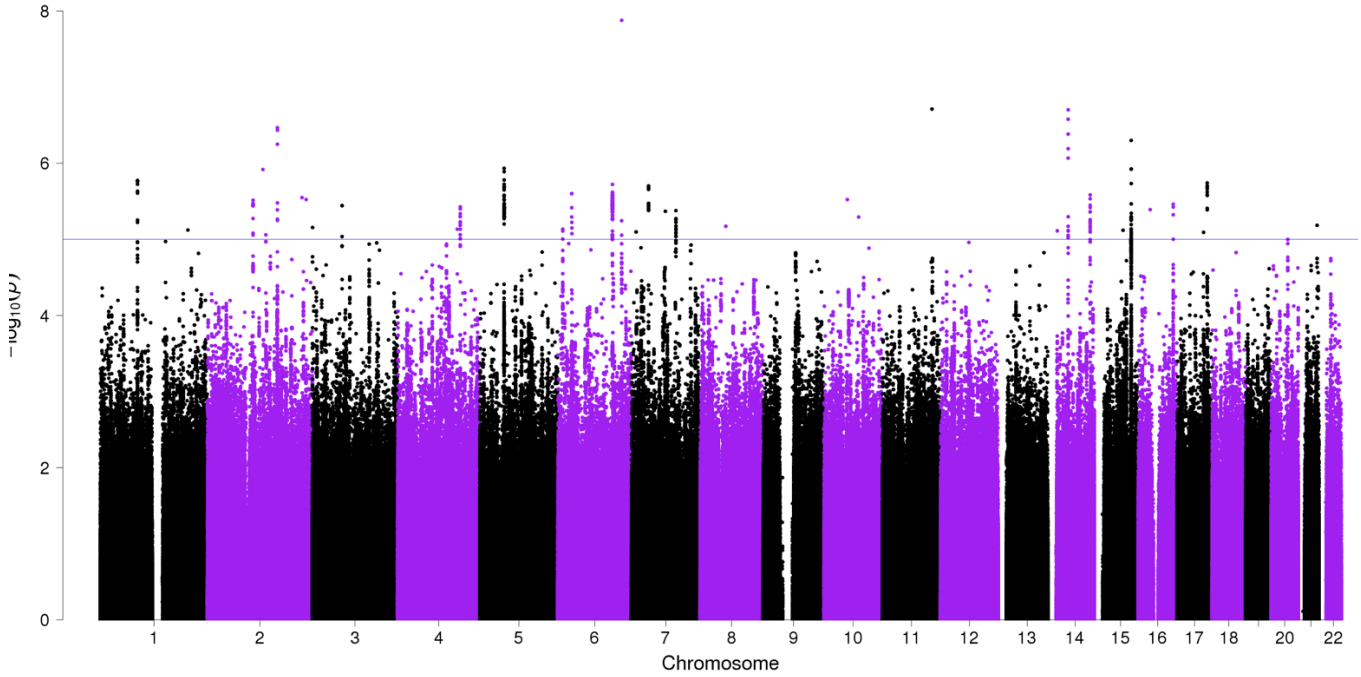


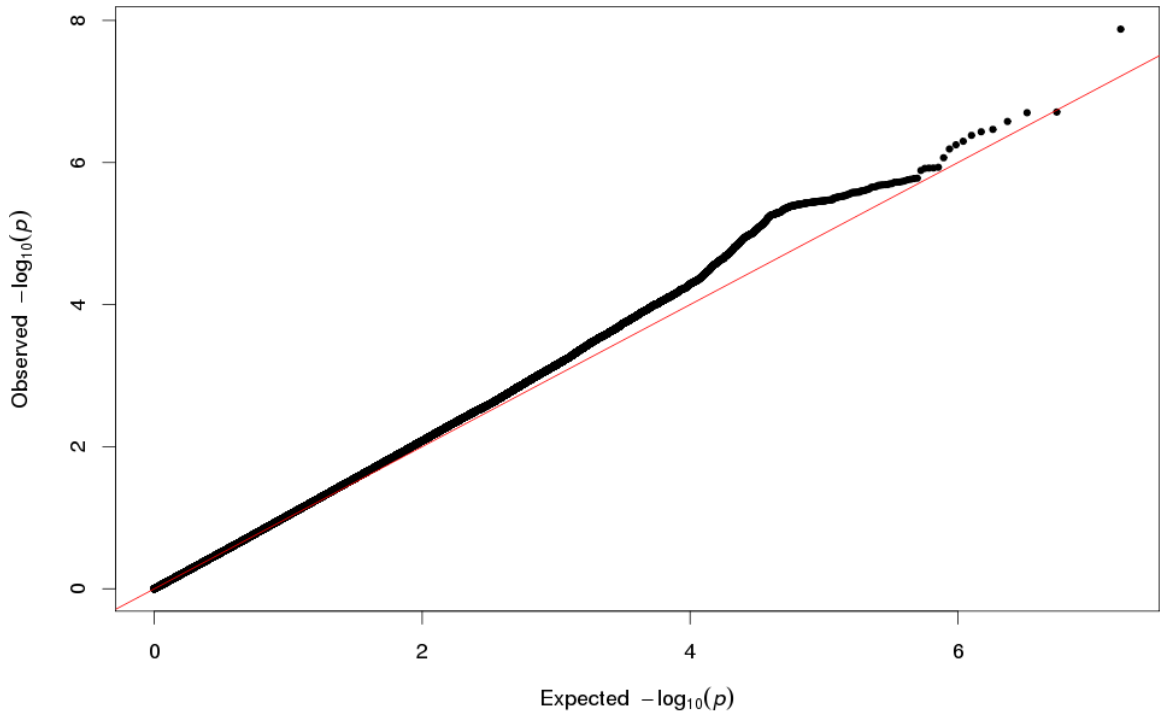
Tail uncorrected for total hippocampal volume



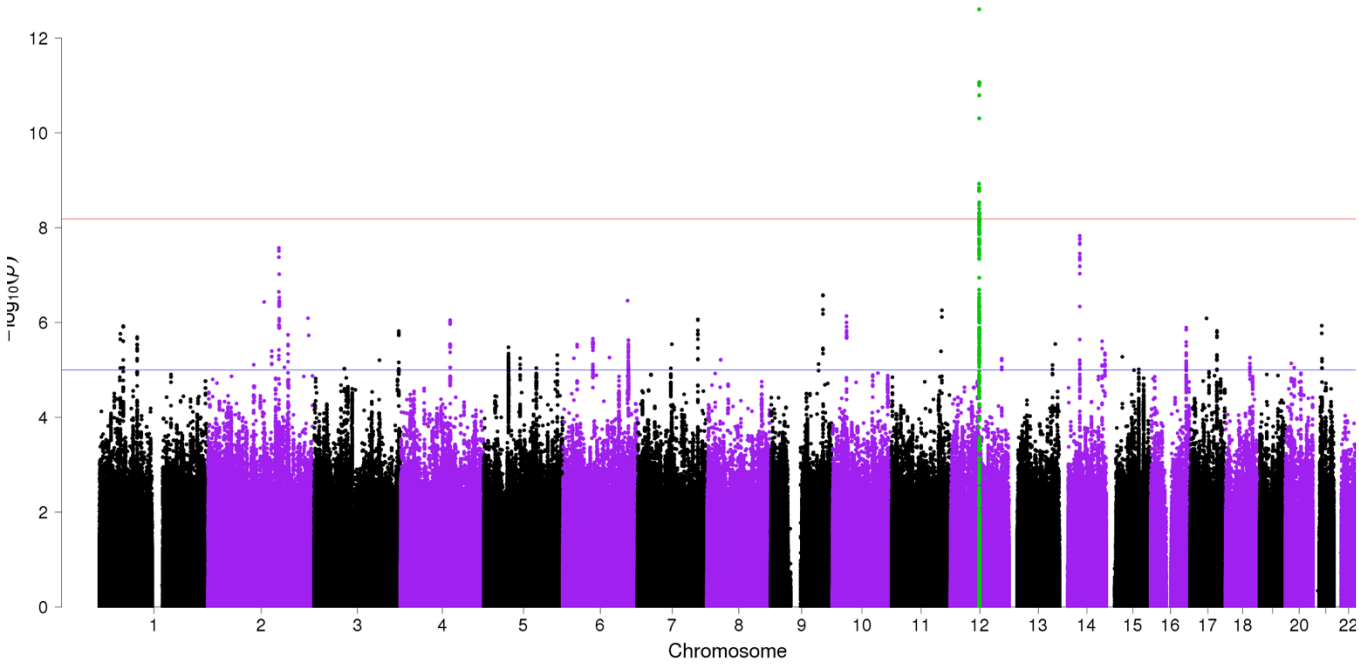


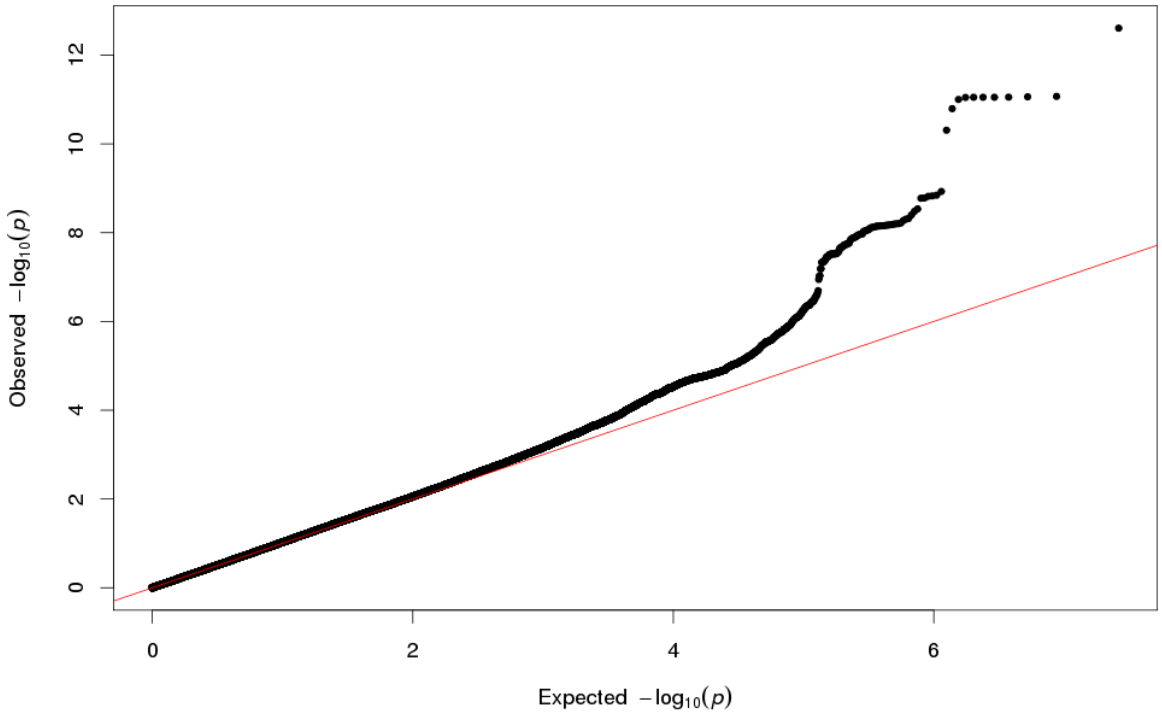
Fissure corrected for total hippocampal volume



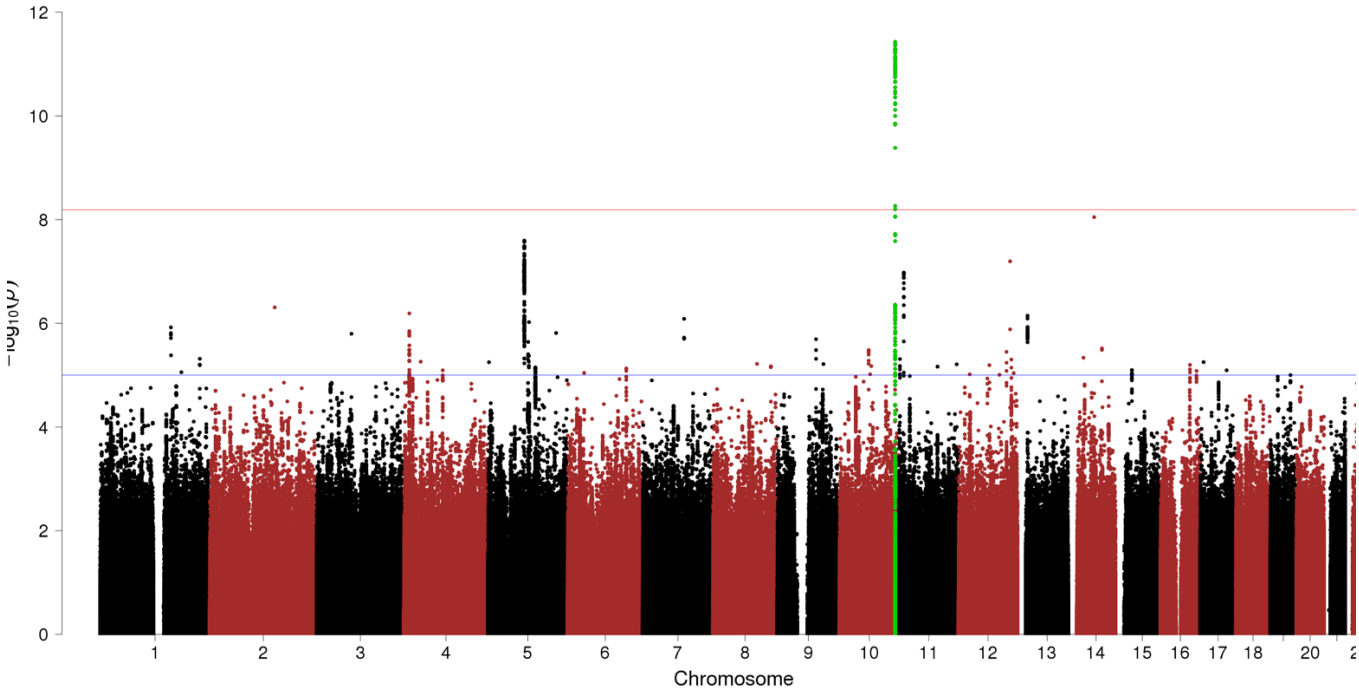


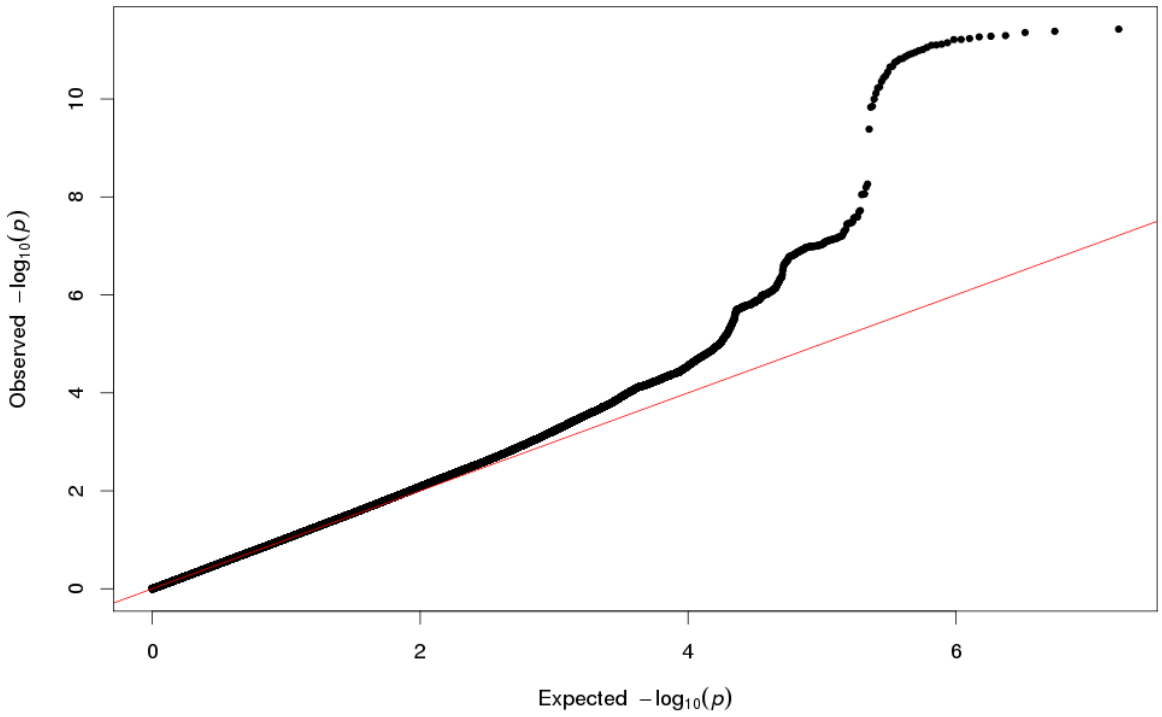
Fissure uncorrected for total hippocampal volume



