Supplementary Information

Genotyping, Quality Control (QC), and Imputation, and Population Substructure

The ADNI-1 and ADNI-GO/2 samples were genotyped using the Illumina Human610-Quad, and HumanOmniExpress microarray chips (Illumina, Inc., San Diego, CA), respectively. QC procedures for the genotype data were performed using PLINK [1]. Samples with genotyping call rates<95% were excluded. Subjects with non-European ancestry were removed based on the self-reported ethnicity. We excluded SNPs with a minor allele frequency (MAF) <5% or significant deviation from Hardy-Weinberg equilibrium ($P<1.0x10^{-6}$). A total of 548,010 SNPs for ADNI-1 and 641,106 SNPs for ADNI-GO/2 were retained after cleaning. Genome-wide imputation of SNP allele dosages was performed using the 1000 Genomes reference panel (v37, March, 2012) and IMPUTE2 software after estimating haplotypes using SHAPEIT [2, 3]. Imputed SNPs with an imputation quality estimate (R^2)≥0.40 were used for association analyses. After QC, the ADNI-1 sample with GWA data consisted of 187 CN, 329 MCI, and 163 AD subjects, and the ADNI-GO/2 contained 118 CN, 252 MCI, and 27 AD subjects with GWA data. Population substructure was evaluated in each dataset with reference populations from the 1000 Genome Project by principal components analysis using EIGENSTRAT [4]. Only individuals clustering with European samples were retained for further analysis. Population substructure in the remaining European ancestry sample was assessed using genotyped SNPs that passed QC. These SNPs were pruned to remove pairs with high linkage disequilibrium (LD) based on pairwise LD (r^2) > 0.2 using PLINK, and using a window size of 1,500 SNPs. Principal components (PCs) of ancestry were derived using the smartpca script in EIGENSTRAT. The first three PCs were included as covariates in association test models to minimize spurious associations and maximize power to detect true associations.

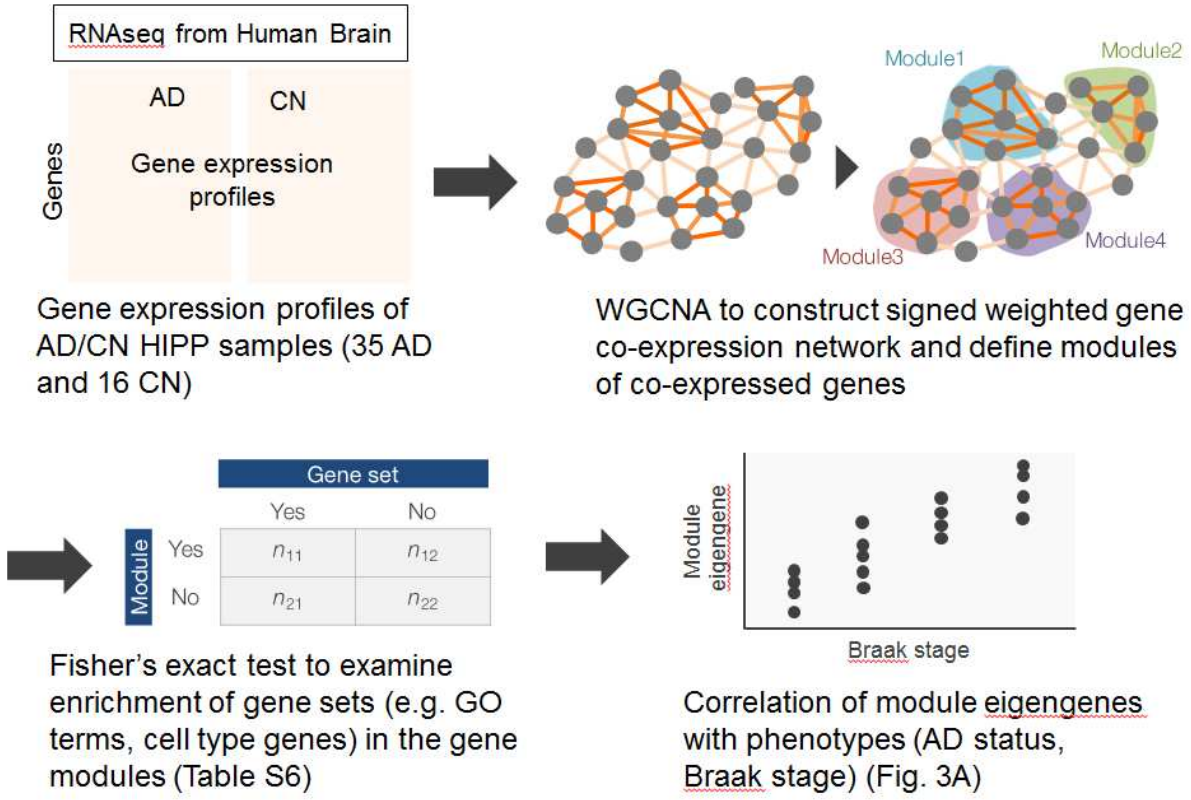
Eisai Bio Bank Description

The Eisai Bio Bank has human brain samples from University of Miami and McLean Hospital. Total RNA purified from hippocampal brain regions were extracted with Qiagen RNeasy Mini Kits (Qiagen, Hilden, Germany). Poly-A-enriched mRNA was reverse transcribed and amplified using the Nugen Ovation Kit (NuGEN, San Carlos, CA, USA). Paired-end cDNA was sequenced with an Illumina MiSeq at 106 base pair length (Illumina, San Diego, CA, USA). RNA-sequencing reads were checked with FASTX-Toolkit (http://hannonlab.cshl.edu/fastx_toolkit), trimmed with Trimmomatic, and aligned to the GRCh38 assembly transcriptome with Bowtie [5]. Transcript expression levels were estimated in transcripts per million (TPM) using RSEM [6]. Samples of RNA integrity numbers (RIN) larger than 5 were kept for downstream analysis.

Source	Total N	Braak Stages								AD cases			Controls		
		NA	0	1	2	3	4	5	6	N (Female)	Age (Mean/SD)	RIN (Mean/SD)	N (Female)	Age (Mean/SD)	RIN (Mean/SD)
McLean	26	0	1	6	3	4	3	3	6	16 (7)	76.1 (5.5)	6.7 (0.95)	10 (5)	66.8 (8.9)	6.6 (1.1)
U of Miami	25	6	0	4	1	5	3	5	1	19 (11)	85.8 (9.0)	6.6 (0.89)	6 (3)	85.7 (6.6)	6.8 (1.0)

Co-expression network analysis

We constructed a gene co-expression network in the human hippocampus transcriptomic data in the Eisai Bio Bank using an R package WGCNA [7]. The Flow chart of co-expression network using RNAseq data from the human hippocampal area is the following.



This software defines module of genes highly co-expressed based on Pearson correlation analysis of gene expression values. The correlation coefficients were applied to the following function for calculating adjacency matrix α.

$$\alpha_{ij} = \left|0.5 + 0.5 \times cor(\boldsymbol{x}_i, \boldsymbol{x}_j)\right|^{\beta}$$

where x_i is a vector including expression levels of gene i in 38 samples. This power function was used for reducing effects of weak correlation and increasing effect of strong correlation. The

parameter β was 12 in this study to meet scale-free topology of the co-expression networks. The adjacency α was used to calculate topological overlap matrix (TOM), an indicator assigned for every pair of genes and representing whether the pair is closely located in the co-expression network. Hierarchical clustering of the genes was performed based on TOM with the average linkage method [8]. Co-expression modules were defined from the hierarchical tree by "dynamic tree cut algorithm" [9]. The modules including less than 100 genes were considered as noisy modules and ignored for the further analyses. Expression patterns of the modules were summarized with their first principal components (module eigengenes). Pearson correlations between gene expressions and the module eigengenes were calculated as module membership values [7].

Definition of brain cell type-specific genes

We used single-cell RNA sequencing data of human brain cells published by Darmanis et al. [10]. Mapping results were downloaded from Gene Expression Omnibus (Accession number: GSE67835) and the mapped read counts were normalized into CPM (count per million) as previously described [10]. Cell type-specific genes were defined when median and mean expression levels (CPM) of genes greater than 4.0.

Supplementary Table 1. Sample size and characteristics of three endophenotypes at the baseline in ADNI 1 and ADNI GO/2.

Trait	Subgroup	ADNI 1			ADNI GO/2		
		N (Female %)	Age (Mean/SD)	Trait (Mean/SD)	N (Female %)	Age (Mean/SD)	Trait (Mean/SD)
CSF $A\beta_{42}$	ALL	365 (40)	74.9 (6.9)	167.6 (55.8)	365 (44.1)	72.9 (7.3)	215.6 (73.1)
	CN	96 (47.9)	75.6 (4.9)	201.2 (55.6)	110 (49.1)	74.8 (5.6)	231.2 (68.7)
	MCI	177 (34.5)	74.6 (7.2)	161.4 (54.1)	230 (42.6)	71.7 (7.4)	215.5 (73.9)
	AD	92 (42.4)	74.6 (7.8)	144.3 (41.6)	25 (36)	75.7 (10.8)	147.3 (39.8)
CSF t-Tau	ALL	365 (40)	74.9 (6.9)	98.2 (53.7)	359 (44.6)	73 (7.3)	88.2 (52.7)
	CN	96 (47.9)	75.6 (4.9)	71.9 (30.6)	107 (49.5)	74.8 (5.6)	72.9 (33)
	MCI	177 (34.5)	74.6 (7.2)	101.1 (55.7)	228 (43)	71.7 (7.4)	90.2 (56.4)
	AD	92 (42.4)	74.6 (7.8)	120.1 (57.8)	24 (37.5)	76.3 (10.7)	137.1 (56.4)
CSF p-Tau	ALL	362 (40.1)	74.9 (6.9)	34.4 (18.6)	364 (44)	72.9 (7.4)	25.2 (12.4)
	CN	94 (47.9)	75.6 (5)	25.5 (14.8)	109 (48.6)	74.8 (5.6)	22.6 (8.9)
	MCI	176 (34.7)	74.6 (7.3)	35.4 (17.7)	230 (42.6)	71.7 (7.4)	25.4 (13.3)
	AD	92 (42.4)	74.6 (7.8)	41.3 (20.3)	25 (36)	75.7 (10.8)	34 (12.7)
HPV	ALL	546 (40.3)	74.9 (6.7)	6500.2 (1191.3)	337 (44.5)	72.3 (7.1)	7155.2 (1101.4)
	CN	166 (43.4)	75.6 (4.8)	7297.8 (922)	102 (50)	74.1 (5.4)	7397.6 (848.2)
	MCI	261 (36.4)	74.6 (7.1)	6378.9 (1082.6)	213 (42.3)	71.1 (7.1)	7177.1 (1125.8)
	AD	119 (44.5)	74.6 (7.8)	5653.9 (1065)	22 (40.9)	74.9 (10.4)	5818.8 (996.2)
LMiT	ALL	679 (39.9)	75.4 (6.7)	8.4 (4.9)	397 (43.8)	72.8 (7.3)	10.8 (4.2)
	CN	187 (43.9)	75.9 (4.9)	14.1 (3.4)	118 (49.2)	74.7 (5.6)	14.4 (2.9)
	MCI	329 (35)	75.3 (7.1)	7.2 (3.2)	252 (42.1)	71.6 (7.4)	9.9 (3.3)
	AD	163 (45.4)	75.3 (7.7)	4.2 (2.9)	27 (37)	75.1 (10.5)	4.1 (2.6)
LMdT	ALL	679 (39.9)	75.4 (6.7)	5.8 (5.5)	397 (43.8)	72.8 (7.3)	9.1 (4.4)
	CN	187 (43.9)	75.9 (4.9)	13.3 (3.6)	118 (49.2)	74.7 (5.6)	13.6 (3.1)
	MCI	329 (35)	75.3 (7.1)	3.8 (2.7)	252 (42.1)	71.6 (7.4)	7.7 (2.8)
	AD	163 (45.4)	75.3 (7.7)	1.2 (1.9)	27 (37)	75.1 (10.5)	1.7 (2)

$A\beta_{42}$, t-Tau, and p-Tau: CSF biomarkers of $A\beta_{42}$ and total and phosphorylated tau proteins. HPV: the MRI scan of hippocampal volume. LMiT and LMdT: the scores from logical memory tests (immediate and delayed recalls). CN: clinically normal subjects. MCI: subjects with mild cognitive impairment. ALL: a composed group of CN, MCI and AD subjects

Supplementary Table 2. Association of *APOE* ε4 carrier status with CSF levels of $A\beta_{42}$, total tau (t-Tau), and phosphorylated tau (p-Tau), with hippocampal volume (HPV), and with logical memory tests of immediate (LMiT) and delayed (LMdT) recall.

Trait	Subgroup	ε4 FREQ	BETA	SE	P
CSF $A\beta_{42}$	ALL	0.22	-0.95	0.07	5.43×10^{-41}
	CN	0.12	-0.87	0.14	5.46×10^{-9}
	MCI	0.24	-0.89	0.09	1.48×10^{-20}
	AD	0.34	-0.73	0.15	6.18×10^{-6}
CSF t-Tau	ALL	0.22	0.69	0.07	5.31×10^{-21}
	CN	0.12	0.26	0.14	0.06
	MCI	0.24	0.76	0.09	1.37×10^{-14}
	AD	0.34	0.23	0.19	0.24
CSF p-Tau	ALL	0.22	0.63	0.07	2.19×10^{-17}
	CN	0.12	0.30	0.15	0.04
	MCI	0.24	0.68	0.10	1.04×10^{-11}
	AD	0.34	0.23	0.18	0.22
HPV	ALL	0.23	-0.55	0.07	1.20×10^{-16}
	CN	0.13	-0.05	0.11	0.66
	MCI	0.26	-0.29	0.09	8.04×10^{-4}
	AD	0.35	-0.59	0.14	5.26×10^{-5}
LMiT	ALL	0.23	-0.49	0.06	4.05×10^{-15}
	CN	0.13	-0.08	0.09	0.36
	MCI	0.25	-0.19	0.06	2.87×10^{-3}
	AD	0.33	0.07	0.12	0.59
LMdT	ALL	0.23	-0.55	0.06	3.77×10^{-19}
	CN	0.13	-0.08	0.08	0.28
	MCI	0.25	-0.21	0.06	2.84×10^{-4}
	AD	0.33	-0.05	0.10	0.61

ε4 FREQ is the ε4 allele frequency.

Supplementary Table 3. Association *P*-values of Alzheimer disease loci previously established by GWAS with AD-related endophenotypes according to cognitive group (Separate spreadsheet)

Supplementary Table 4. Effect sizes and P-values for additional SNPs that show a suggestive association ($P<1.0x10^{-6}$) for CSF $A\beta_{42}$, total tau and phosphorylated tau levels; MRI measure of hippocampal volume; and test scores for immediate and delayed recall in cognitively normal, mild cognitively impaired, and AD subjects. (Separate spreadsheet)

Supplementary Table 5. Top-ranked genes based on the genetic association tests in the CN and MCI subgroups with $P<10^{-6}$.

ID	Symbol	Entrez Gene Name
ADAMTS18	ADAMTS18	ADAM metallopeptidase with thrombospondin type 1 motif 18
ADAMTS3	ADAMTS3	ADAM metallopeptidase with thrombospondin type 1 motif 3
AKR7A3	AKR7A3	aldo-keto reductase family 7 member A3
ANAPC4	ANAPC4	anaphase promoting complex subunit 4
ANO2	ANO2	anoctamin 2
APOE	APOE	apolipoprotein E
ARHGAP24	ARHGAP24	Rho GTPase activating protein 24
ART3	ART3	ADP-ribosyltransferase 3
BCL2L14	BCL2L14	BCL2 like 14
BEST3	BEST3	bestrophin 3
BRIP1	BRIP1	BRCA1 interacting protein C-terminal helicase 1
C20orf96	C20orf96	chromosome 20 open reading frame 96
C6orf58	C6orf58	chromosome 6 open reading frame 58
CAMK2B	CAMK2B	calcium/calmodulin dependent protein kinase II beta
CCDC3	CCDC3	coiled-coil domain containing 3
CDCP1	CDCP1	CUB domain containing protein 1
CLIC5	CLIC5	chloride intracellular channel 5
CMAHP	CMAHP	cytidine monophospho-N-acetylneuraminic acid hydroxylase, pseudogene
CYTH3	CYTH3	cytohesin 3
DAB1	DAB1	DAB1, reelin adaptor protein
DENND4A	DENND4A	DENN domain containing 4A
DMGDH	DMGDH	dimethylglycine dehydrogenase
ERBB2IP	ERBIN	erbb2 interacting protein
FILIP1	FILIP1	filamin A interacting protein 1
FLJ37035	FLJ37035	uncharacterized LOC399821
FRA10AC1	FRA10AC1	fragile site, folic acid type, rare, fra(10)(q23.3) or fra(10)(q24.2) candidate 1
FSHR	FSHR	follicle stimulating hormone receptor
FSIP1	FSIP1	fibrous sheath interacting protein 1
GOLM1	GOLM1	golgi membrane protein 1
GRIN2B	GRIN2B	glutamate ionotropic receptor NMDA type subunit 2B
IFITM10	IFITM10	interferon induced transmembrane protein 10
JPH3	JPH3	junctophilin 3
KCNE4	KCNE4	potassium voltage-gated channel subfamily E regulatory subunit 4
KCNK10	KCNK10	potassium two pore domain channel subfamily K member 10
KIAA2026	KIAA2026	KIAA2026
LRRTM4	LRRTM4	leucine rich repeat transmembrane neuronal 4
MCM5	MCM5	minichromosome maintenance complex component 5
MMP28	MMP28	matrix metallopeptidase 28
MTUS1	MTUS1	microtubule associated tumor suppressor 1
NRG1	NRG1	neuregulin 1
INADL	PATJ	PATJ, crumbs cell polarity complex component
PDGFRL	PDGFRL	platelet derived growth factor receptor like
PDS5B	PDS5B	PDS5 cohesin associated factor B

PLD4	PLD4	phospholipase D family member 4
PRKG1	PRKG1	protein kinase, cGMP-dependent, type I
RCAN1	RCAN1	regulator of calcineurin 1
RGS19	RGS19	regulator of G-protein signaling 19
RNF165	RNF165	ring finger protein 165
SDAD1	SDAD1	SDA1 domain containing 1
SNTB2	SNTB2	syntrophin beta 2
SORCS1	SORCS1	sortilin related VPS10 domain containing receptor 1
SRRM4	SRRM4	serine/arginine repetitive matrix 4
SYT9	SYT9	synaptotagmin 9
TEKT5	TEKT5	tektin 5
TNIK	TNIK	TRAF2 and NCK interacting kinase
TRPV2	TRPV2	transient receptor potential cation channel subfamily V member 2
WBSCR17	WBSCR17	Williams-Beuren syndrome chromosome region 17
WDR5	WDR5	WD repeat domain 5
ZCCHC4	ZCCHC4	zinc finger CCHC-type containing 4
ZNF7	ZNF7	zinc finger protein 7
ZNF804B	ZNF804B	zinc finger protein 804B

Supplementary Table 6. Co-expression network profiles for the modules that contain known AD genes as well as the genes with significant association ($P<1.0x10^{-6}$) with at least one trait for CN, MCI, or all subjects.