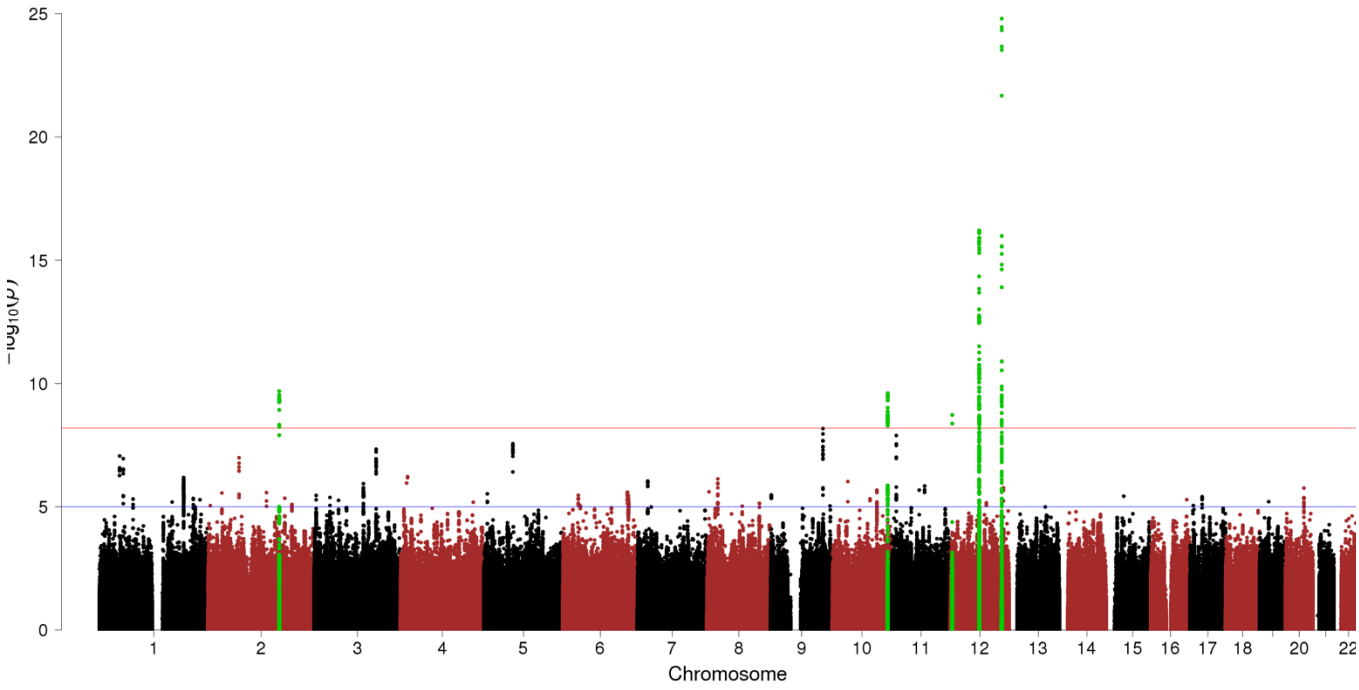


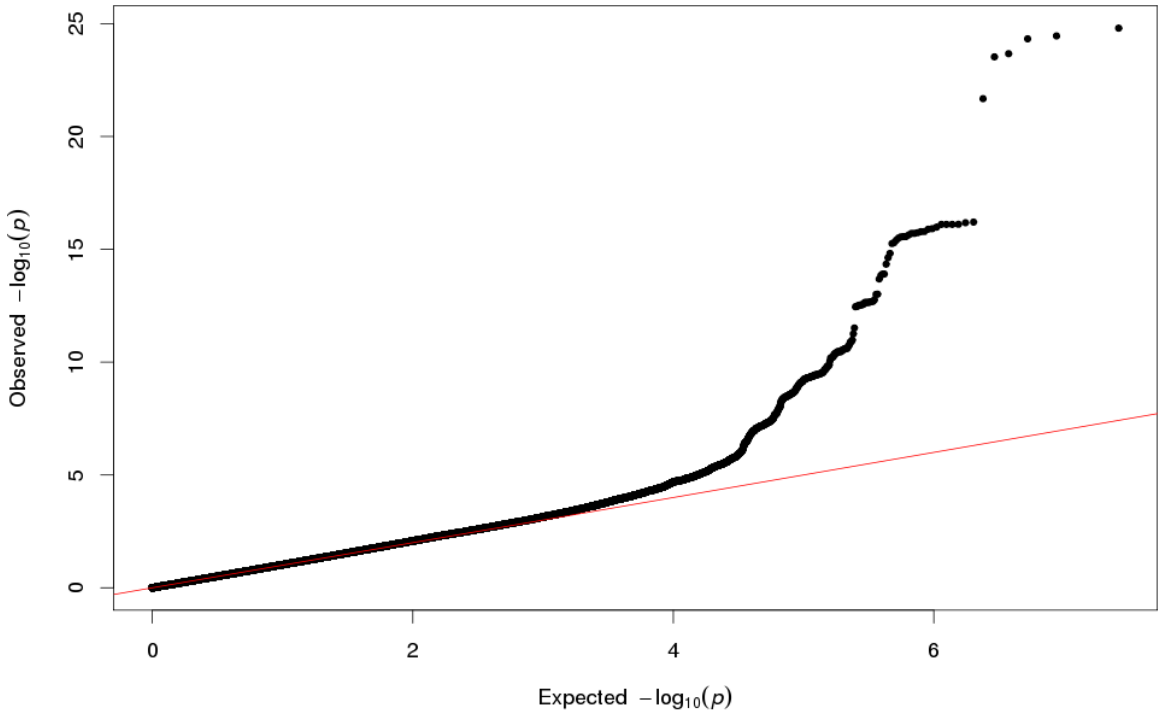
Molecular Layer corrected for total hippocampal volume



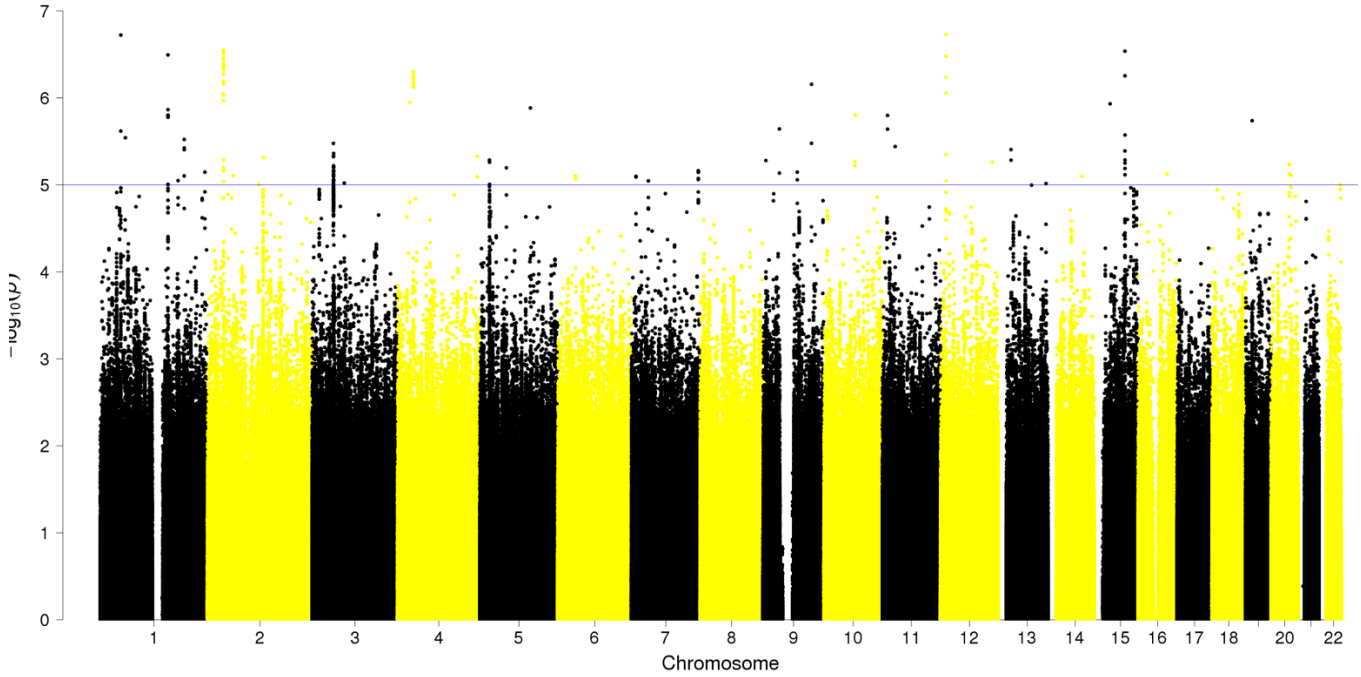


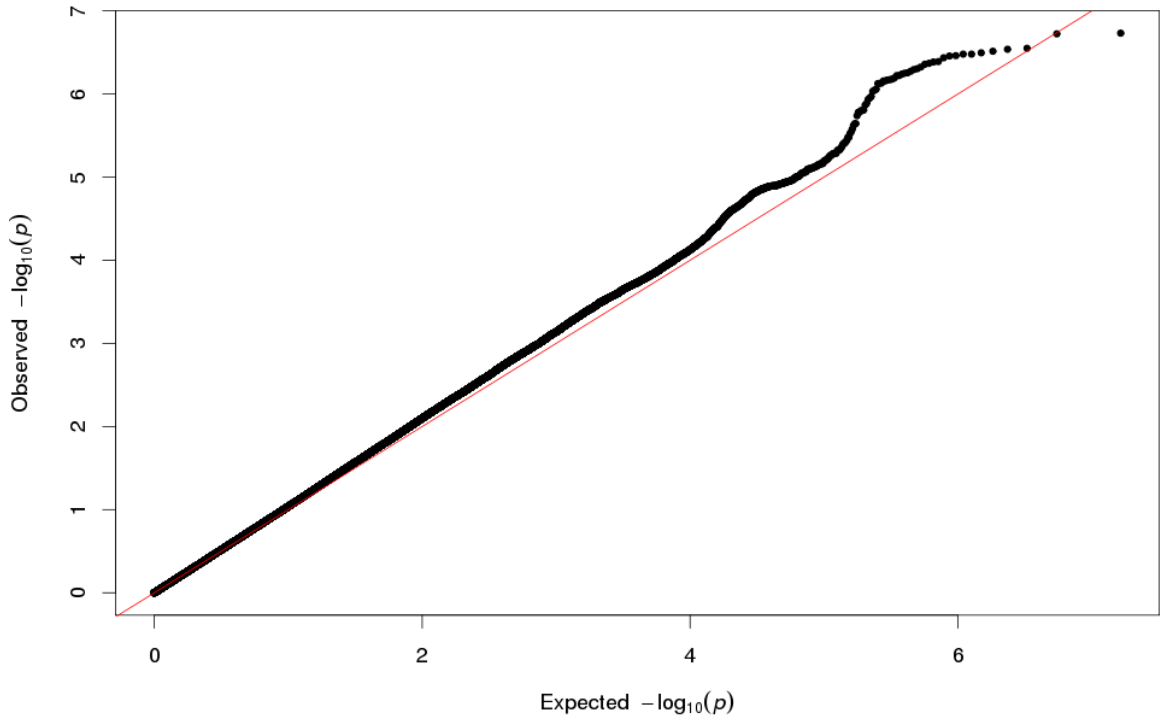
Molecular Layer uncorrected for total hippocampal volume



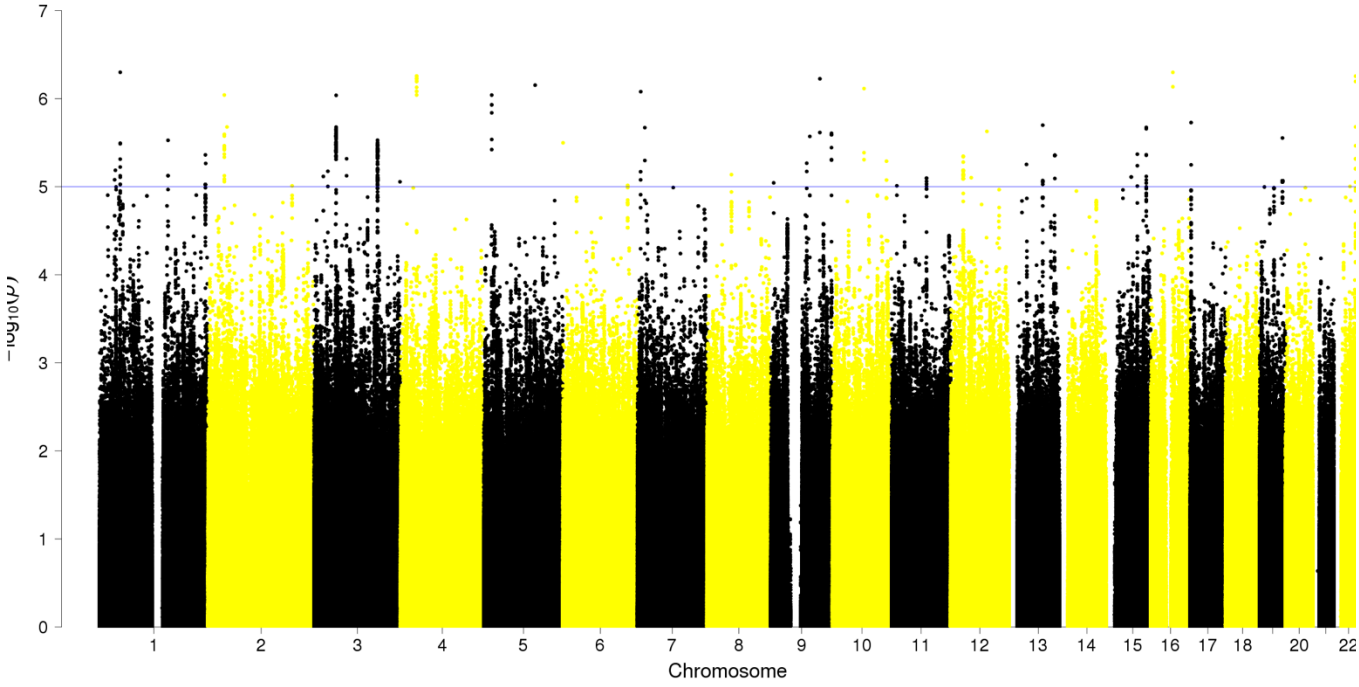


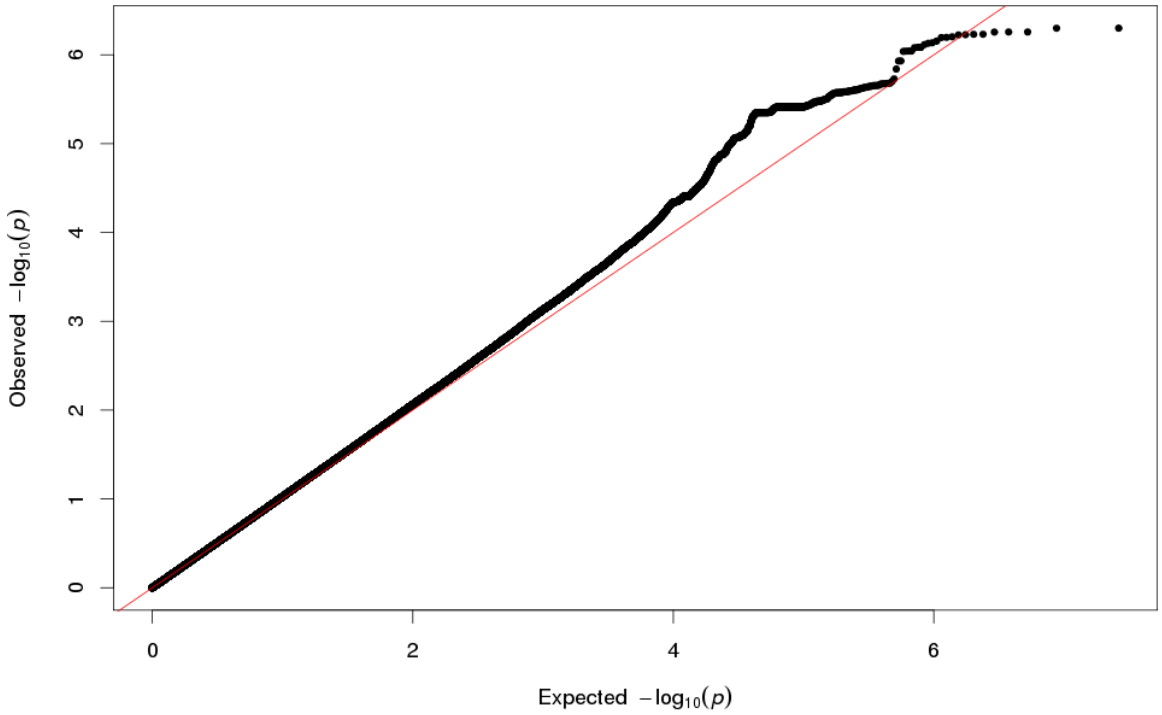
Parasubiculum corrected for total hippocampal volume



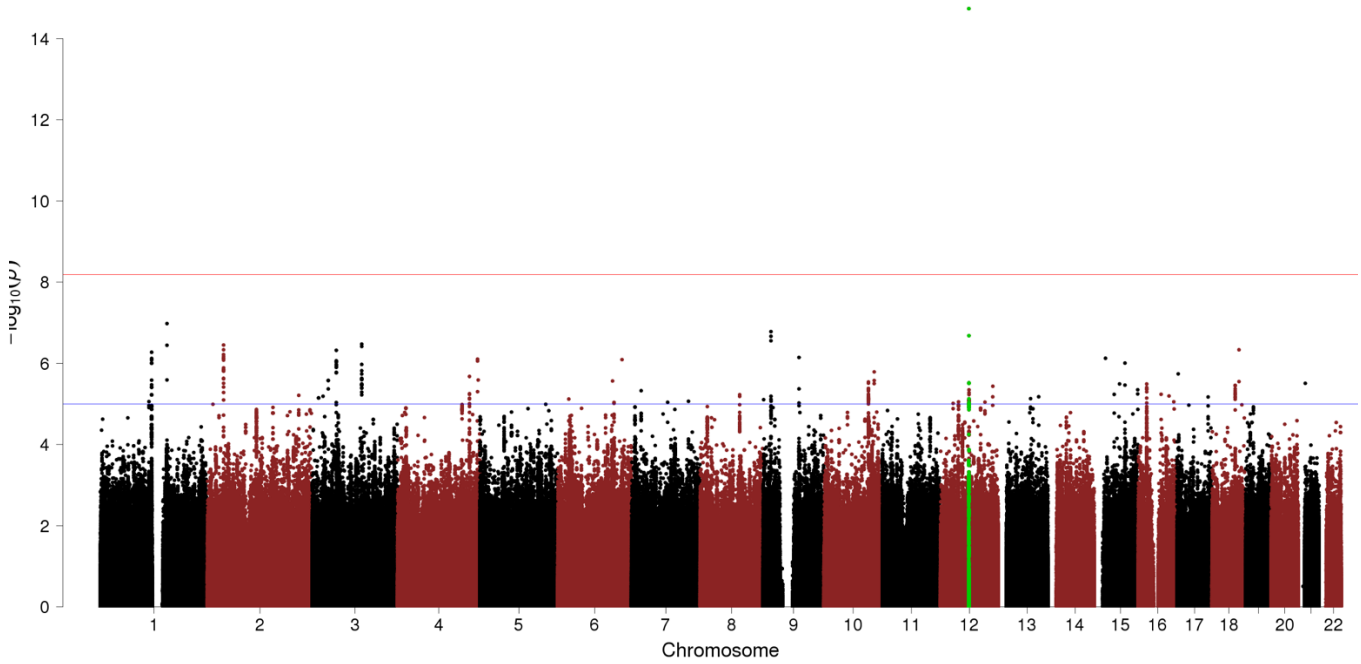


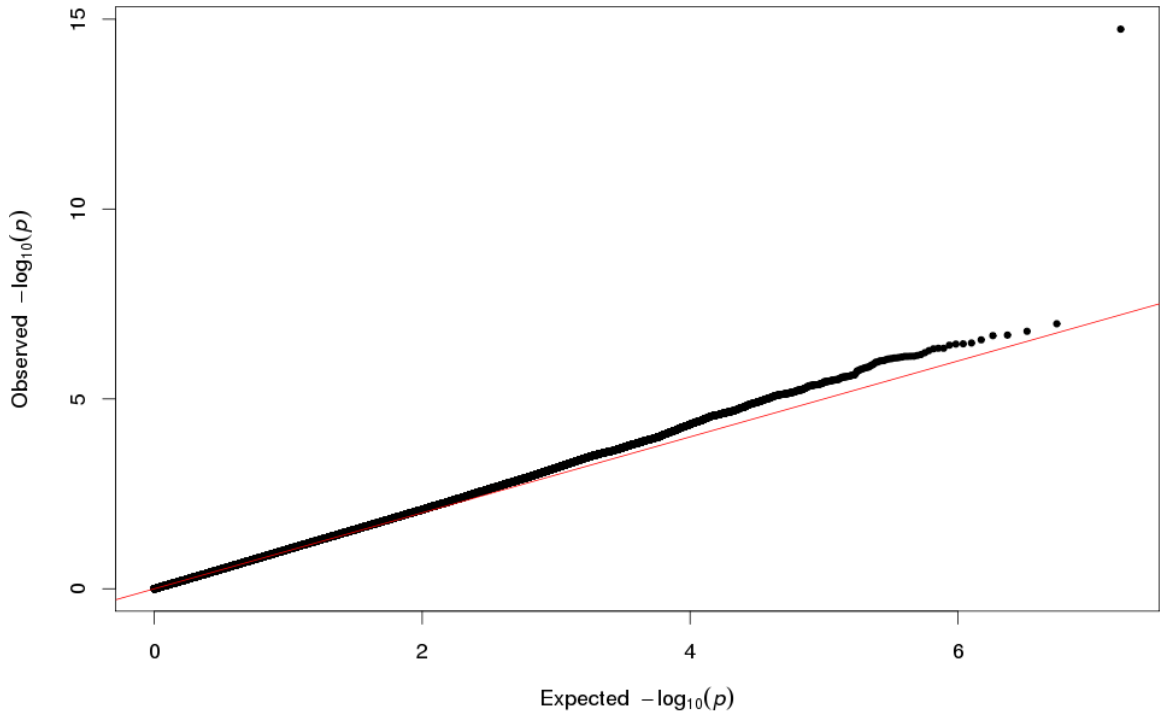
Parasubiculum uncorrected for total hippocampal volume