Module (Size)	Gene (MM)	Known AD genes (MM) in a same module	Enriched Gene Ontology (FDR)	Enriched Diseases (FDR)
M1 (1618)	***C14orf79*** *(0.49)*	*MAPT-AS1 (0.37)*		AD ($6.2x10^{-3}$)
M2 (314)	*PRKG1(0.88)*	*GLIS3 (0.89)* *FERMT2 (0.80)*	Protein binding ($6.8x10^{-39}$) Focal adhesion ($1.9x10^{-10}$) Signal transduction ($8.8x10^{-10}$)	AD ($2.2x10^{-9}$) CP ($3.1x10^{-9}$) PD ($8.4x10^{-7}$)
M3 (528)	*ARHGAP24 (0.07)*	*BZRAP1-AS1 (0.59)*		
M4 (229)	***MTUS1(0.87)*** *ERBIN (0.86)*	*BACE1-AS (0.72)* *ZCWPW1 (0.67)*	Protein binding ($3.5x10^{-8}$)	
M5 (879)	*AKAP9 (0.66)*	*CELF1 (0.82)*	DNA binding ($2.0x10^{-43}$) Protein binding ($7.6x10^{-40}$) Transcription ($3.3x10^{-39}$)	Schizophrenia ($3.0x10^{-4}$) AD (0.01) PD (0.01)
M6 (843)	***APOE (0.65)***	*APOE (0.65)*	Type I interferon signaling (0.03)	
M7 (3885)	*GRIN2B (0.95)* *CAMK2B (0.88)* ***SRRM4 (0.84)*** *NRG1 (0.83)* *JPH3 (0.78)* *DAB1 (0.73)* *ZNF804B (0.55)* *BRIP1 (0.51)*	*PTK2B (0.89)* *APP (0.86)* *PLXNA4 (0.84)* *MAPT (0.75)* *BZRAP1 (0.67)* *PSEN2 (0.64)*	Chemical synaptic transmission ($1.8x10^{-84}$) Neuron projection ($1.7x10^{-30}$) Nervous system development Axon guidance ($1.6x10^{-24}$) Postsynaptic density ($8.6x10^{-22}$)	AD ($1.8x10^{-46}$) PD ($1.3x10^{-25}$) CP ($2.4x10^{-23}$)
M8 (476)	*RCAN1 (0.74)*	*BIN1 (0.87)* *PSEN1 (0.79)*	Protein binding ($2.8x10^{-16}$) Microtubule binding ($4.1x10^{-5}$) Regulation cell shape ($2.3x10^{-4}$)	AD ($3.8x10^{-5}$) Schizophrenia (0.01) CP (0.01)

Module membership (MM) means a hub-gene score in a module of co-expression network. The FDR indicates false discovery rate estimated using the Benjamin-Hochberg procedure. Enriched diseases were the first three enriched diseases for the module. Bold SNPs denote the study-wide significant association ($P<8.33x10^{-9}$) with a trait. AD, PD, or CP indicates Alzheimer disease, Parkinson disease, and cognitive performance, respectively.

Supplementary Table 7. Correlation expression matrix for genes which were suggestively associated with at least one endophenotypes or were previously identifed in GWAS of AD risk (Separate spreadsheet)

Supplementary Table 8. Rank of the identified modules in enrichment analysis in co-expression networks from the human hippocampal area

Module	# of Genes in a Module	# of AD-associated Genes in a Module	P-value	FDR
M7	3885	265	1.06×10^{-47}	1.81×10^{-46}
M2	314	32	1.27×10^{-10}	2.17×10^{-9}
Module X1	289	23	3.86×10^{-6}	2.19×10^{-5}
Module X2	379	28	1.57×10^{-6}	2.67×10^{-5}
M8	476	32	2.23×10^{-6}	3.7×10^{-5}
Module X3	379	27	4.71×10^{-6}	$4.c01 \times 10^{-5}$
Module X4	299	13	1.69×10^{-4}	0.001
M1	1618	66	4.86×10^{-4}	0.006
Module X5	286	18	7.59×10^{-4}	0.006
M5	879	39	0.002	0.011
Module X6	252	16	0.001	0.011
Module X7	244	15	0.003	0.021
Module X8	590	27	0.005	0.022
Module X9	379	12	0.004	0.025

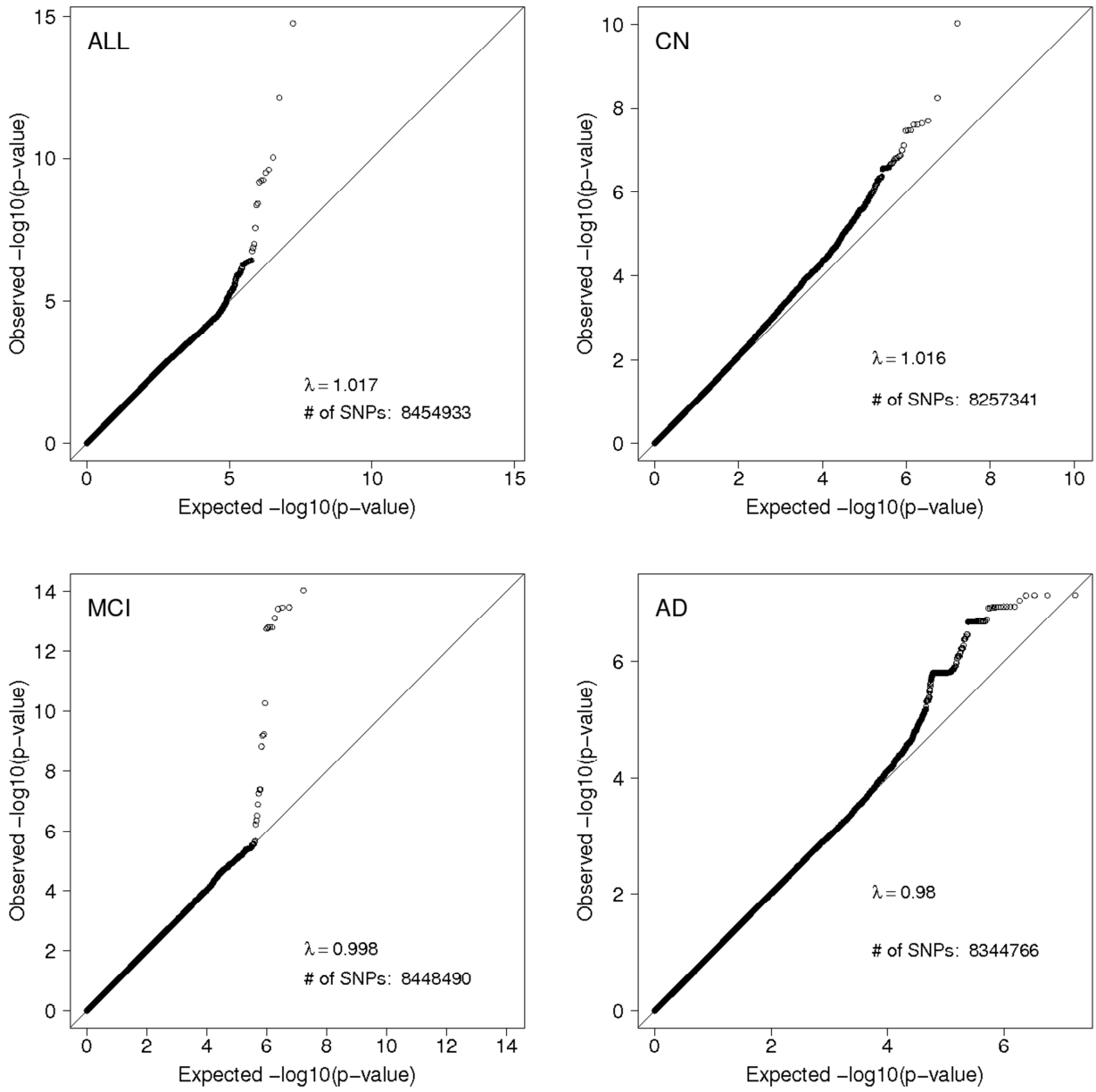
The number of total AD-associated genes is 1,101 obtained from GWASdb2 [11]. The bold modules contain top ranked genes ($P<1.0 \times 10^{-6}$) in this study.