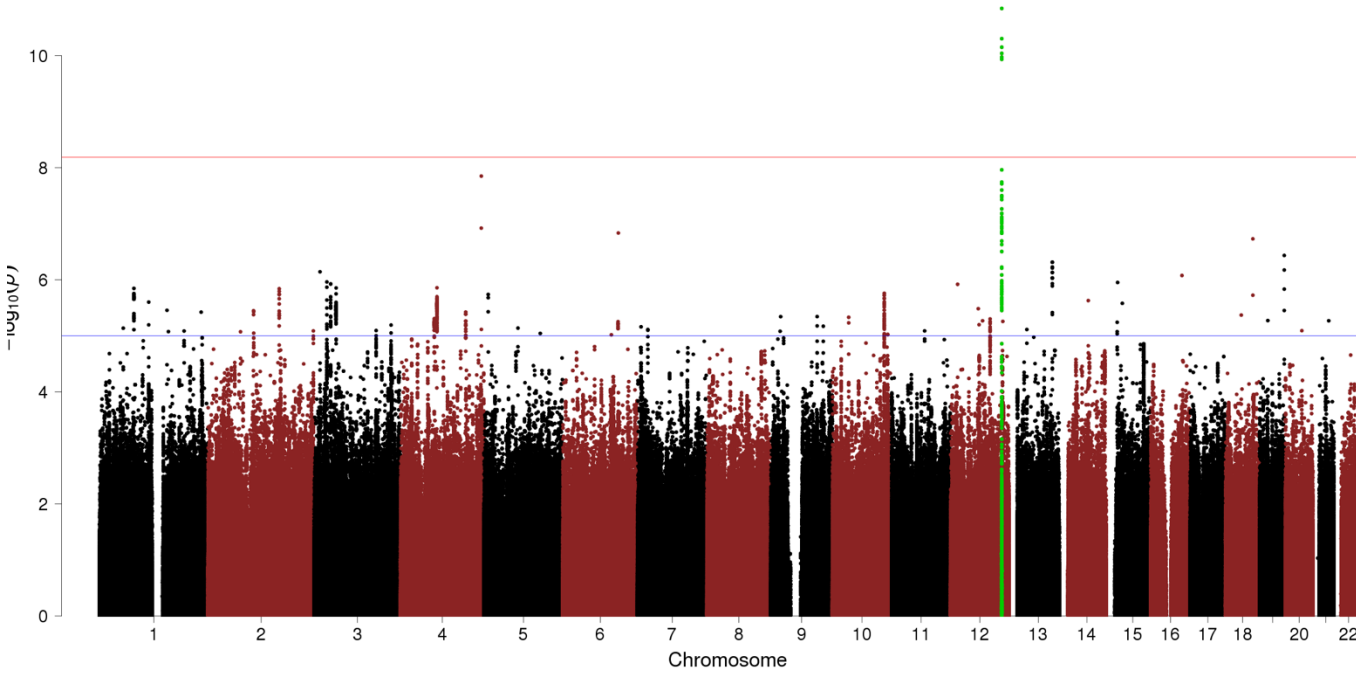


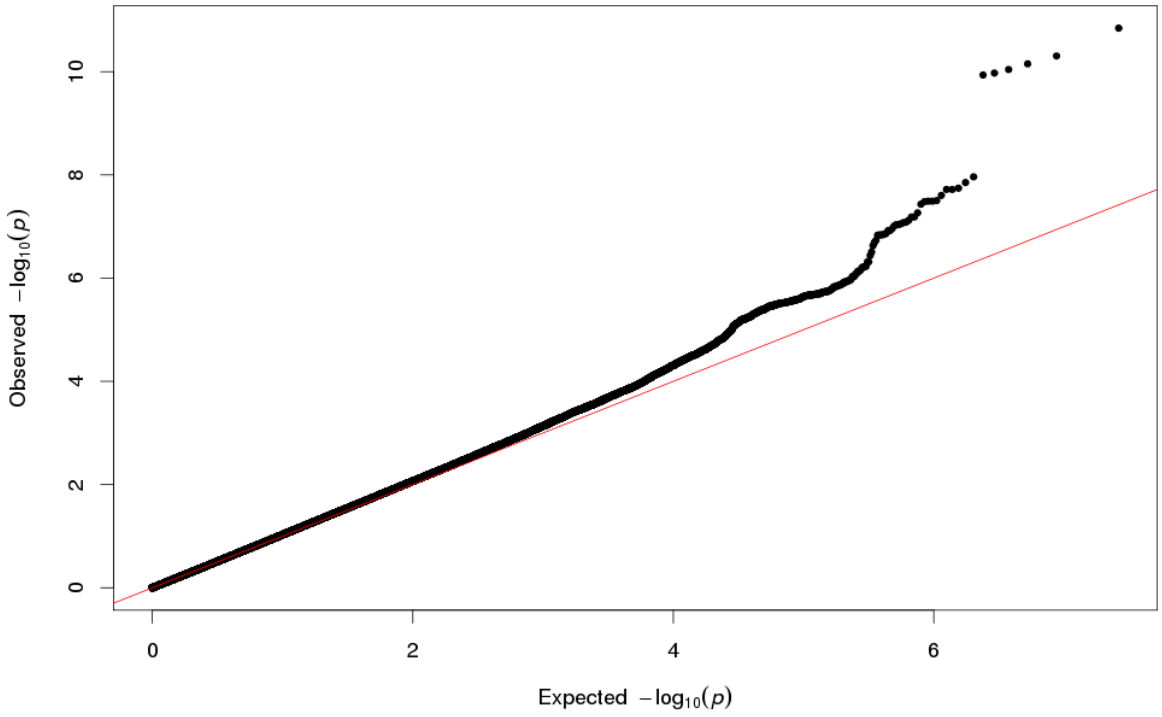
Presubiculum corrected for total hippocampal volume



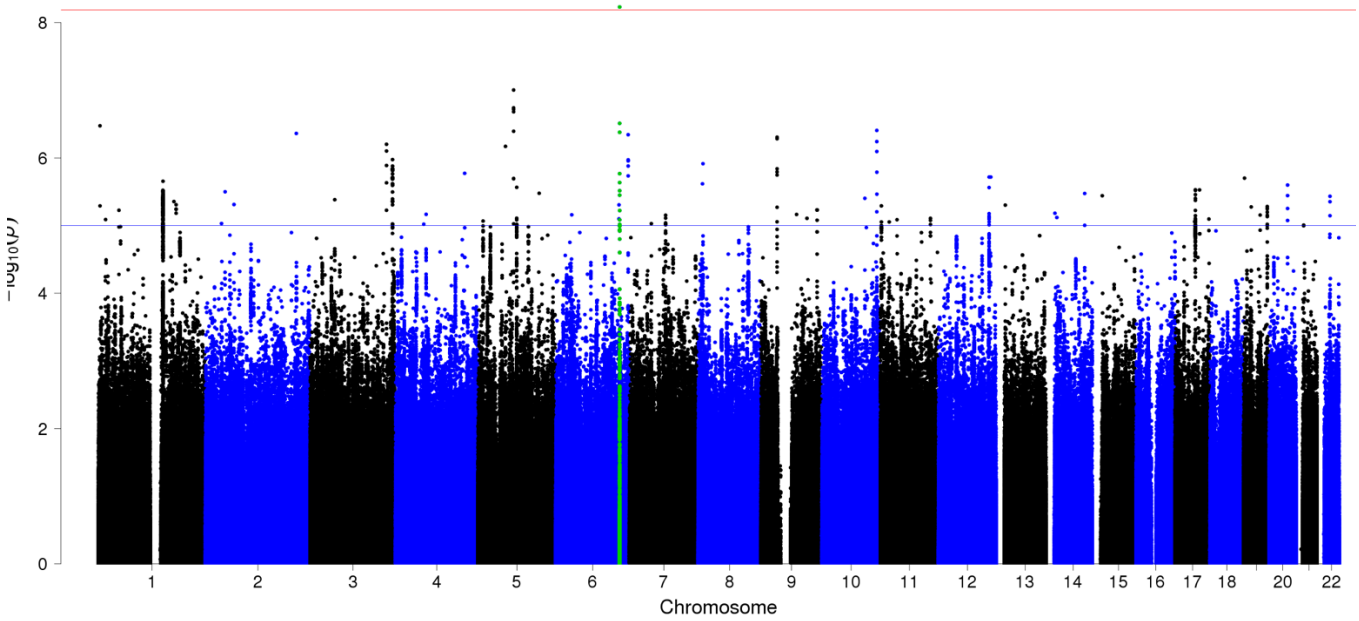


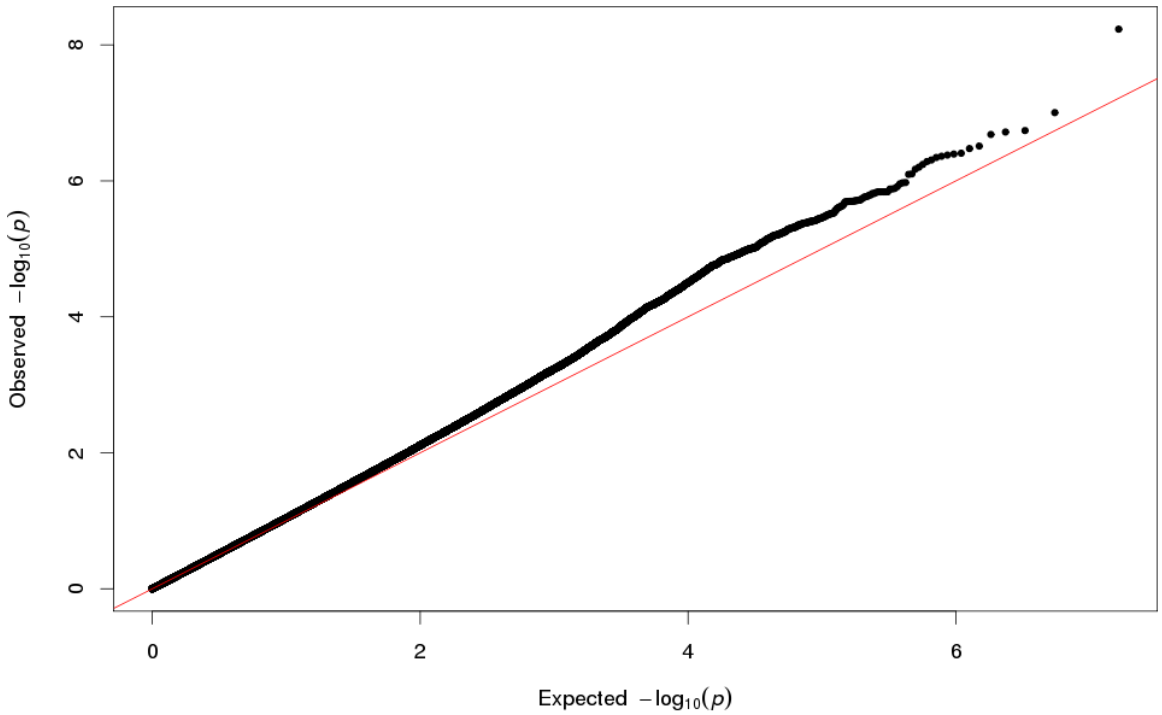
Presubiculum uncorrected for total hippocampal volume