Supplementary Table 9. Genetic associations with CSF biomarkers for the SNPs which were identified in the Deming *et al.* study [12] with genome-wide significant association with CSF biomarkers (Separate spreadsheet)

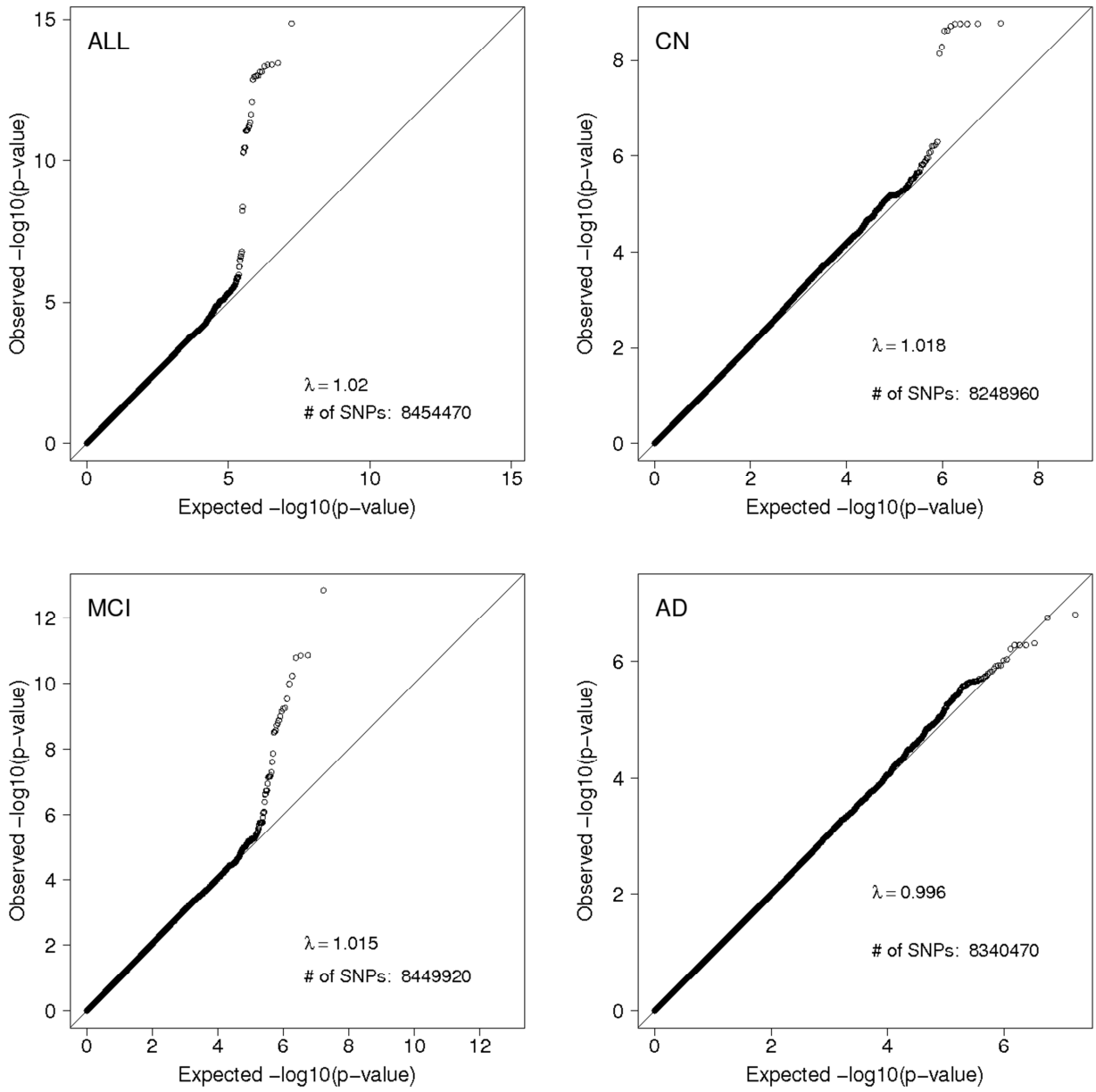
Supplementary Table 10. Previous findings for loci showing at least suggestive evidence for association ($P < 1.0x10^{-6}$) in the current study for AD-related endophenotypes.

		Current Study						Previous Studies			
Trait	**Sub**	**GENE**	**CH**	**SNP**	**Beta**	**SE**	**P-value**	**Statistical Method/Trait**	**SNP**	**P-value**	**Ref**
$A\beta_{42}$	**CN**	*AKR7A3*	1	rs59348345	0.88	0.18	$5.06x10^{-7}$	Entire brain (voxel-GWAS)	rs710865	$1.10x10^{-7}$	[13]
		GRIN2B	12	rs74442473	-1.02	0.18	$2.52x10^{-8}$	Temporal lobe atrophy	rs11055612	$1.20x10^{-7}$	[14]
		KCNK10	14	rs17692117	-1.05	0.21	$5.30x10^{-7}$	Information processing speed	rs17124581	$2.71x10^{-6}$	[15]
	AD	*ERBB4*	2	rs839506	-0.60	0.11	$1.73x10^{-7}$	Copy number variant (AD patients only)	.	.	[16, 17]
t-Tau	**CN**	*SRRM4*	12	rs10775009	0.51	0.09	$1.59x10^{-9}$	GWAS of CSF t-Tau	rs1997111	$2.11x10^{-7}$	[18]
	AD	*RELN*	7	rs3819489	-0.78	0.15	$2.20x10^{-7}$	GWAS of Braak score (from controls)	rs6943822	0.02	[20]
HPV	**CN**	*MTUS1*	8	rs4921790	0.61	0.10	$4.58x10^{-8}$	GWAS of CSF p-Tau	rs7842088	$2.12x10^{-7}$	[18]
	AD	*AKAP9*	7	rs149454736	1.91	0.33	$4.76x10^{-9}$	AD using whole exome sequencing in African Americans	rs144662445 rs149979685	0.002	[20]
LMT	**MCI**	*NRG1*	8	rs118130881	-0.61	0.11	$1.27x10^{-8}$	AD using linkage analysis	rs392499	0.01	[21]

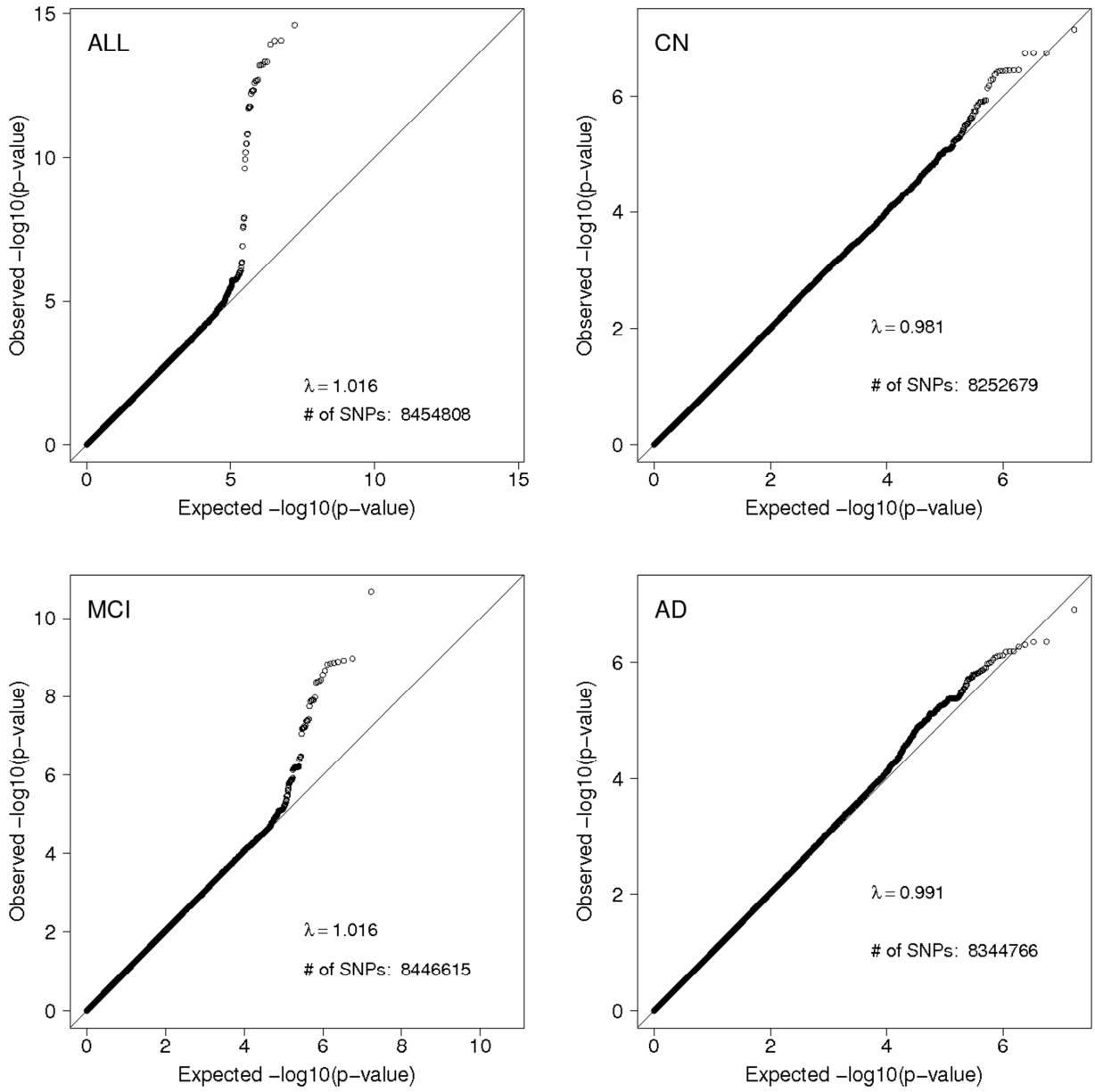
Supplementary Figure 1. Quantile-quantile plots of observed (y-axis) vs. expected (x-axis) P-values for CSF $A\beta_{42}$ in the total sample (ALL), Clinically normal (CN), Mild Cognitively Impaired (MCI), and AD subjects.