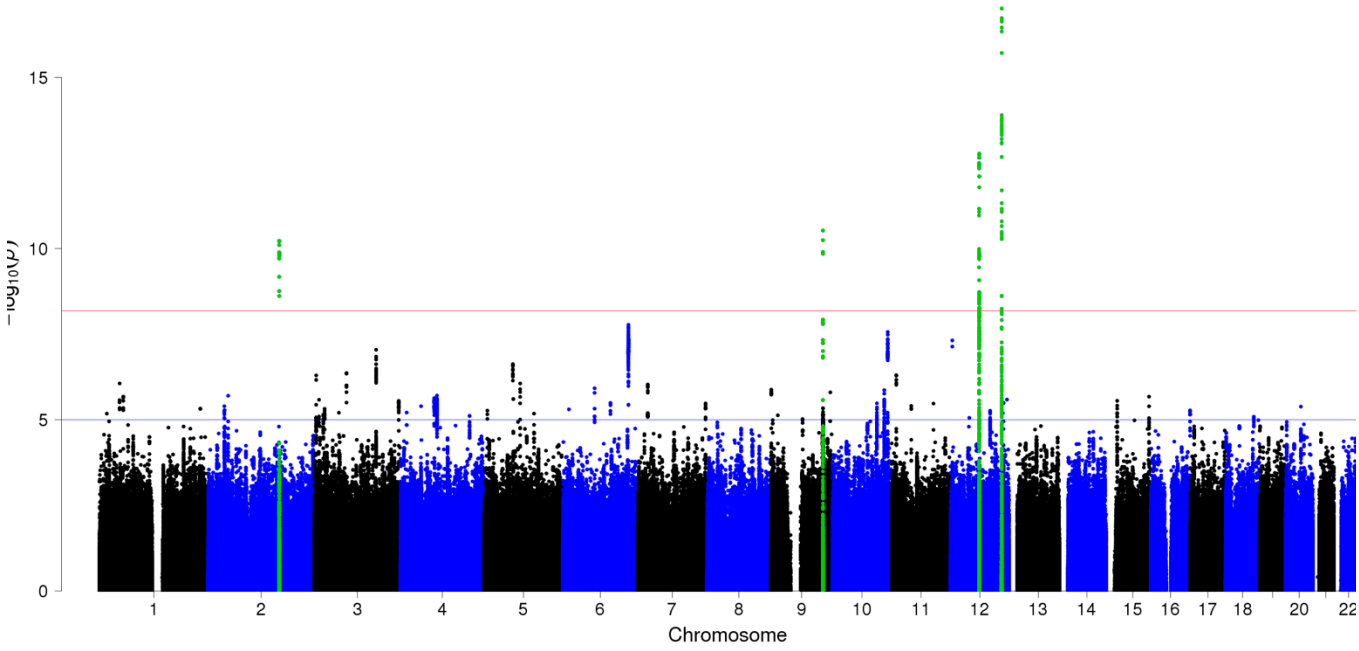


Subiculum corrected for total hippocampal volume





Subiculum uncorrected for total hippocampal volume



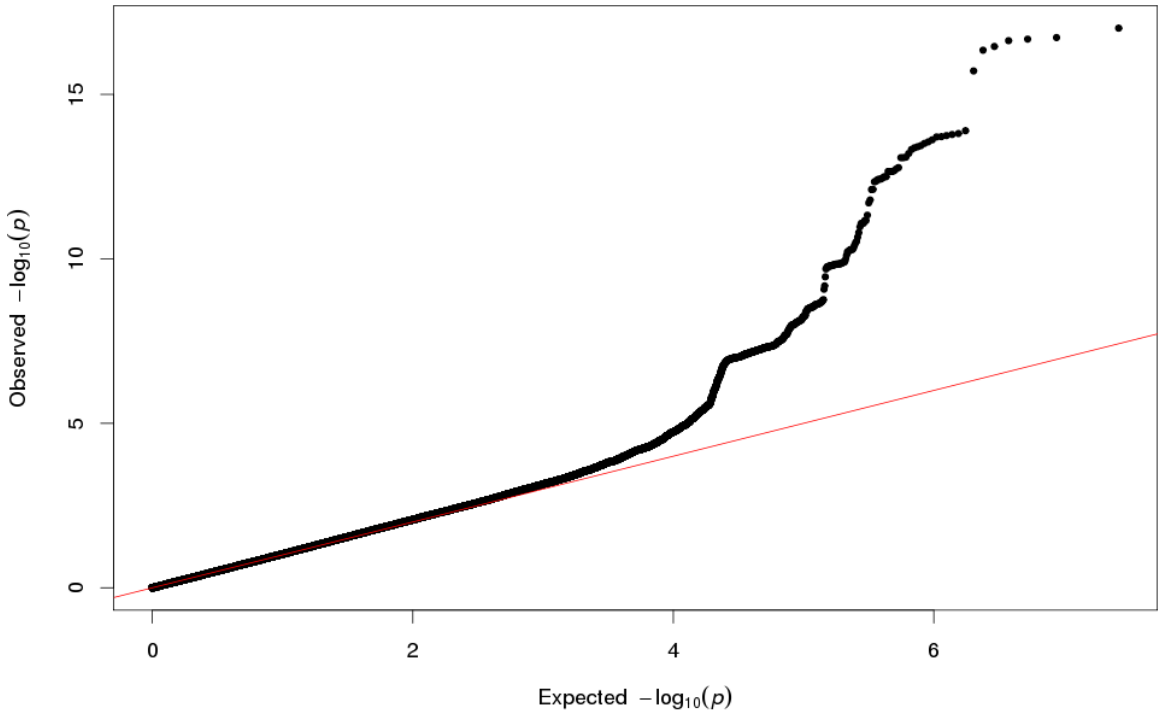
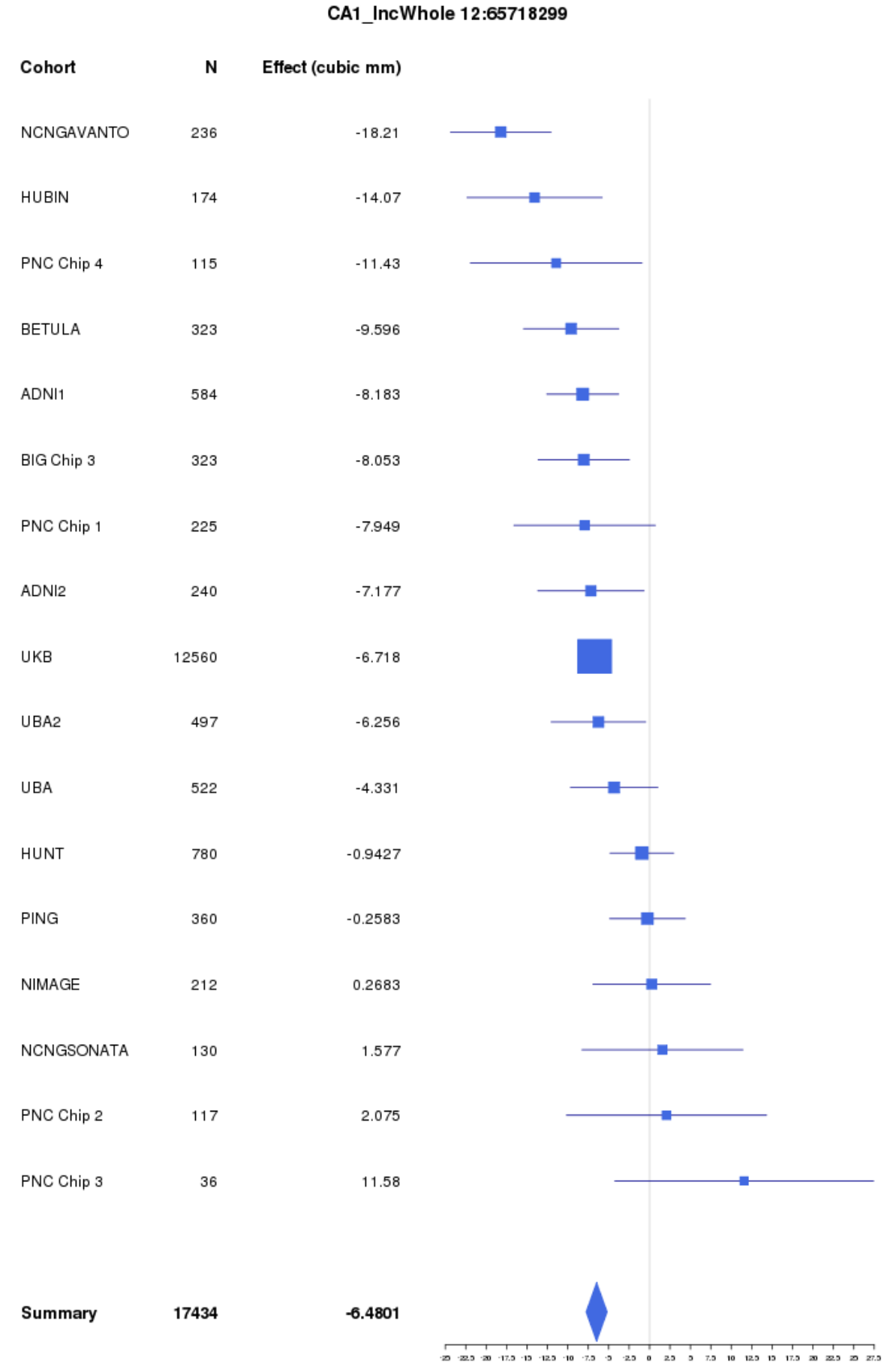
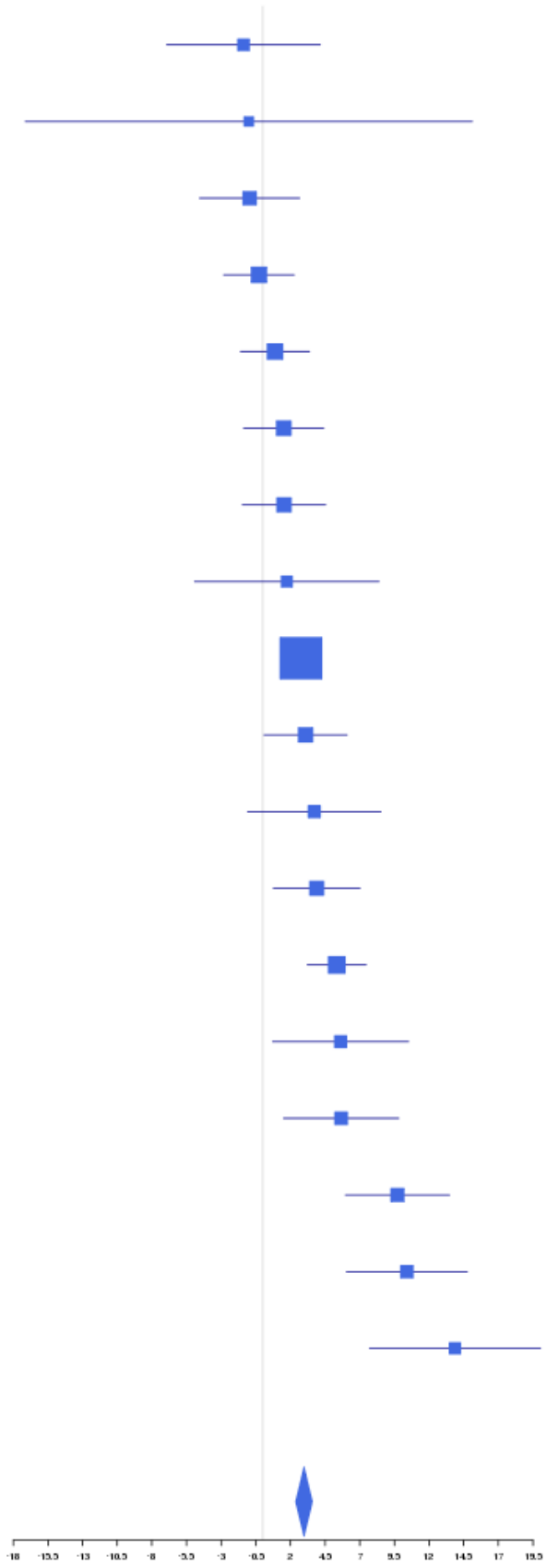


Figure S4 Forest plot per lead SNP of the whole-genome significant loci across all the subfields.



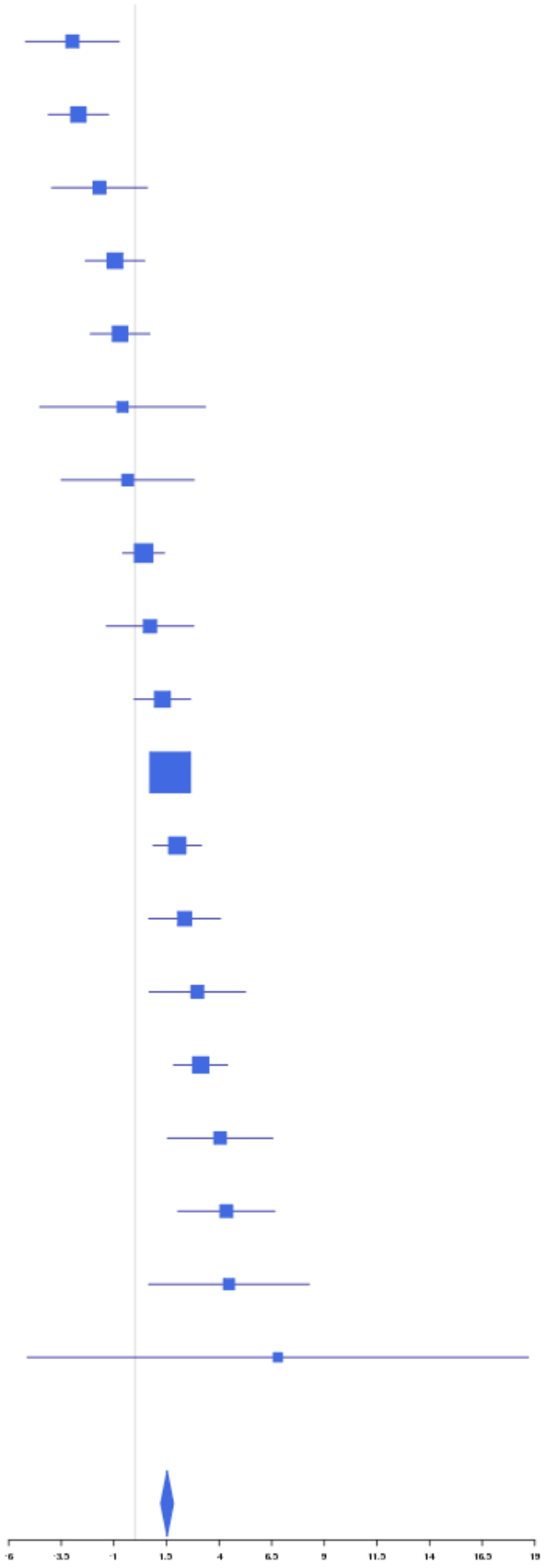
CA1_lncWhole 14:59074136

Cohort	N	Effect (cubic mm)
NCNGSONATA	130	-1.389
PNC Chip 3	36	-1.004
ADNI2	240	-0.9483
ADNI1	584	-0.2725
BIG Chip 2	779	0.8827
UNIBA	355	1.512
UBA2	497	1.531
PNC Chip 4	115	1.735
UKB	12560	2.755
UBA	522	3.088
PNC Chip 1	225	3.717
PING	360	3.893
HUNT	780	5.34
HUBIN	174	5.615
NCNGAVANTO	236	5.656
BETULA	323	9.721
NIMAGE	212	10.4
PNC Chip 2	117	13.87
Summary	**18245**	**2.9772**



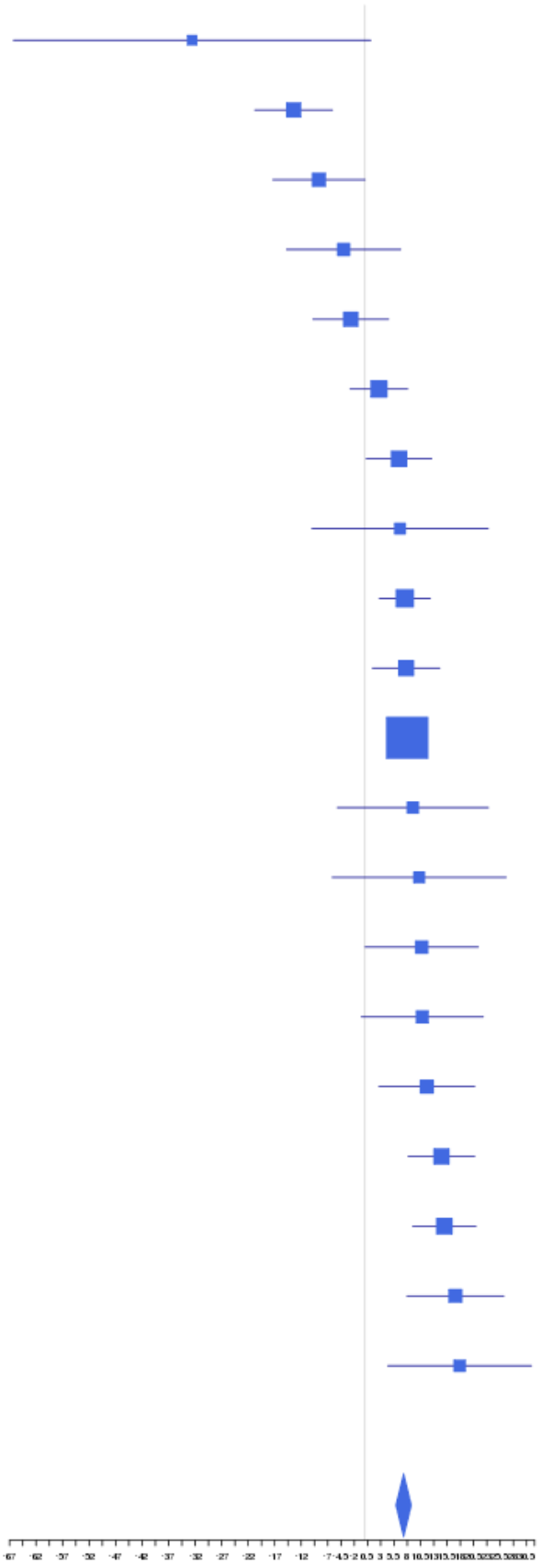
GC.ML.DG_IncWhole 14:59074136

Cohort	N	Effect (cubic mm)
NIMAGE	212	-2.973
UBA2	497	-2.686
ADNI2	240	-1.682
ADNI1	584	-0.9468
UNIBA	355	-0.7054
PNC Chip 4	115	-0.5848
NCNGSONATA	130	-0.3411
BIG Chip 1	1159	0.414
BETULA	323	0.7198
UBA	522	1.305
UKB	12560	1.675
HUNT	780	2.013
PING	360	2.36
NCNGAVANTO	236	2.966
BIG Chip 2	779	3.121
HUBIN	174	4.05
PNC Chip 1	225	4.345
PNC Chip 2	117	4.47
PNC Chip 3	36	6.791
Summary	**19404**	**1.5297**



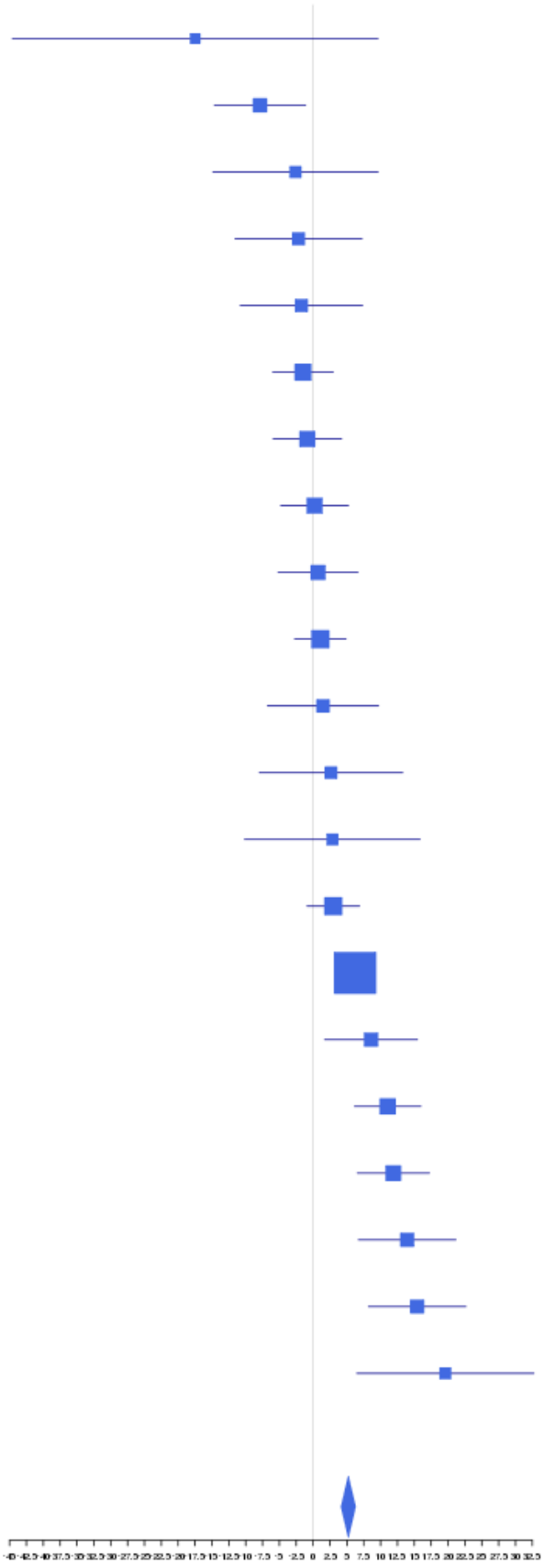
Hippocampal_tail_lncWhole 1:47945370

Cohort	N	Effect (cubic mm)
PNC Chip 3	36	-32.58
UNIBA	355	-13.43
ADNI2	240	-8.658
NIMAGE	212	-4.001
PING	360	-2.668
ADNI1	584	2.651
UBA	522	6.433
PNC Chip 2	117	6.627
BIG Chip 1	1156	7.531
HUNT	780	7.774
UKB	12504	7.986
NCNGSONATA	130	9.046
PNC Chip 4	115	10.24
NCNGAVANTO	236	10.71
PNC Chip 1	225	10.83
BIG Chip 3	317	11.68
BIG Chip 2	764	14.44
UBA2	497	14.99
BETULA	323	17.07
HUBIN	174	17.87
Summary	**19647**	**7.3102**



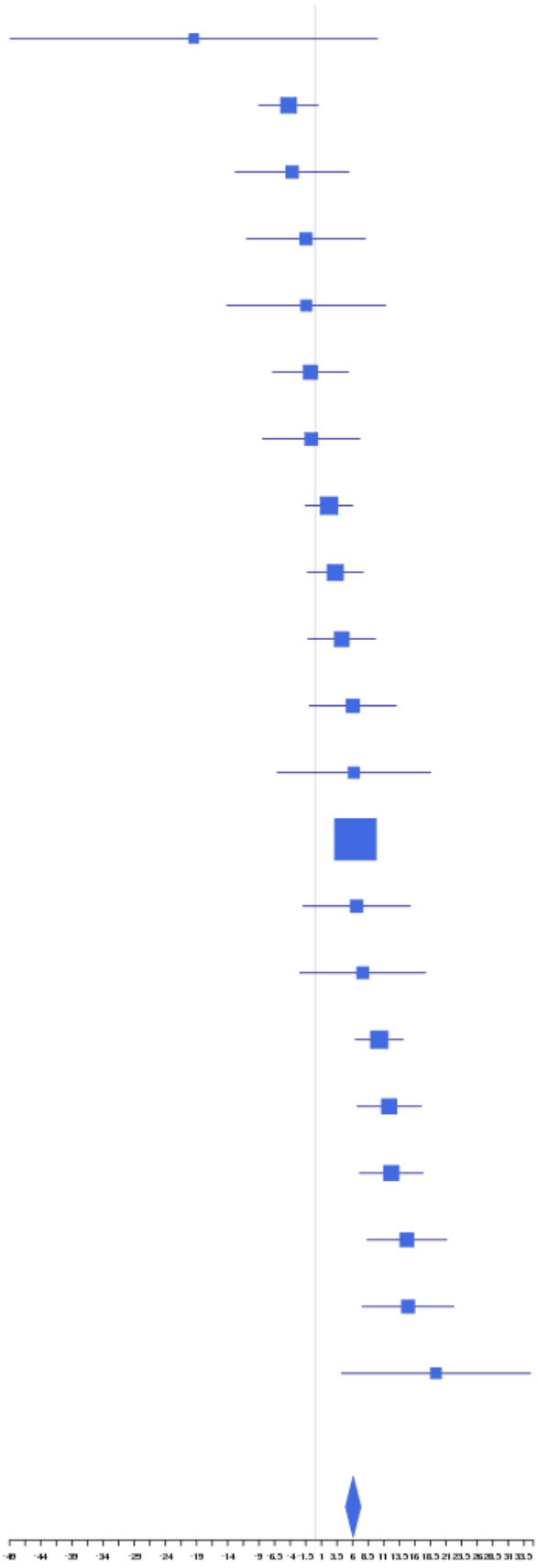
Hippocampal_tail_IncWhole 1:51016603

Cohort	N	Effect (cubic mm)
PNC Chip 3	36	-17.48
UNIBA	355	-7.874
NCNGSONATA	130	-2.611
PNC Chip 1	225	-2.153
NIMAGE	212	-1.733
ADNI1	584	-1.505
BIG Chip 2	779	-0.8543
UBA	522	0.2188
PING	360	0.7314
BIG Chip 1	1158	1.07
NCNGAVANTO	236	1.467
HUBIN	174	2.656
PNC Chip 2	117	2.848
TOP	1158	2.99
UKB	12515	6.233
BETULA	323	8.592
HUNT	780	11.06
UBA2	497	11.9
BIG Chip 3	323	13.94
ADNI2	240	15.43
PNC Chip 4	115	19.6
Summary	**20839**	**5.2216**



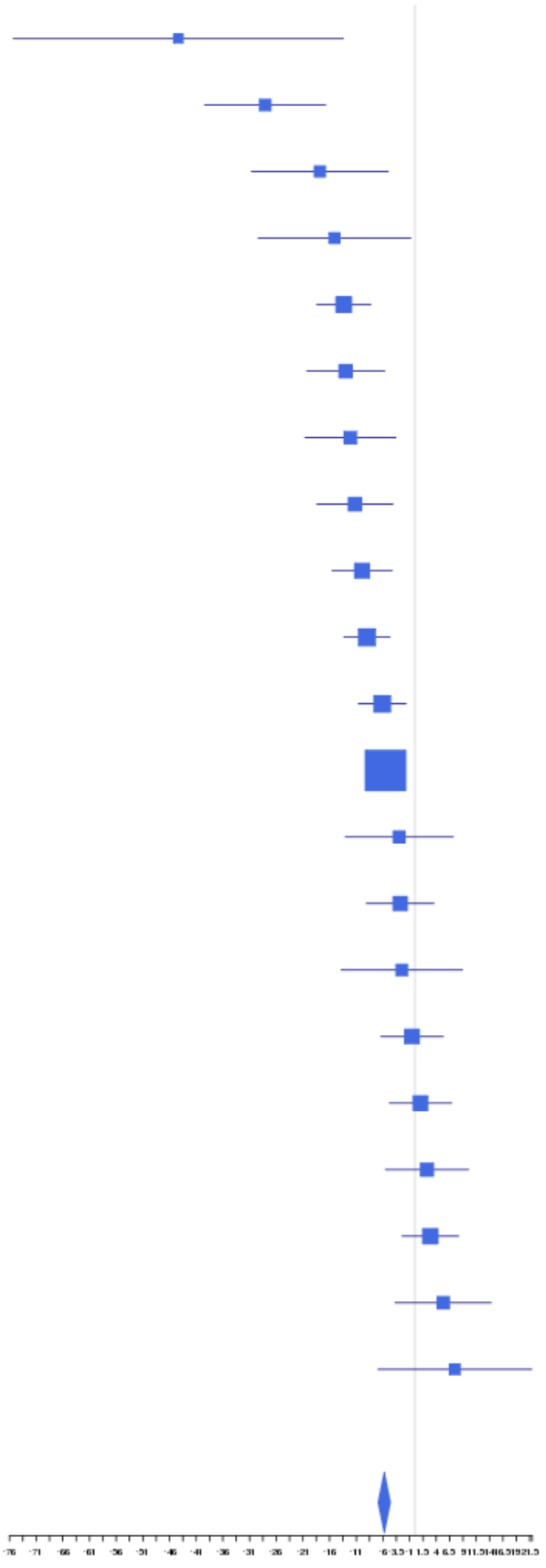
Hippocampal_tail_IncWhole 2:162846439

Cohort	N	Effect (cubic mm)
PNC Chip 3	36	-19.45
HUNT	780	-4.259
NIMAGE	212	-3.683
HUBIN	174	-1.468
PNC Chip 4	115	-1.426
PING	360	-0.7522
BIG Chip 3	323	-0.6336
TOP	1158	2.222
ADNI1	584	3.228
UBA2	497	4.262
ADNI2	240	6.042
NCNGSONATA	130	6.217
UKB	12556	6.45
NCNGAVANTO	236	6.654
PNC Chip 1	225	7.639
BIG Chip 1	1159	10.28
UBA	522	11.87
BIG Chip 2	778	12.22
UNIBA	355	14.72
BETULA	323	14.9
PNC Chip 2	117	19.38
Summary	**20880**	**6.1075**



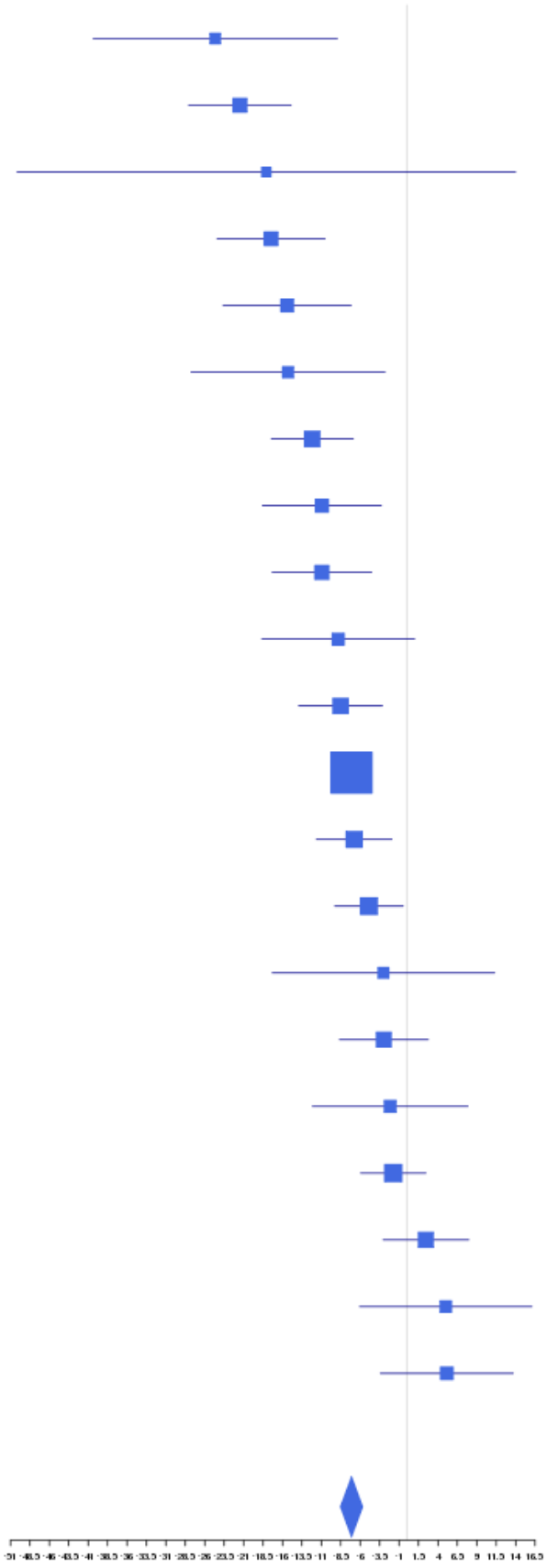
Hippocampal_tail_IncWhole 5:81929360

Cohort	N	Effect (cubic mm)
PNC Chip 3	36	-44.36
PNC Chip 1	225	-28.09
NCNGSONATA	130	-17.82
PNC Chip 4	115	-15.07
ADNI1	584	-13.34
BETULA	323	-12.97
BIG Chip 3	322	-12.1
UNIBA	355	-11.24
BIG Chip 2	776	-9.907
BIG Chip 1	1158	-9.002
TOP	1158	-6.127
UKB	12549	-5.52
NIMAGE	212	-2.941
PING	360	-2.762
HUBIN	174	-2.456
UBA2	497	-0.5421
UBA	522	1.039
ADNI2	240	2.267
HUNT	780	2.891
NCNGAVANTO	236	5.309
PNC Chip 2	117	7.479
Summary	**20869**	**-5.7429**



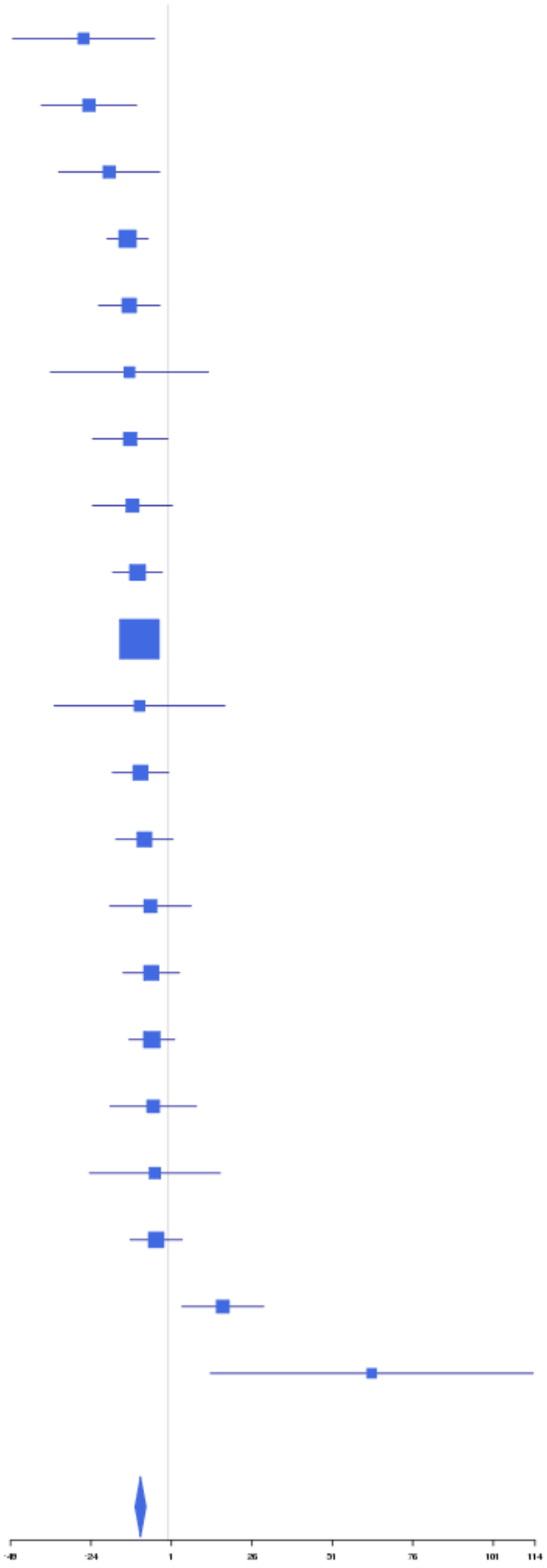
Hippocampal_tail_IncWhole 5:90816402

Cohort	N	Effect (cubic mm)
PNC Chip 2	117	-24.65
PING	360	-21.48
PNC Chip 3	36	-18.08
BETULA	323	-17.47
BIG Chip 3	322	-15.4
NCNGSONATA	130	-15.28
HUNT	780	-12.16
ADNI2	240	-10.93
UNIBA	355	-10.93
PNC Chip 1	225	-8.828
UBA2	497	-8.529
UKB	12529	-7.119
ADNI1	584	-6.779
BIG Chip 1	1159	-4.874
PNC Chip 4	115	-3.011
BIG Chip 2	779	-2.958
NIMAGE	212	-2.142
TOP	1158	-1.748
UBA	522	2.46
HUBIN	174	5.009
NCNGAVANTO	236	5.143
Summary	**20853**	**-7.1115**



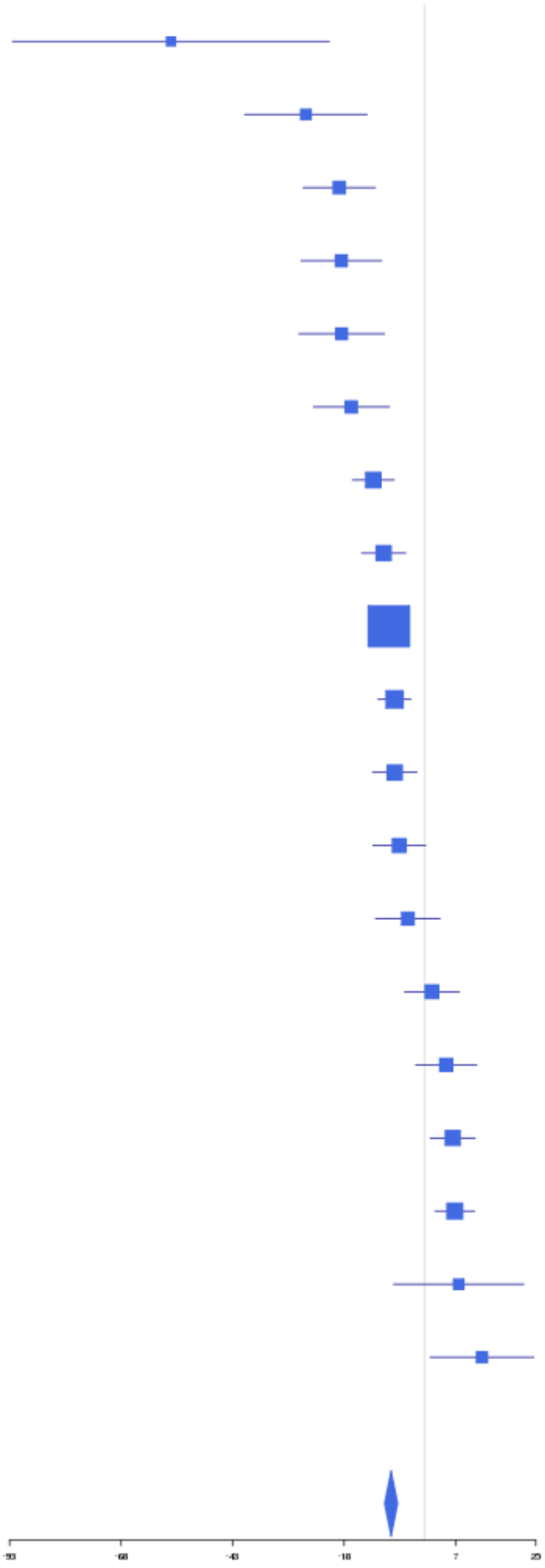
Hippocampal_tail_IncWhole 5:93094118

Cohort	N	Effect (cubic mm)
PNC Chip 4	115	-26.26
NIMAGE	212	-24.61
PNC Chip 1	225	-18.32
TOP	1158	-12.61
PING	360	-12.1
PNC Chip 2	117	-12.03
UNIBA	355	-11.79
NCNGAVANTO	236	-11.1
ADNI1	584	-9.524
UKB	12549	-8.897
NCNGSONATA	130	-8.888
UBA	522	-8.589
UBA2	497	-7.379
ADNI2	240	-5.51
BIG Chip 2	778	-5.255
BIG Chip 1	1144	-5.076
BIG Chip 3	322	-4.648
HUBIN	174	-4.133
HUNT	780	-3.726
BETULA	323	16.98
PNC Chip 3	36	63.26
Summary	**20857**	**-8.5878**



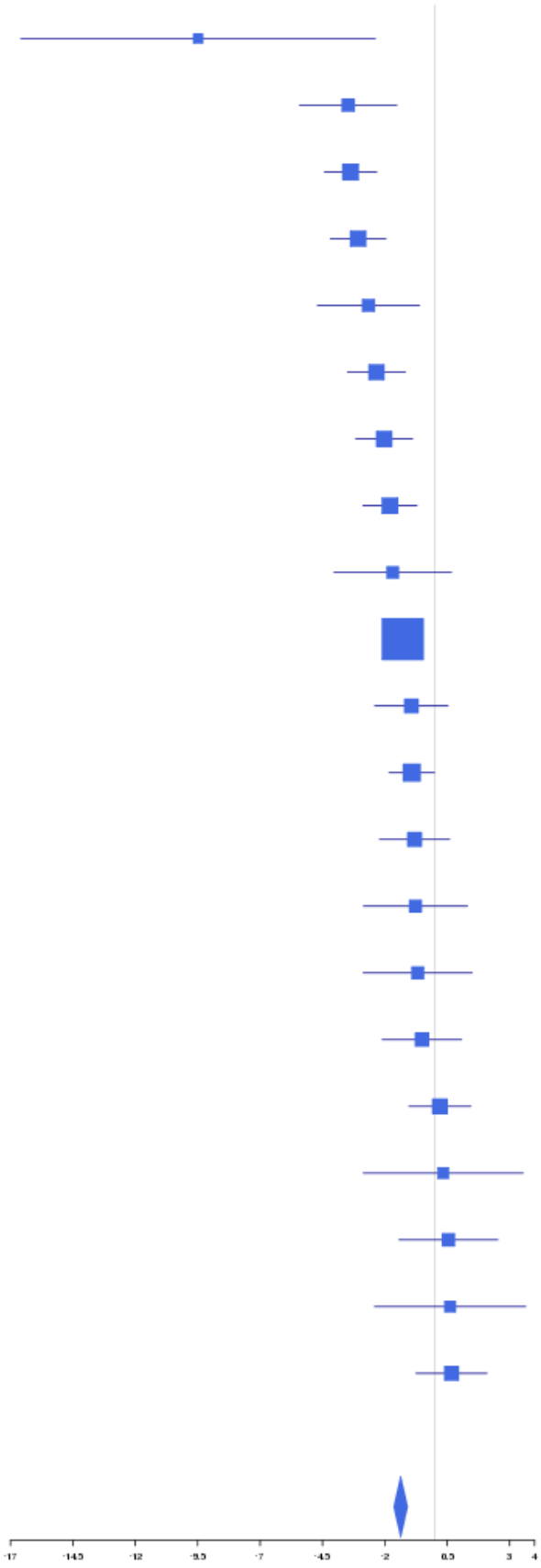
Hippocampal_tail_lncWhole 14:59074136

Cohort	N	Effect (cubic mm)
PNC Chip 3	36	-56.81
PNC Chip 2	117	-26.54
NCNGAVANTO	236	-19.07
PNC Chip 1	225	-18.6
HUBIN	174	-18.54
NIMAGE	212	-16.37
HUNT	780	-11.44
BIG Chip 2	779	-9.115
UKB	12560	-7.954
BIG Chip 1	1159	-6.688
UBA	522	-6.625
PING	360	-5.619
BETULA	323	-3.7
UNIBA	355	1.706
ADNI2	240	4.903
UBA2	497	6.37
ADNI1	584	6.844
PNC Chip 4	115	7.722
NCNGSONATA	130	12.93
Summary	**19404**	**-7.4462**