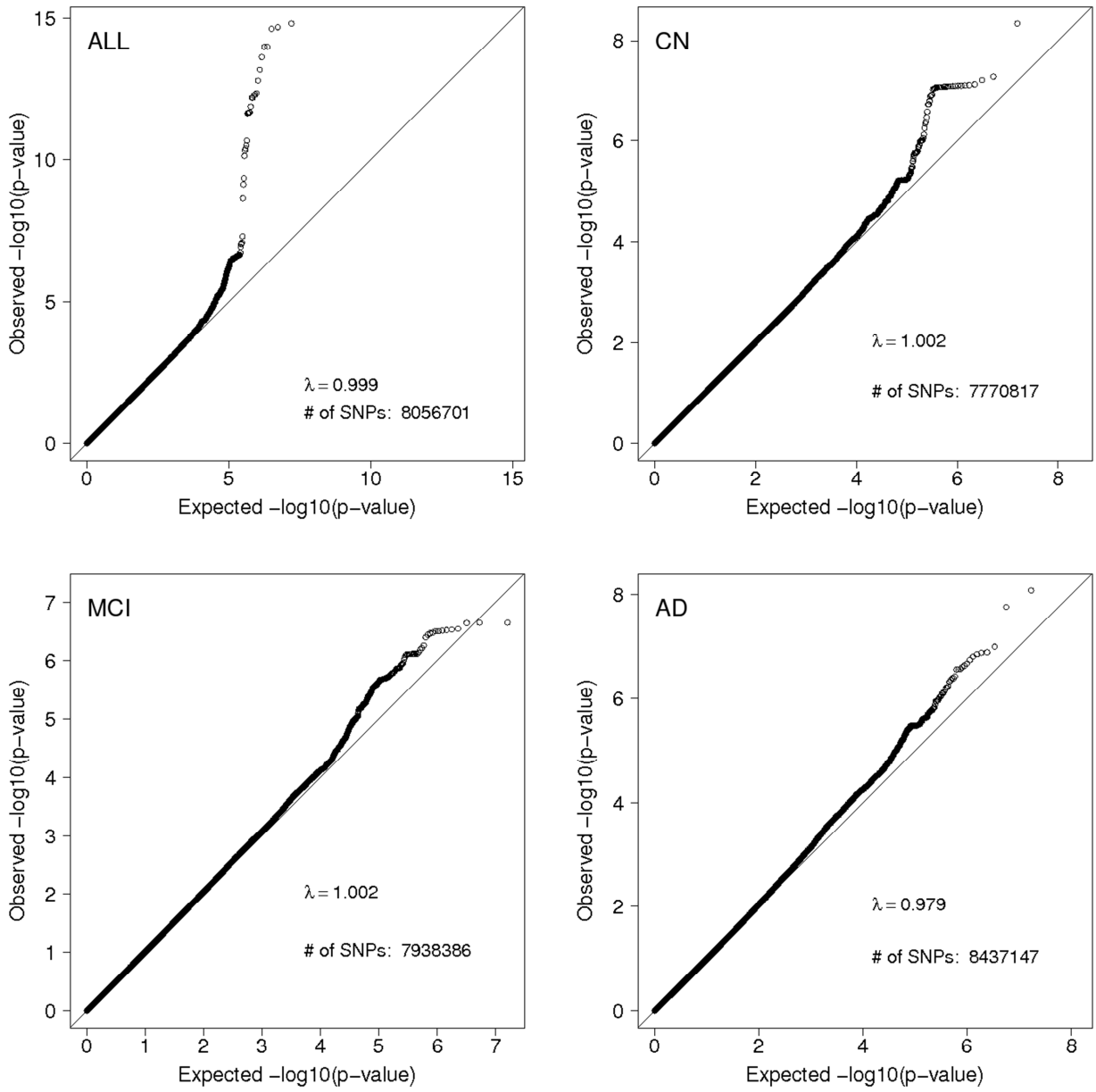
Supplementary Figure 2. Quantile-quantile plots of observed (y-axis) vs. expected (x-axis) P-values for CSF t-Tau in the total sample (ALL), Clinically normal (CN), Mild Cognitively Impaired (MCI), and AD subjects.



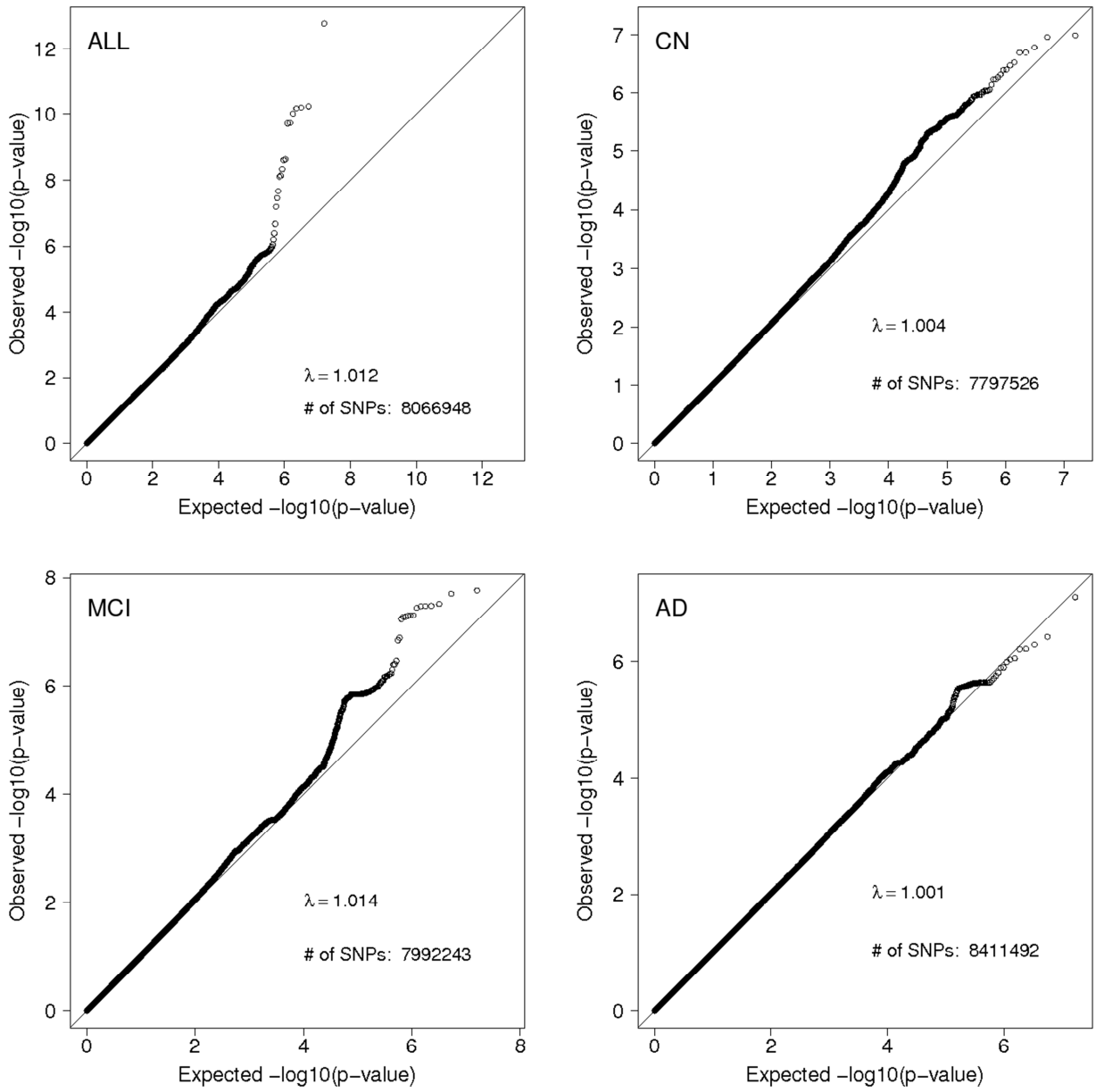
Supplementary Figure 3. Quantile-quantile plots of observed (y-axis) vs. expected (x-axis) P-values for CSF p-Tau from the sample in ALL, Clinically normal (CN), Mild Cognitive Impairment (MCI), and AD.