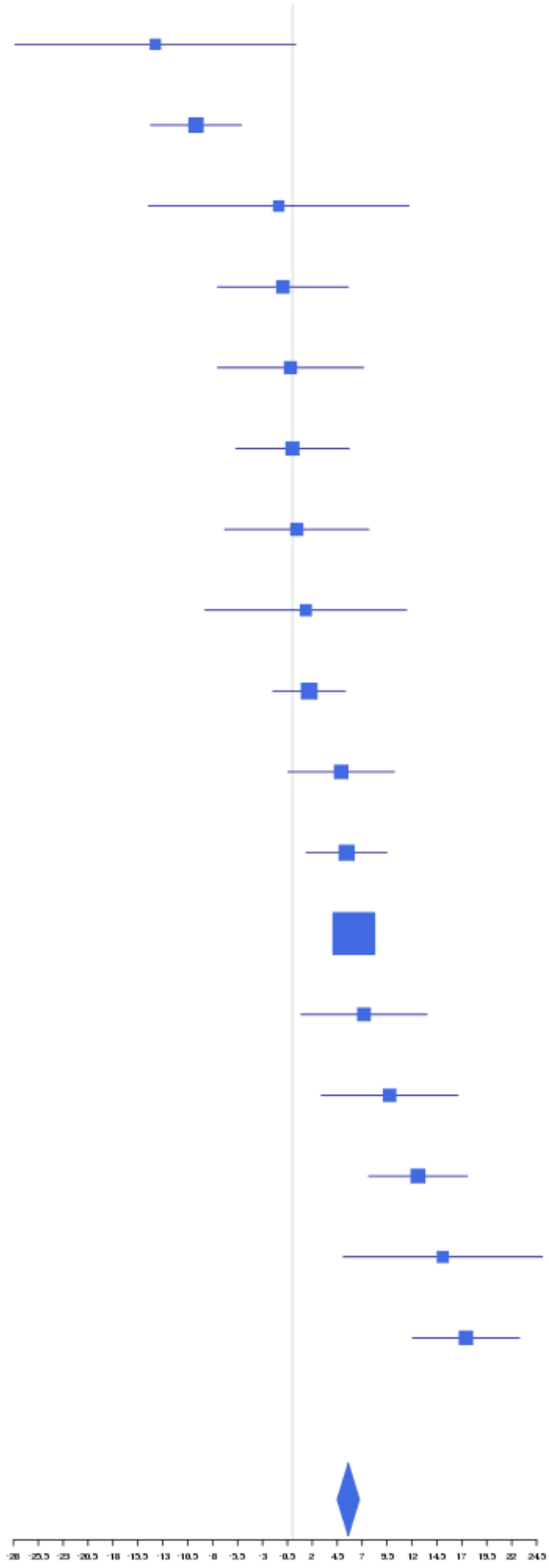
molecular_layer_HP_lncWhole 10:126436717

Cohort	N	Effect (cubic mm)
PNC Chip 3	36	-9.481
BIG Chip 3	322	-3.468
HUNT	780	-3.372
ADNI1	584	-3.067
PNC Chip 1	225	-2.656
BIG Chip 2	777	-2.335
UBA	522	-2.028
BIG Chip 1	1150	-1.795
NCNGSONATA	130	-1.684
UKB	12511	-1.282
ADNI2	240	-0.9361
TOP	1158	-0.9208
PING	360	-0.8082
NIMAGE	212	-0.7735
HUBIN	174	-0.6823
BETULA	323	-0.5137
UBA2	497	0.2073
PNC Chip 4	115	0.3392
NCNGAVANTO	236	0.548
PNC Chip 2	117	0.6157
UNIBA	355	0.6714
Summary	**20824**	**-1.3636**



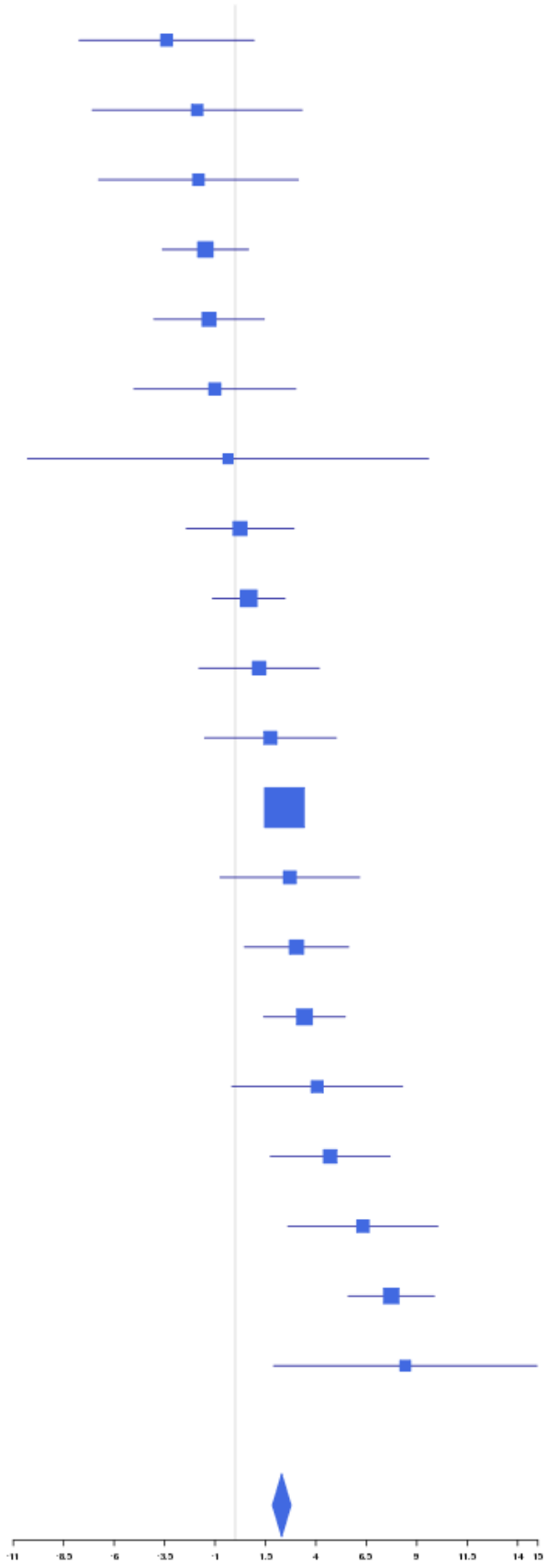
presubiculum_lncWhole 12:65718299

Cohort	N	Effect (cubic mm)
PNC Chip 3	36	-13.75
PING	360	-9.671
PNC Chip 2	117	-1.372
NIMAGE	212	-0.9532
HUBIN	174	-0.1904
BETULA	323	0.01548
PNC Chip 1	225	0.4428
PNC Chip 4	115	1.349
HUNT	780	1.685
UBA2	497	4.898
ADNI1	584	5.443
UKB	12560	6.165
NCNGAVANTO	236	7.183
ADNI2	240	9.769
UBA	522	12.6
NCNGSONATA	130	15.1
BIG Chip 3	323	17.42
Summary	**17434**	**5.6108**



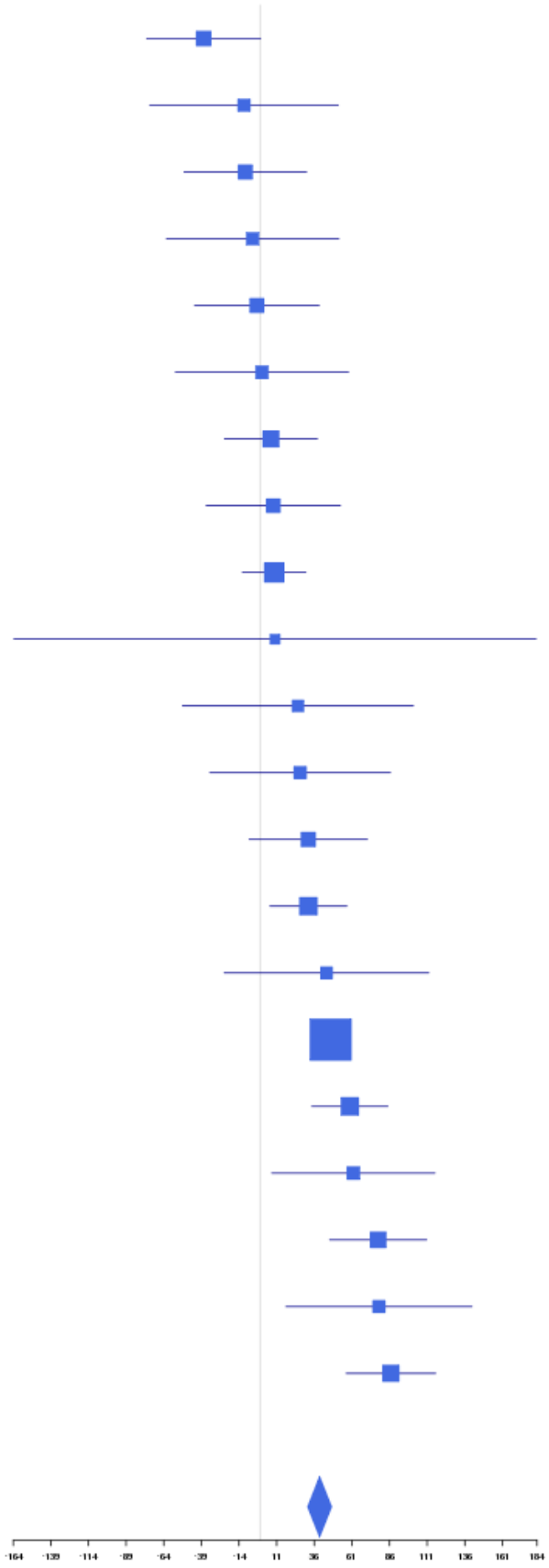
subiculum_lncWhole 6:148056480

Cohort	N	Effect (cubic mm)
HUBIN	174	-3.398
PNC Chip 2	117	-1.881
NCNGSONATA	130	-1.819
ADNI1	584	-1.474
UNIBA	355	-1.294
NIMAGE	212	-1.008
PNC Chip 3	36	-0.3544
UBA2	497	0.2463
TOP	1158	0.6717
PING	360	1.187
ADNI2	240	1.746
UKB	12560	2.441
BIG Chip 3	323	2.709
UBA	522	3.041
HUNT	780	3.435
PNC Chip 1	225	4.066
BETULA	323	4.71
NCNGAVANTO	236	6.332
BIG Chip 2	779	7.737
PNC Chip 4	115	8.433
Summary	**19726**	**2.3071**



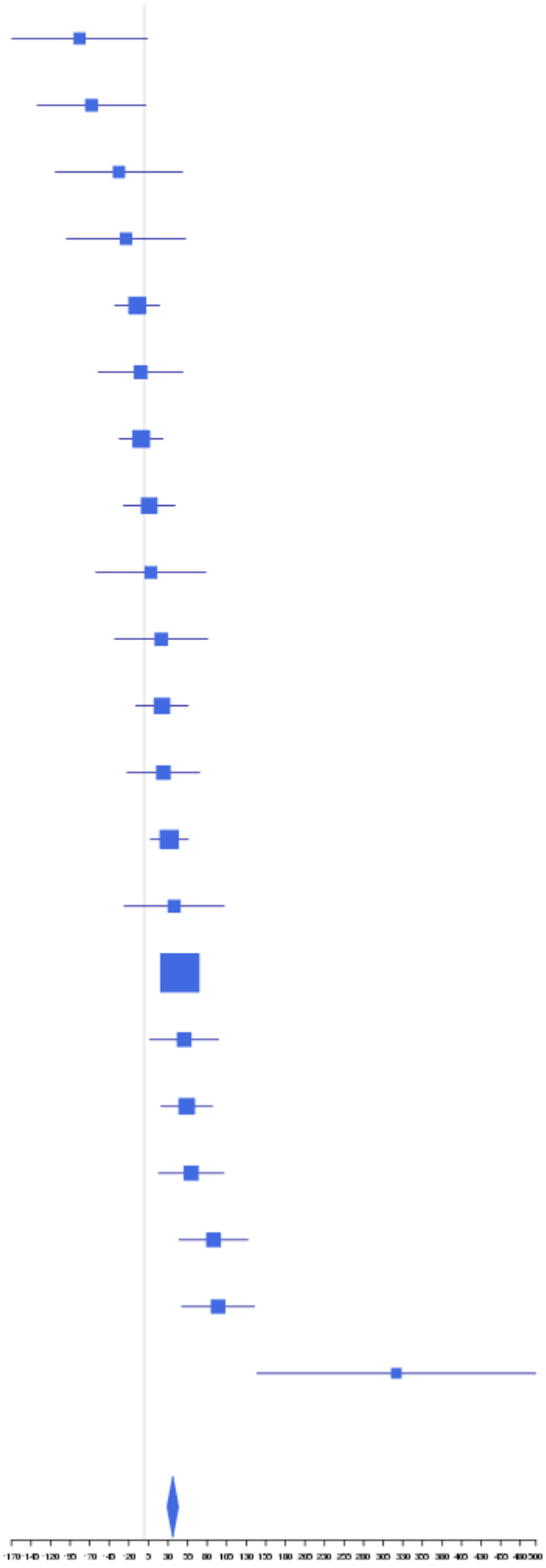
Whole_hippocampus 2:162845565

Cohort	N	Effect (cubic mm)
UNIBA	355	-37.49
ADNI2	240	-10.68
ADNI1	584	-9.829
PNC Chip 1	225	-4.934
BIG Chip 3	323	-2.14
HUBIN	174	1.247
BIG Chip 2	778	7.202
NIMAGE	212	8.768
TOP	1158	9.321
PNC Chip 3	36	9.898
PNC Chip 2	117	25.15
NCNGAVANTO	236	26.6
PING	360	32.02
BIG Chip 1	1158	32.11
NCNGSONATA	130	44.12
UKB	12546	46.84
HUNT	780	59.61
BETULA	323	61.97
UBA2	497	78.44
PNC Chip 4	115	78.96
UBA	522	86.91
Summary	**20869**	**39.5437**



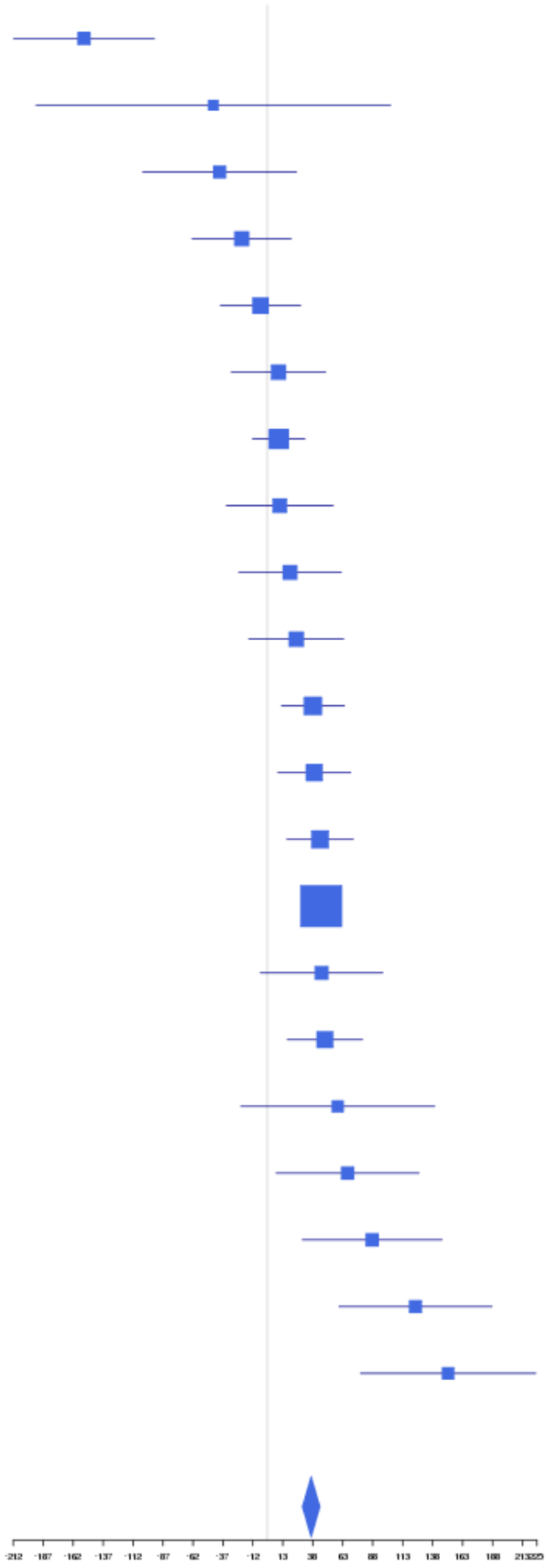
Whole_hippocampus 3:141759380

Cohort	N	Effect (cubic mm)
PNC Chip 4	115	-82.89
HUBIN	174	-67.61
PNC Chip 2	117	-32.59
ADNI2	240	-23.54
BIG Chip 1	1150	-9.24
BETULA	323	-4.933
HUNT	780	-4.264
UBA2	497	6.038
NCNGSONATA	130	8.184
PNC Chip 1	225	21.34
UBA	522	22.36
ADNI1	584	24.12
TOP	1158	31.66
NCNGAVANTO	236	37.96
UKB	12536	45.15
UNIBA	355	50.77
BIG Chip 2	776	53.96
PING	360	59.7
BIG Chip 3	322	88.25
NIMAGE	212	94.01
PNC Chip 3	36	321.7
Summary	**20848**	**36.184**



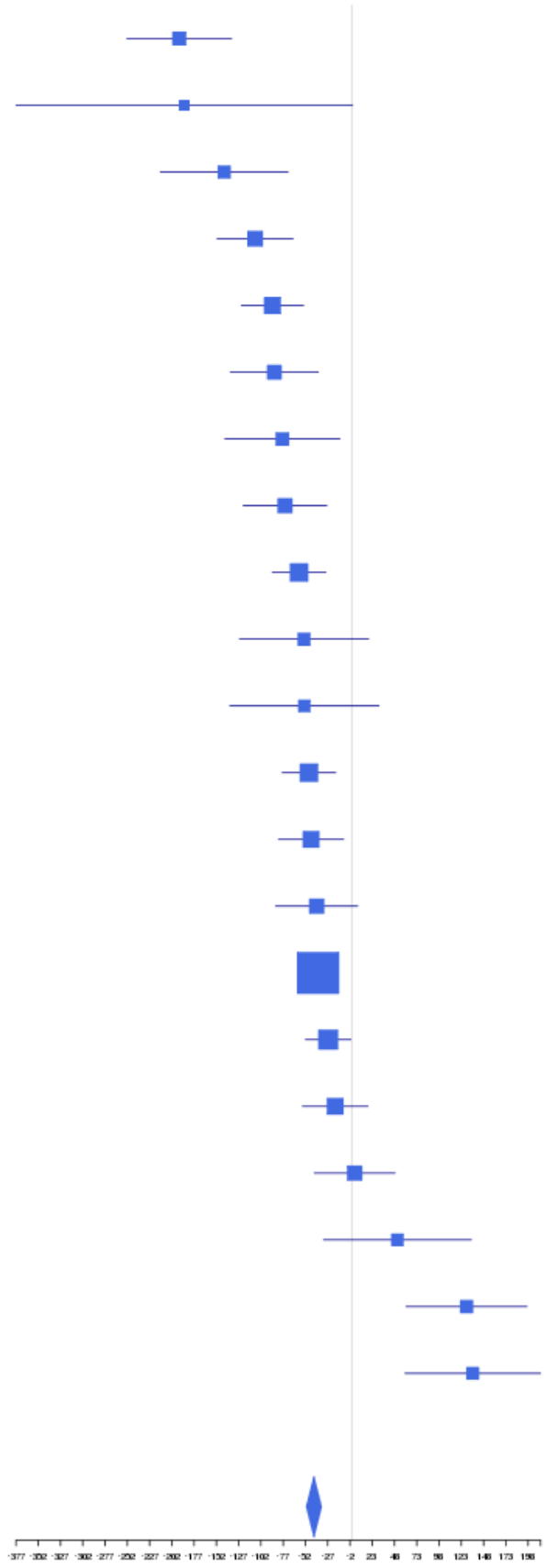
Whole_hippocampus 5:66112715

Cohort	N	Effect (cubic mm)
HUBIN	174	-152.9
PNC Chip 3	36	-45.03
NCNGSONATA	130	-39.74
PING	360	-21.35
UBA2	497	-5.631
BIG Chip 3	323	9.289
TOP	1158	9.552
NIMAGE	212	10.45
ADNI1	584	18.99
UNIBA	355	24.19
BIG Chip 1	1156	38.1
BIG Chip 2	777	39.24
HUNT	780	44.07
UKB	12535	45.01
BETULA	323	45.32
UBA	522	48.11
PNC Chip 2	117	58.81
NCNGAVANTO	236	67.05
PNC Chip 1	225	87.54
ADNI2	240	123.7
PNC Chip 4	115	150.9
Summary	**20855**	**36.6334**



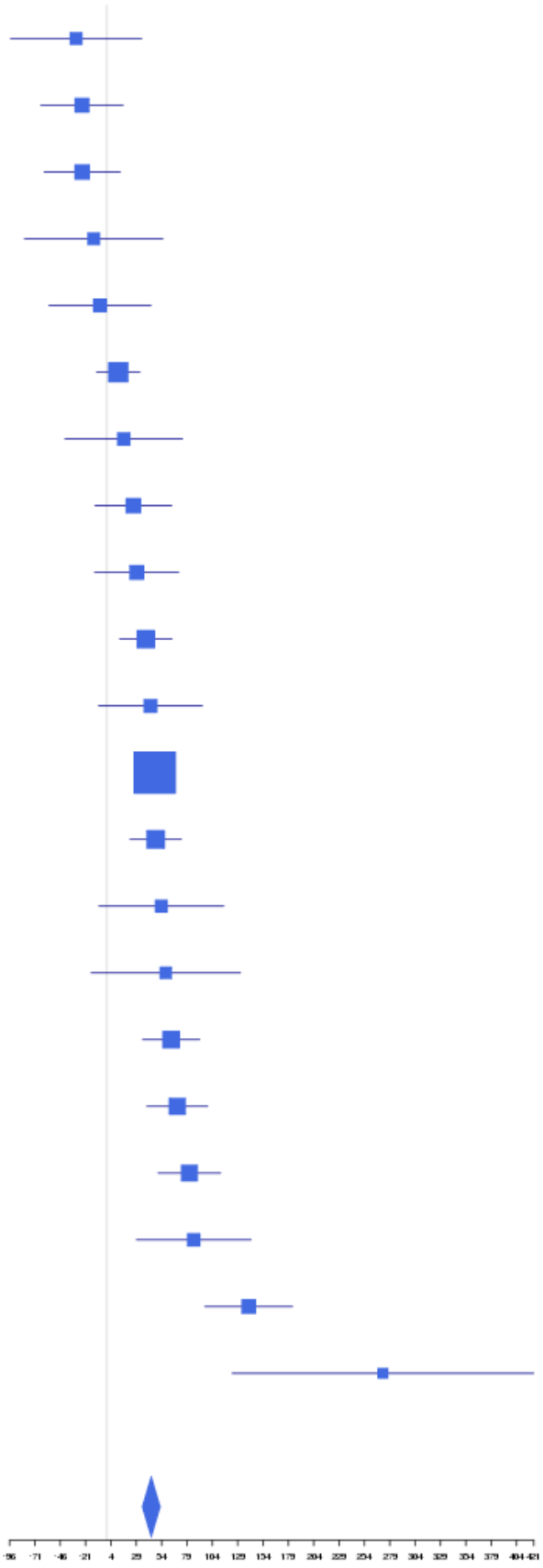
Whole_hippocampus 9:119245127

Cohort	N	Effect (cubic mm)
PNC Chip 1	225	-193.7
PNC Chip 3	36	-188
HUBIN	174	-143.2
PING	360	-108.5
BIG Chip 2	776	-88.98
NIMAGE	212	-86.95
BETULA	323	-77.89
BIG Chip 3	323	-74.95
BIG Chip 1	1156	-59.16
NCNGSONATA	130	-53.58
PNC Chip 2	117	-53.21
HUNT	780	-48.05
UBA2	497	-45.7
ADNI1	584	-39.4
UKB	12544	-37.78
TOP	1158	-26.47
UBA	522	-18.61
UNIBA	355	3.279
PNC Chip 4	115	51.29
NCNGAVANTO	236	128.9
ADNI2	240	135.8
Summary	**20863**	**-42.4218**



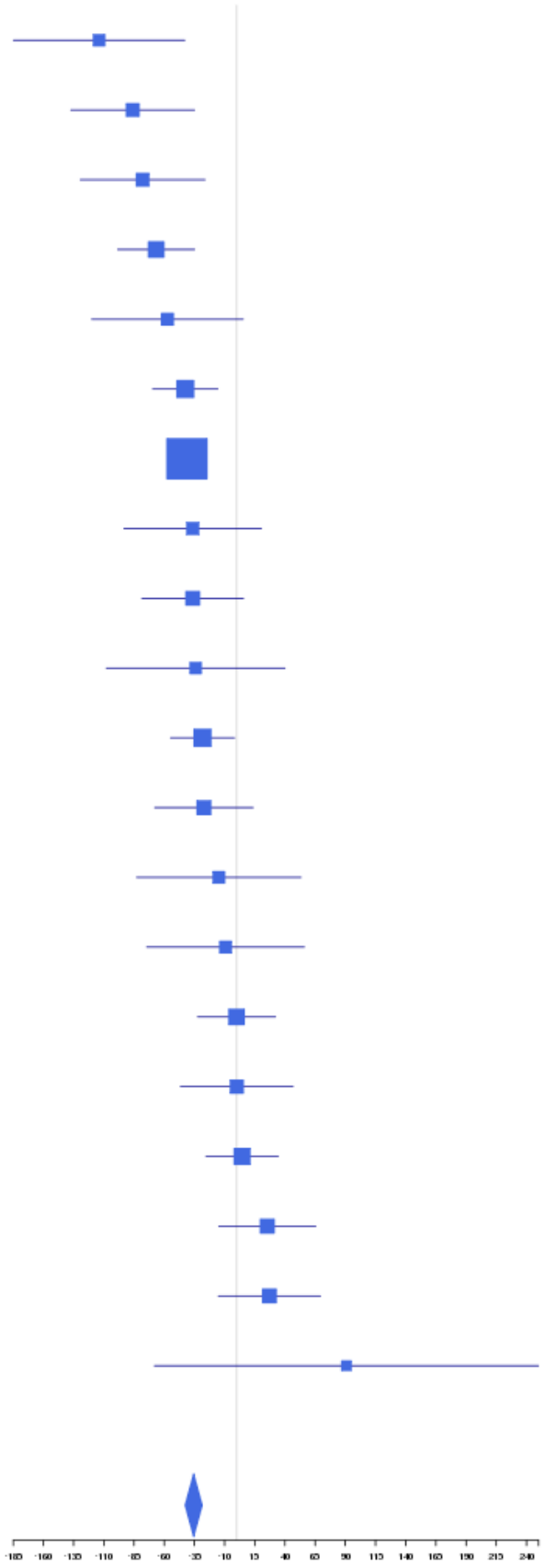
Whole_hippocampus 10:126474200

Cohort	N	Effect (cubic mm)
NCNGSONATA	130	-30.34
ADNI1	584	-24.6
PING	360	-24.38
PNC Chip 2	117	-12.99
PNC Chip 1	225	-6.819
TOP	1158	11.18
HUBIN	174	16.6
UNIBA	355	26.06
BIG Chip 3	321	29.38
BIG Chip 1	1154	38.37
BETULA	323	43.02
UKB	12505	47.23
HUNT	780	48.11
ADNI2	240	53.71
PNC Chip 4	115	58.08
UBA	522	63.35
BIG Chip 2	776	69.39
UBA2	497	81.34
NCNGAVANTO	236	85.61
NIMAGE	212	139.8
PNC Chip 3	36	272.2
Summary	**20820**	**43.747**



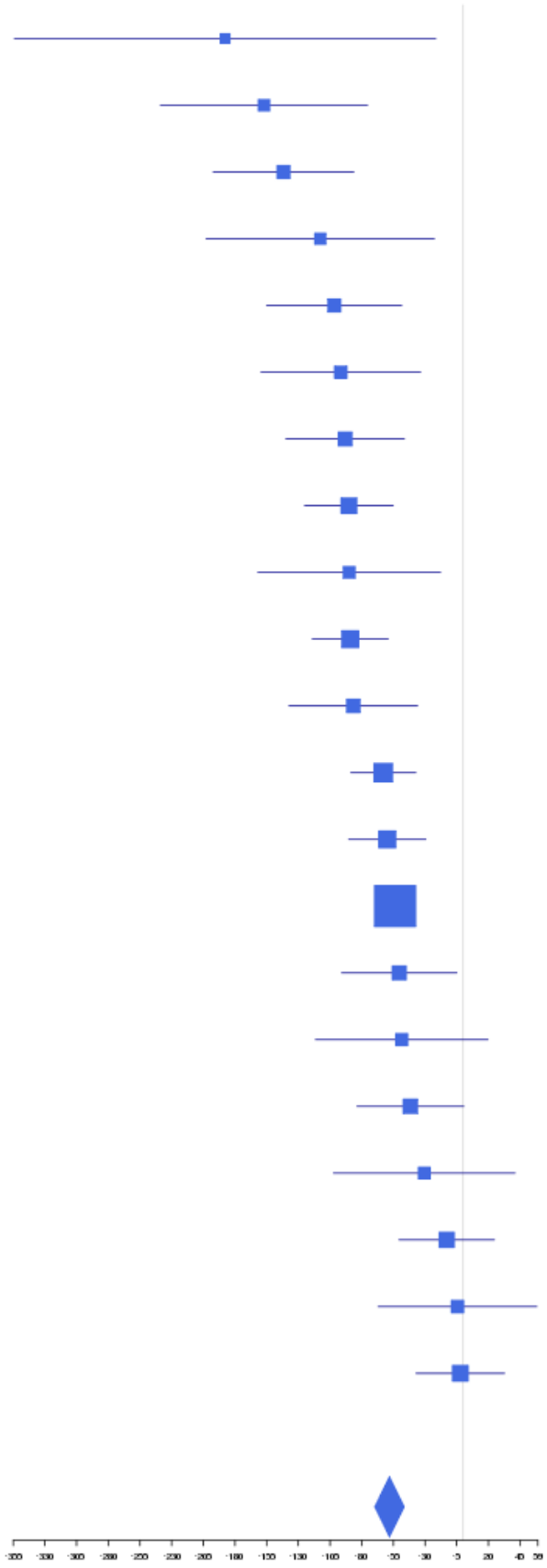
Whole_hippocampus 12:4007898

Cohort	N	Effect (cubic mm)
PNC Chip 4	115	-113.9
BETULA	323	-86.08
PNC Chip 1	225	-77.81
UBA2	497	-66.67
ADNI2	240	-57.3
BIG Chip 1	1141	-42.55
UKB	12532	-41.11
NCNGAVANTO	236	-36.41
BIG Chip 3	323	-36.4
PNC Chip 2	117	-33.95
HUNT	780	-28.27
PING	360	-27.1
HUBIN	174	-14.76
NCNGSONATA	130	-9.169
BIG Chip 2	779	-0.08168
NIMAGE	212	0.09667
UBA	522	4.529
ADNI1	584	25.37
UNIBA	355	27.12
PNC Chip 3	36	90.86
Summary	**19681**	**-35.5976**



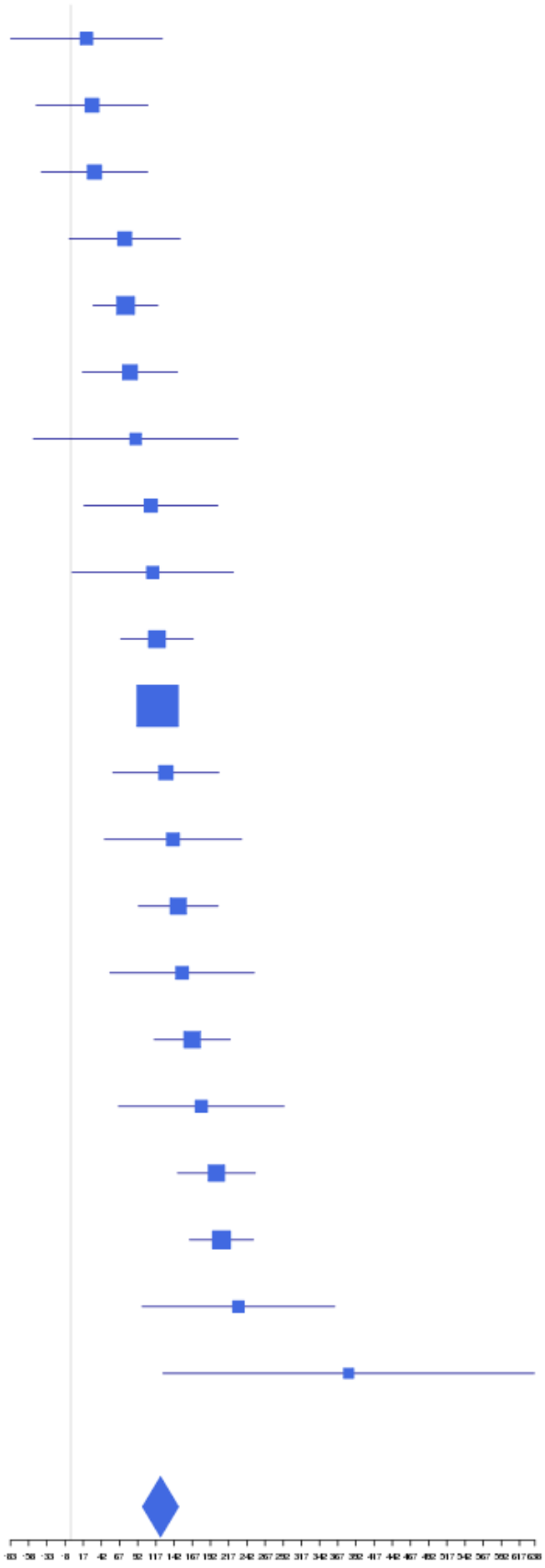
Whole_hippocampus 12:65765944

Cohort	N	Effect (cubic mm)
PNC Chip 3	36	-187.8
PNC Chip 4	115	-157.1
BETULA	323	-141.7
PNC Chip 2	117	-112.7
UNIBA	355	-101.7
NCNGAVANTO	236	-96.52
ADNI1	584	-93.05
BIG Chip 2	779	-90.08
NCNGSONATA	130	-89.85
HUNT	780	-89.03
NIMAGE	212	-86.62
TOP	1158	-62.93
BIG Chip 1	1156	-59.81
UKB	12525	-53.63
BIG Chip 3	323	-50.39
HUBIN	174	-48.4
PING	360	-41.55
ADNI2	240	-30.58
UBA2	497	-12.89
PNC Chip 1	225	-4.378
UBA	522	-2.161
Summary	**20847**	**-58.0823**



Whole_hippocampus 12:117323367

Cohort	N	Effect (cubic mm)
HUBIN	174	21.53
NIMAGE	212	29.11
ADNI1	584	32.52
BIG Chip 3	318	74.04
TOP	1158	75.15
UNIBA	355	81.29
NCNGSONATA	130	89.11
BETULA	323	110.1
NCNGAVANTO	236	112.6
HUNT	780	118.4
UKB	12551	119.3
PING	360	130.7
PNC Chip 1	225	140.5
UBA2	497	147.7
PNC Chip 2	117	153
BIG Chip 2	776	166.9
ADNI2	240	179.4
UBA	522	200.2
BIG Chip 1	1150	207.1
PNC Chip 4	115	230.4
PNC Chip 3	36	381.9
Summary	**20859**	**123.3129**