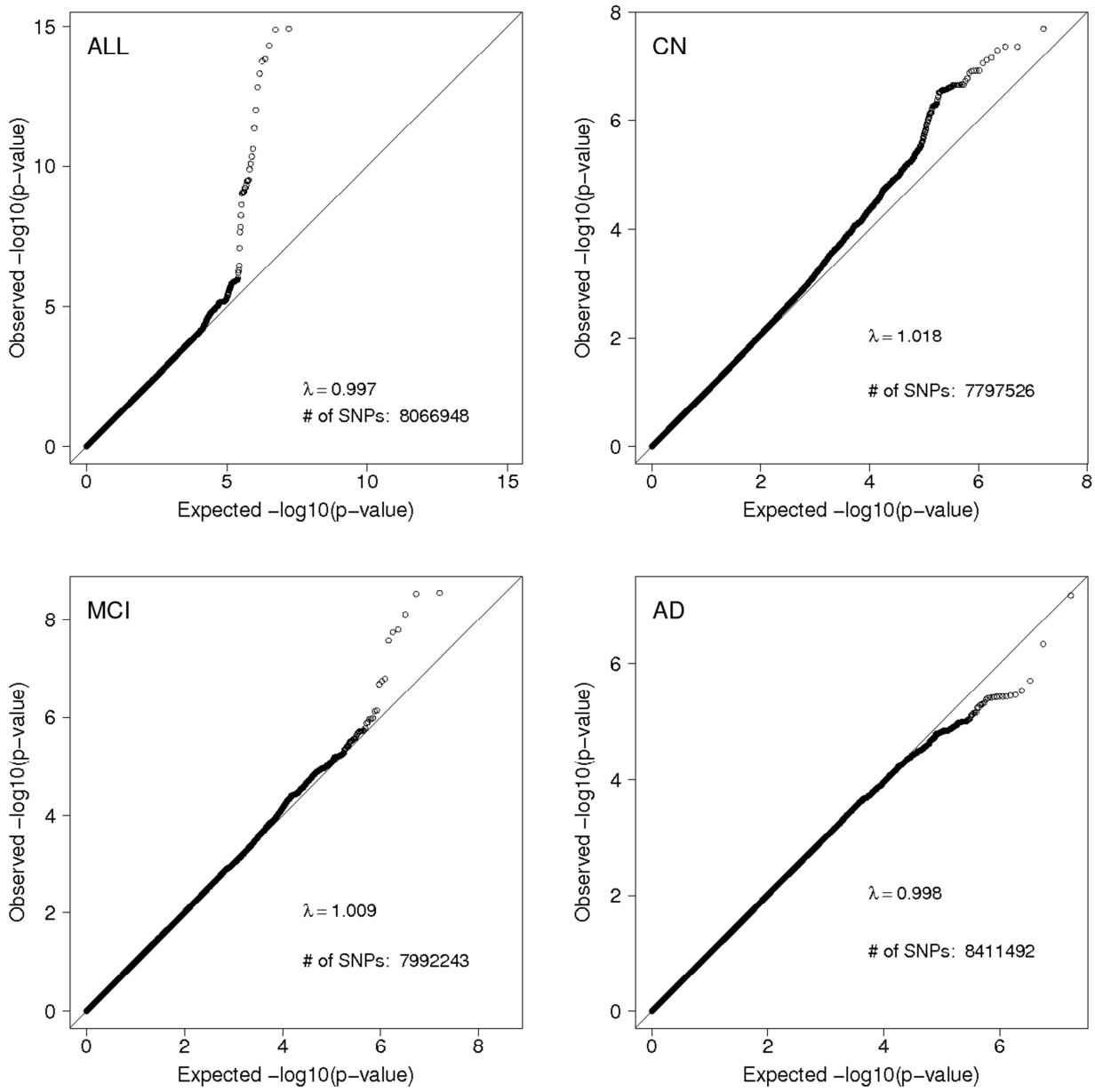
Supplementary Figure 4. Quantile-quantile plots of observed (y-axis) vs. expected (x-axis) P-values for Hippocampal volume (HPV) from the sample in ALL, Clinically normal (CN), Mild Cognitive Impairment (MCI), and AD.



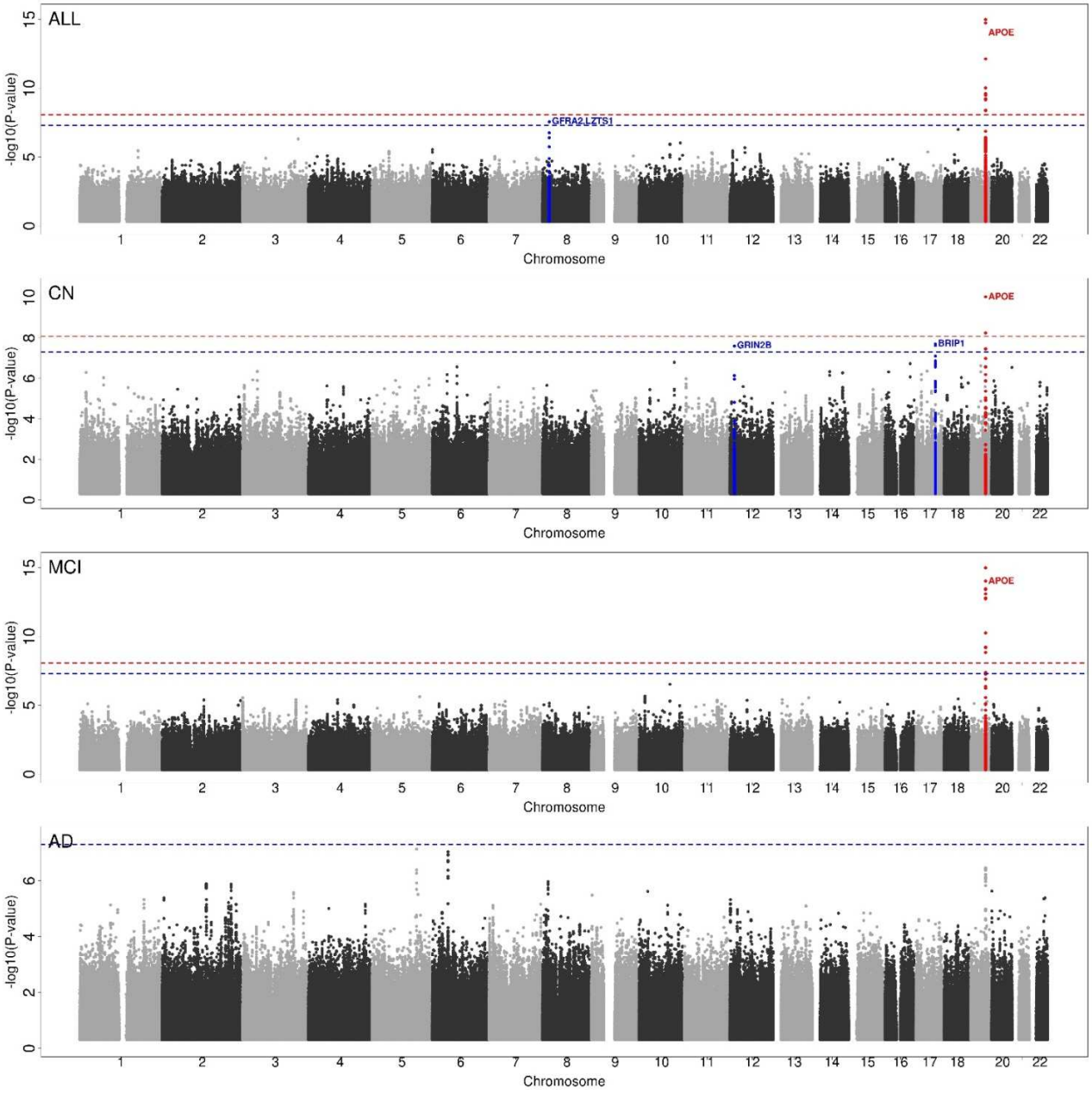
Supplementary Figure 5. Quantile-quantile plots of observed (y-axis) vs. expected (x-axis) P-values for logical memory test (LMT)-immediate recalls from the sample in ALL, Clinically normal (CN), Mild Cognitive Impairment (MCI), and AD.



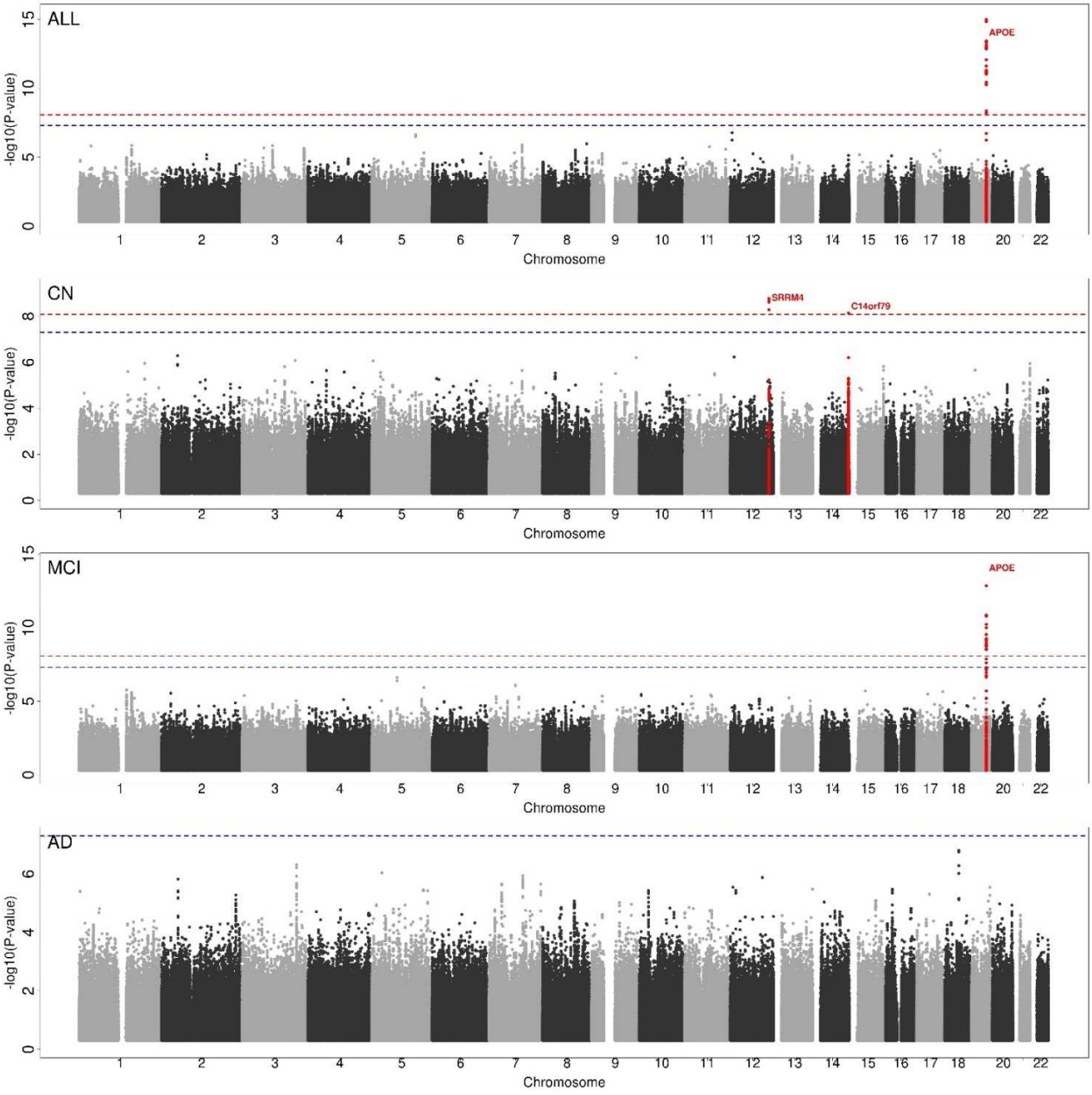
Supplementary Figure 6. Quantile-quantile plots of observed (y-axis) vs. expected (x-axis) P-values for logical memory test (LMT)-delayed recalls from the sample in ALL, Clinically normal (CN), Mild Cognitive Impairment (MCI), and AD.



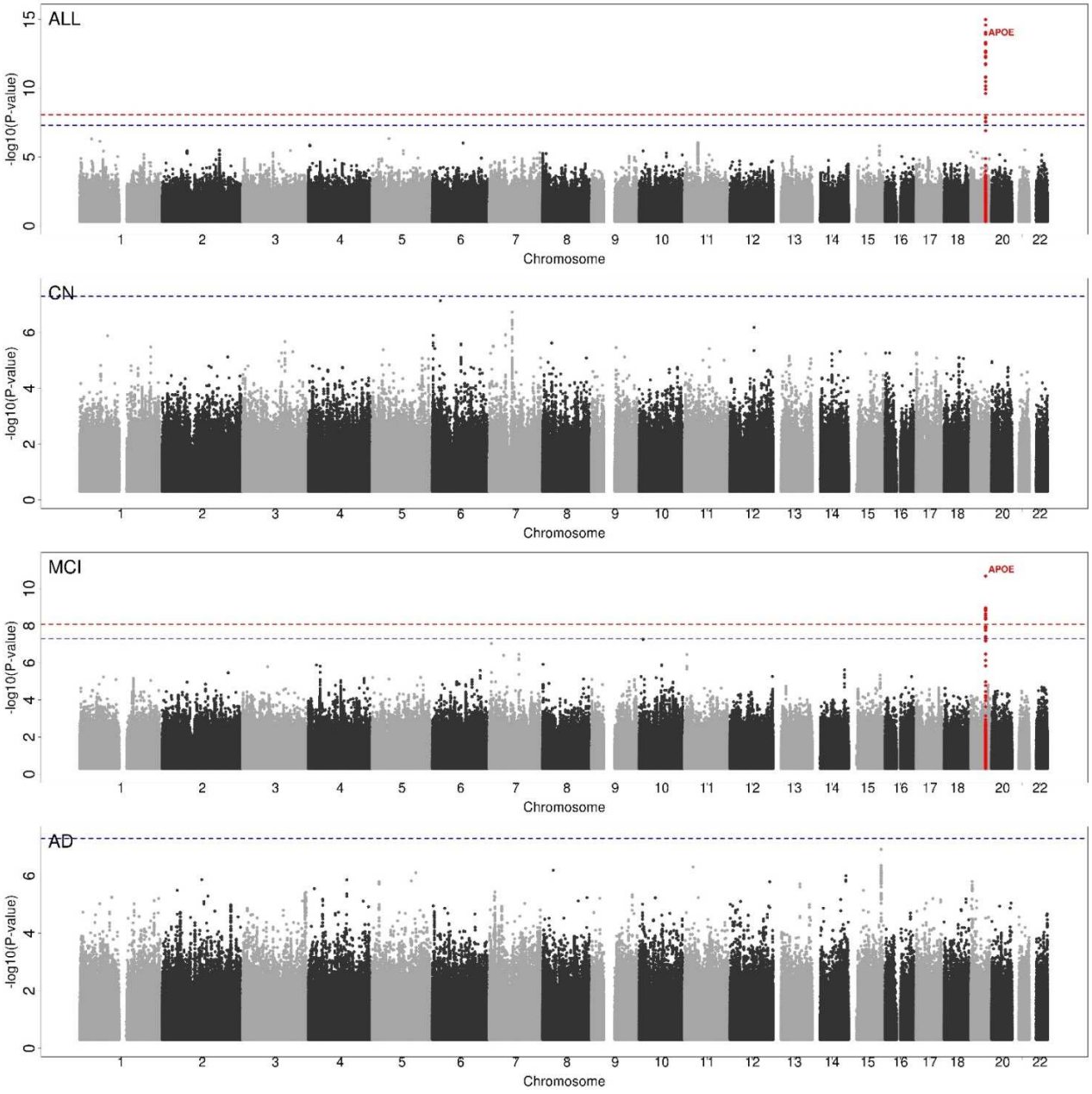
Supplementary Figure 7. Manhattan plot showing the meta-analyzed results of CSF $A\beta_{42}$ from all the subjects and three subgroups (CN: clinically normal, MCI: mild cognitive impairment, and AD). Blue dot line represents the genome-wide significance threshold of $P<5.0x10^{-8}$, and the red dot line indicates study-wide significant threshold of $P<8.33x10^{-9}$. Loci achieving study-wide significance are highlighted in red, and loci at genome-wide significance are in blue.



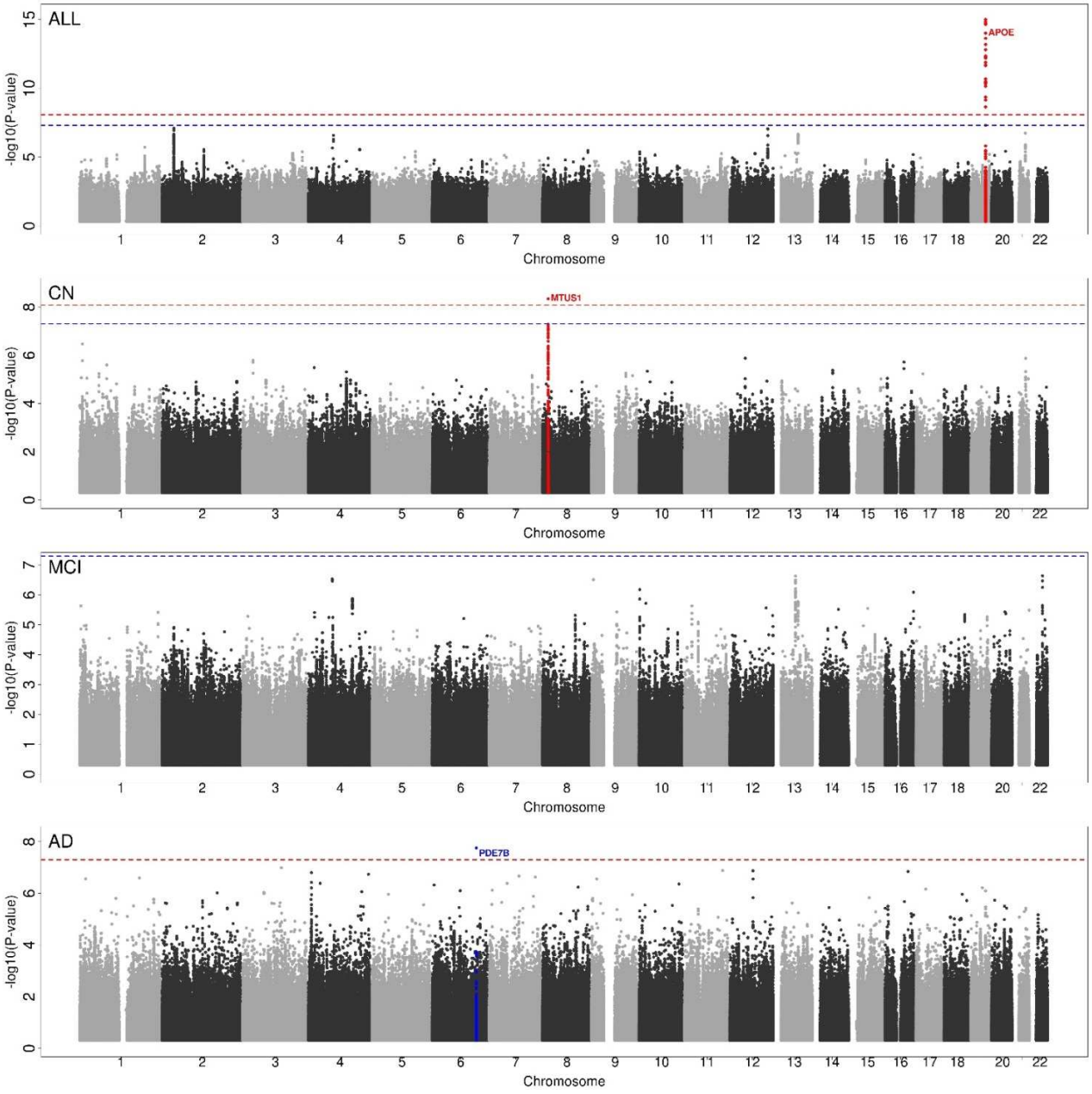
Supplementary Figure 8. Manhattan plot showing the meta-analyzed results of CSF total Tau from all the subjects and three subgroups (CN: clinically normal, MCI: mild cognitive impairment, and AD). Blue dot line represents the genome-wide significance threshold of $P<5.0\times10^{-8}$, and the red dot line indicates study-wide significant threshold of $P<8.33\times10^{-9}$. Loci achieving study-wide significance are highlighted in red, and loci at genome-wide significance are in blue.