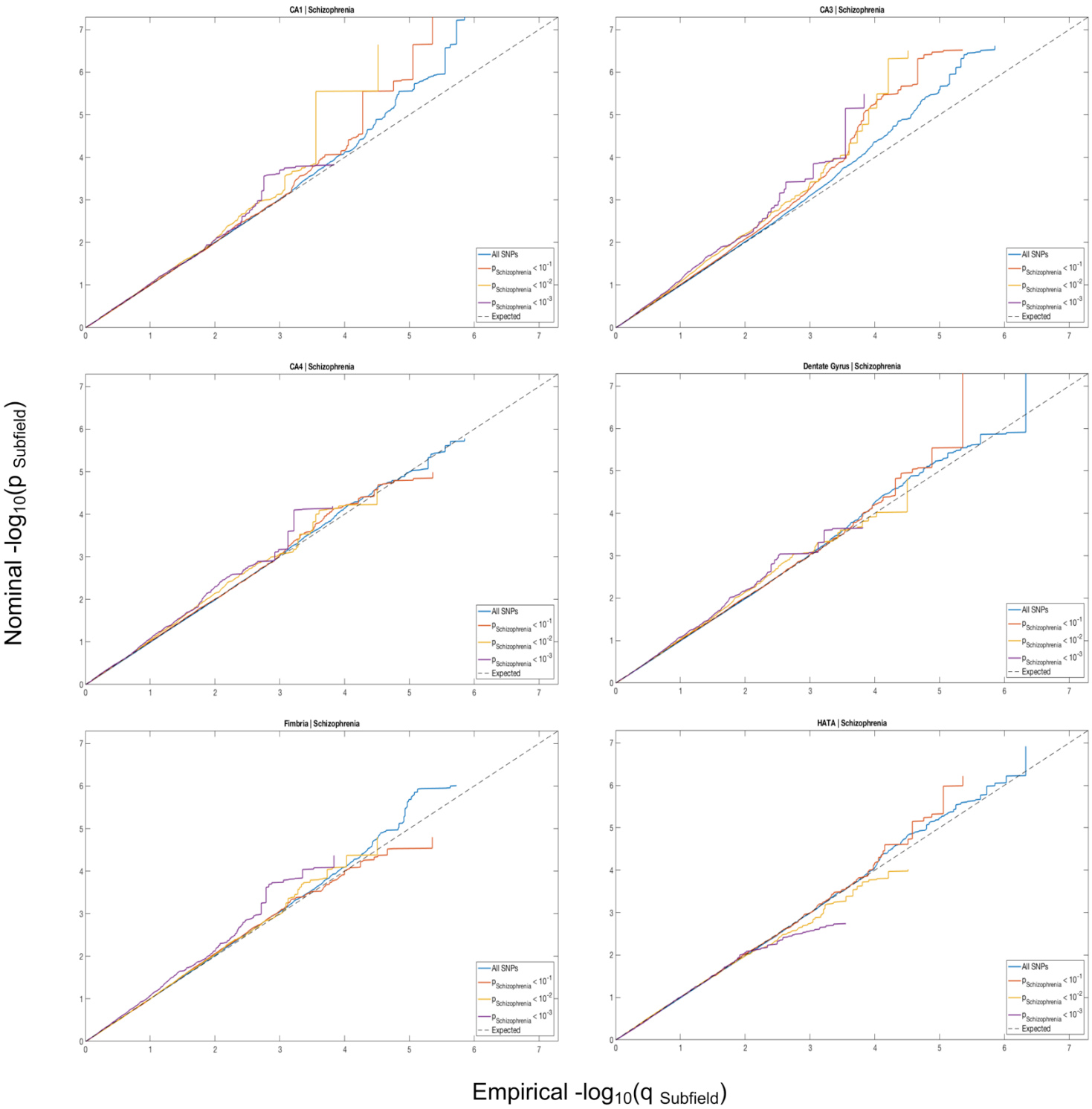
Linkage disequilibrium score regression (LDSR)

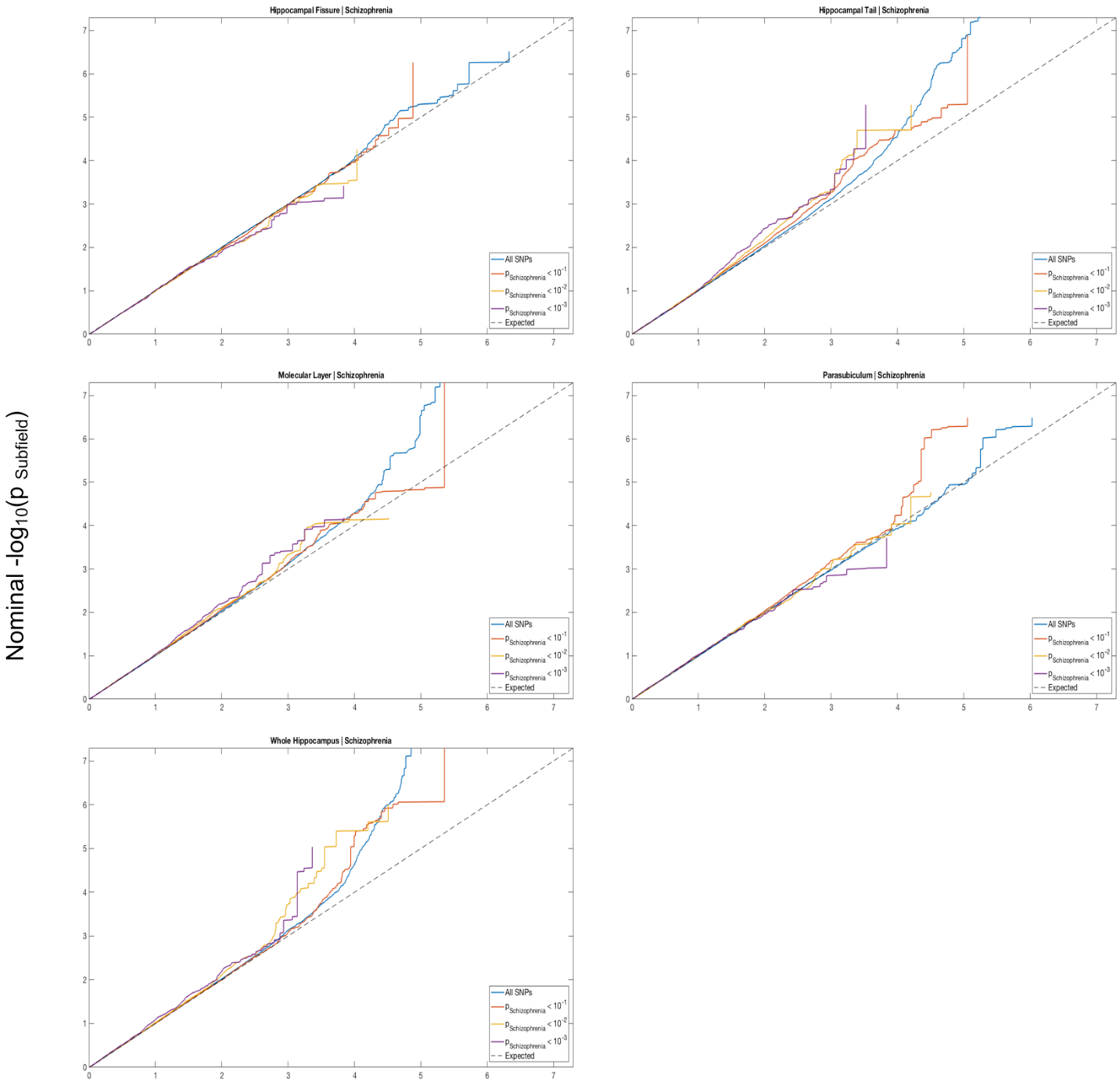
LDSR utilizes the fact that the effect size of any given SNP relates to its LD structure with causal variants, whereas inflation of test statistics by cryptic relatedness or population stratification will be independent of LD. As such, it can isolate true polygenic signals, expressed in an 'LD Score'. Cross-trait LDSR builds on this by taking the product of Z-scores from two traits to estimate their genetic overlap. Note that this technique is robust against sample overlap, which is accounted for by the intercept. For more information, please see Bulik-Sullivan *et al.* (22).

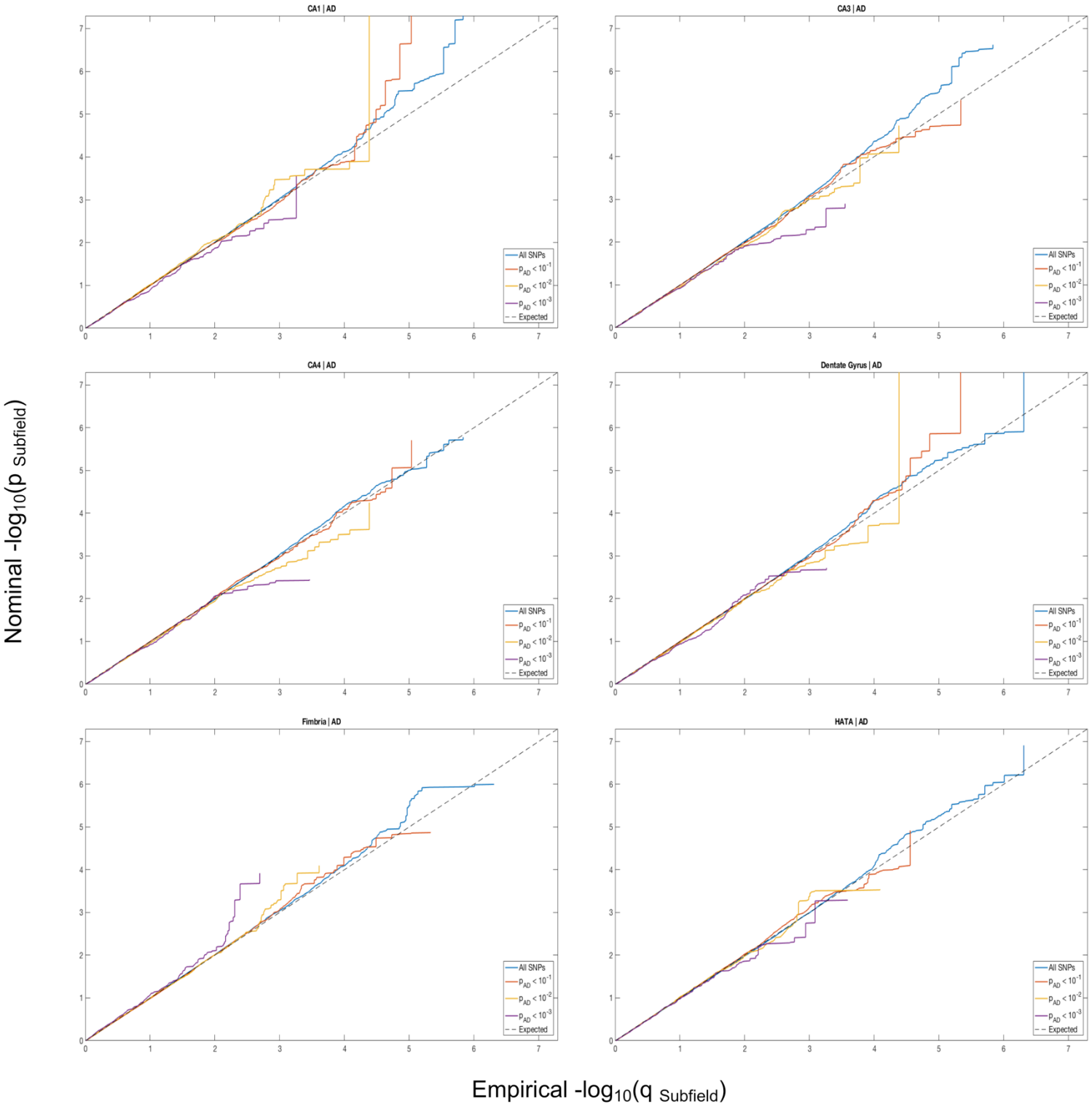
Conditional/conjunction false discovery rate (FDR)

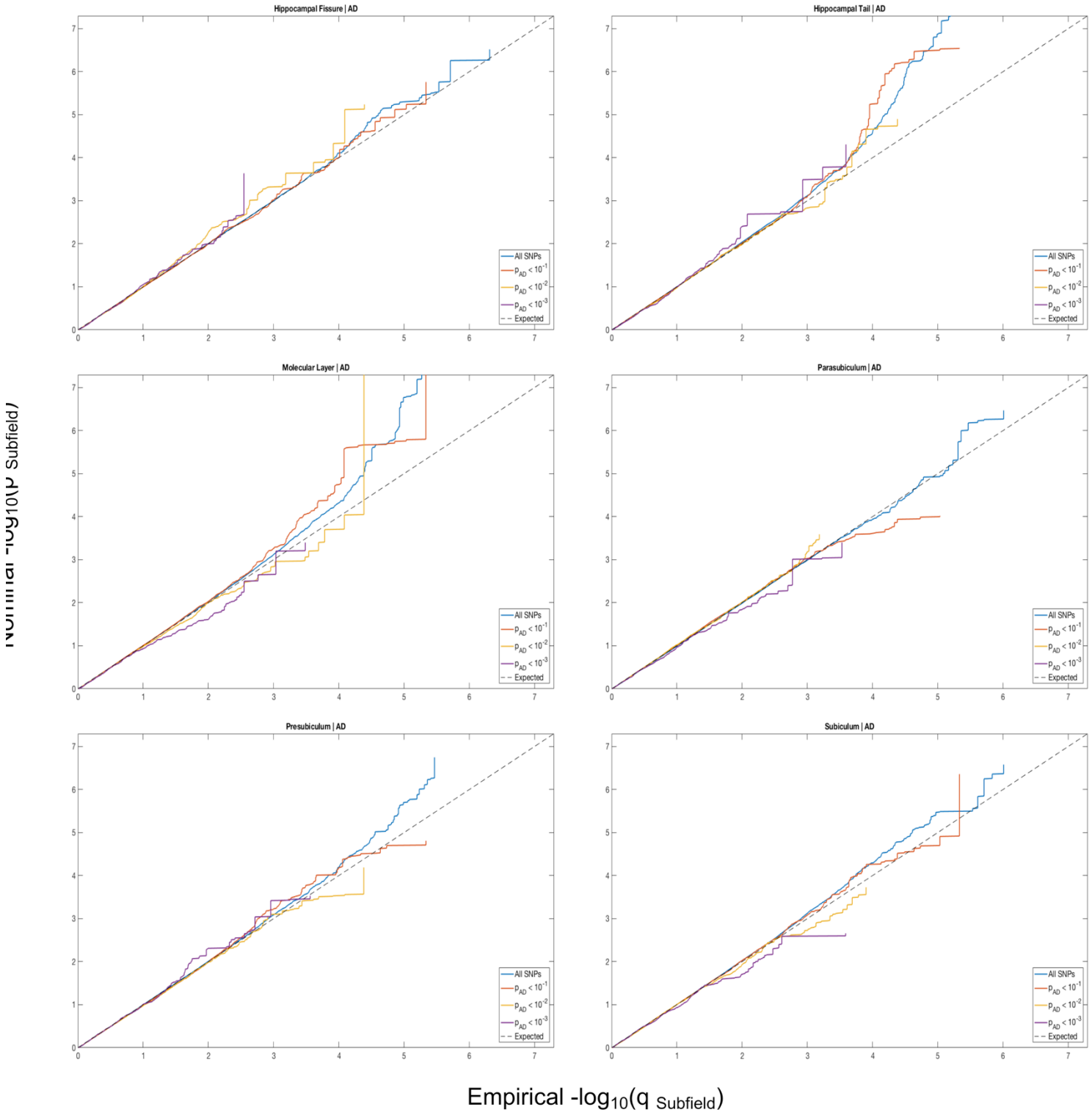
Conditional FDR re-ranks test statistics of SNPs for one trait (here, hippocampal subfield volumes) based on their strength of association with a second trait (here, AD and schizophrenia). Genetic overlap can be visualized through conditional QQ-plots, plotting the observed distribution of test statistics from the first trait thresholded at increasing levels of association with the second trait (here we used $p<.1$, $p<.01$, and $p<.001$). Pleiotropic enrichment will show up as increasing deflections from the null distribution, see Figure 3 in the main text and the figures below. Conjunctional FDR can identify specific shared variants, by selecting those SNPs that have a conditional FDR value below .05 on both traits. The strength of these techniques, compared to LDSR, lies in the fact that overlap between the traits is detected regardless of the direction of allelic effects, which could be mixed. For more information, please see Andreassen *et al.* (23,24).

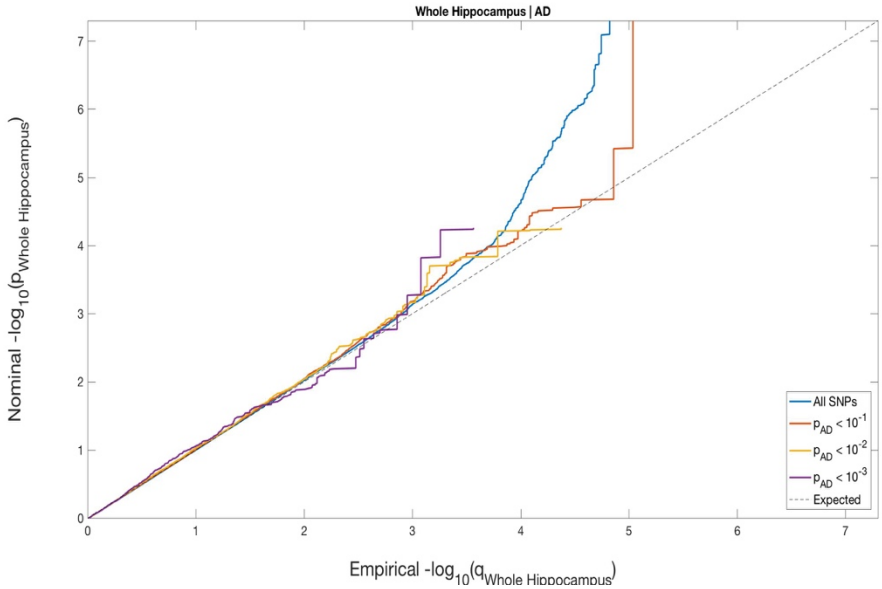
Figure S5. Conditional QQ plots, conditioning the subfields genome-wide significance statistics on those for schizophrenia and Alzheimer's disease.




Hippocampal Fissure | Schizophrenia
Hippocampal Tail | Schizophrenia
Molecular Layer | Schizophrenia
Parasubiculum | Schizophrenia
Whole Hippocampus | Schizophrenia
All SNPs
$p_{Schizophrenia} < 10^{-1}$
$p_{Schizophrenia} < 10^{-2}$
$p_{Schizophrenia} < 10^{-3}$
Expected
Nominal $-\log_{10}(p_{Subfield})$
Empirical $-\log_{10}(q_{Subfield})$


CA1 | AD
CA3 | AD
CA4 | AD
Dentate Gyrus | AD
Fimbria | AD
HATA | AD
All SNPs
$p_{AD} < 10^{-1}$
$p_{AD} < 10^{-2}$
$p_{AD} < 10^{-3}$
Expected
Nominal $-\log_{10}(p_{Subfield})$
Empirical $-\log_{10}(q_{Subfield})$


Hippocampal Fissure | AD
Hippocampal Tail | AD
Molecular Layer | AD
Parasubiculum | AD
Presubiculum | AD
Subiculum | AD
All SNPs
$p_{AD} < 10^{-1}$
$p_{AD} < 10^{-2}$
$p_{AD} < 10^{-3}$
Expected
Empirical -log10(q Subfield)
Nominal -log10(p Subfield)


Whole Hippocampus | AD
Nominal -log10(pWhole Hippocampus)
Empirical -log10(qWhole Hippocampus)
All SNPs
pAD < 10-1
pAD < 10-2
pAD < 10-3
Expected
0
1
2
3
4
5
6
7

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