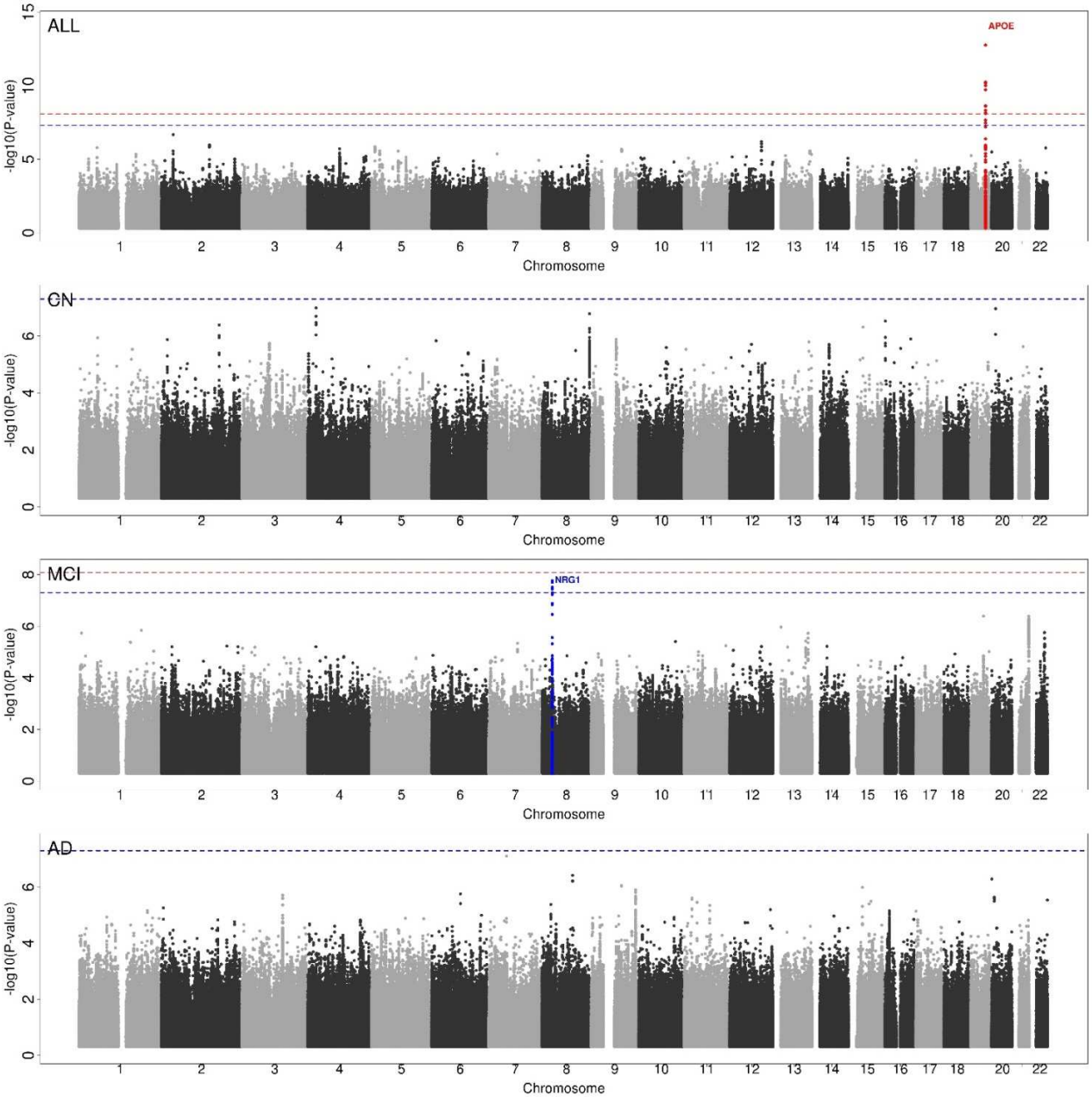
Supplementary Figure 9. Manhattan plot showing the meta-analyzed results of CSF phosphorylated tau from all the subjects and three subgroups (CN: clinically normal, MCI: mild cognitive impairment, and AD). Blue dot line represents the genome-wide significance threshold of $P<5.0\times10^{-8}$, and the red dot line indicates study-wide significant threshold of $P<8.33\times10^{-9}$. Loci achieving study-wide significance are highlighted in red, and loci at genome-wide significance are in blue.



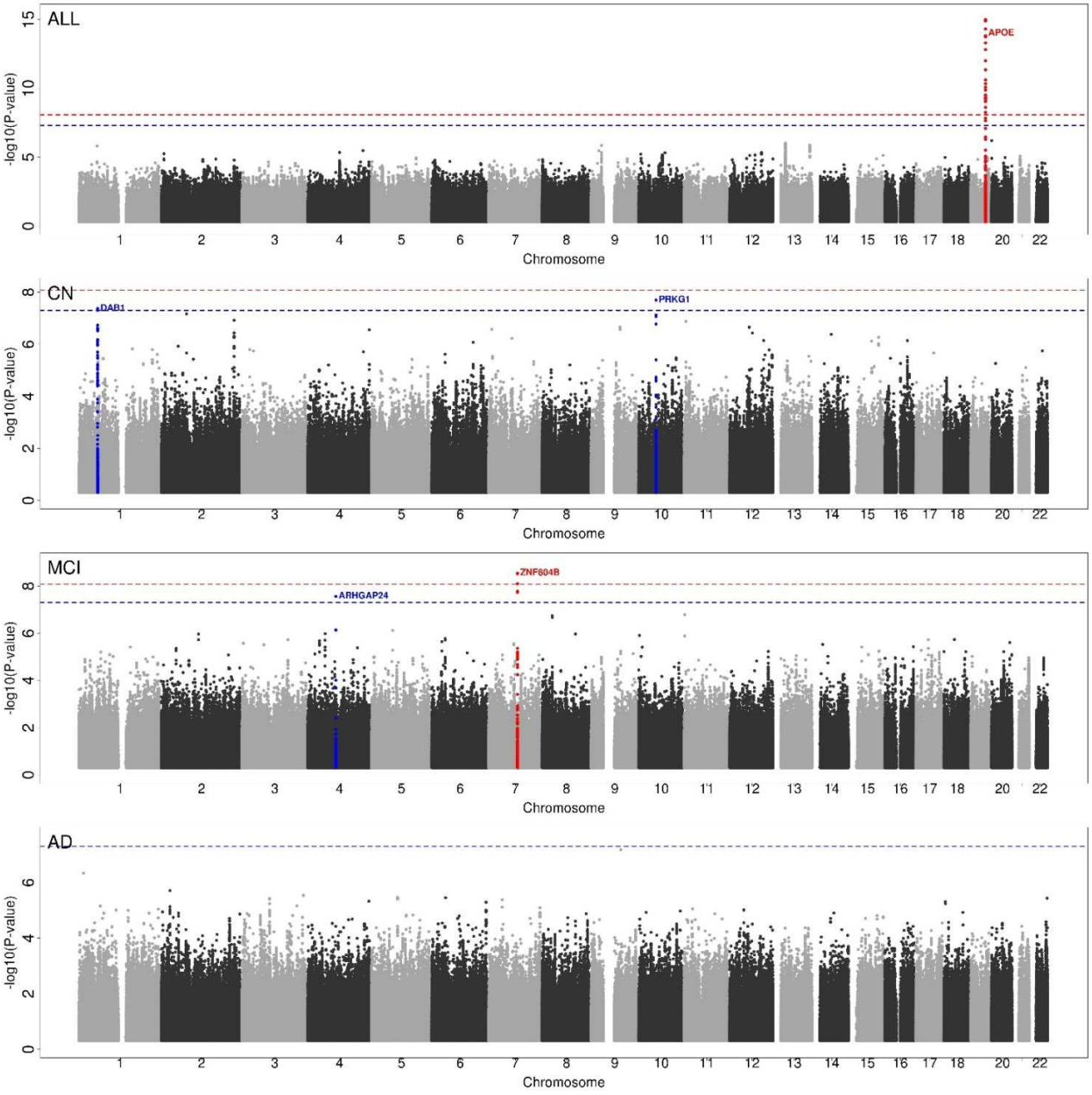
Supplementary Figure 10. Manhattan plot showing the meta-analyzed results of hippocampal volume (HPV) in brains from all the subjects and three subgroups (CN: clinically normal, MCI: mild cognitive impairment, and AD). Blue dot line represents the genome-wide significance threshold of $P<5.0\times10^{-8}$, and the red dot line indicates study-wide significant threshold of $P<8.33\times10^{-9}$. Loci achieving study-wide significance are highlighted in red, and loci at genome-wide significance are in blue.



Supplementary Figure 11. Manhattan plot showing the meta-analyzed results of logical memory test (LMT)-immediate recall from all the subjects and three subgroups (CN: clinically normal and MCI: mild cognitive impairment). Blue dot line represents the genome-wide significance threshold of $P<5.0\times10^{-8}$, and the red dot line indicates study-wide significant threshold of $P<8.33\times10^{-9}$. Loci achieving study-wide significance are highlighted in red, and loci at genome-wide significance are in blue.

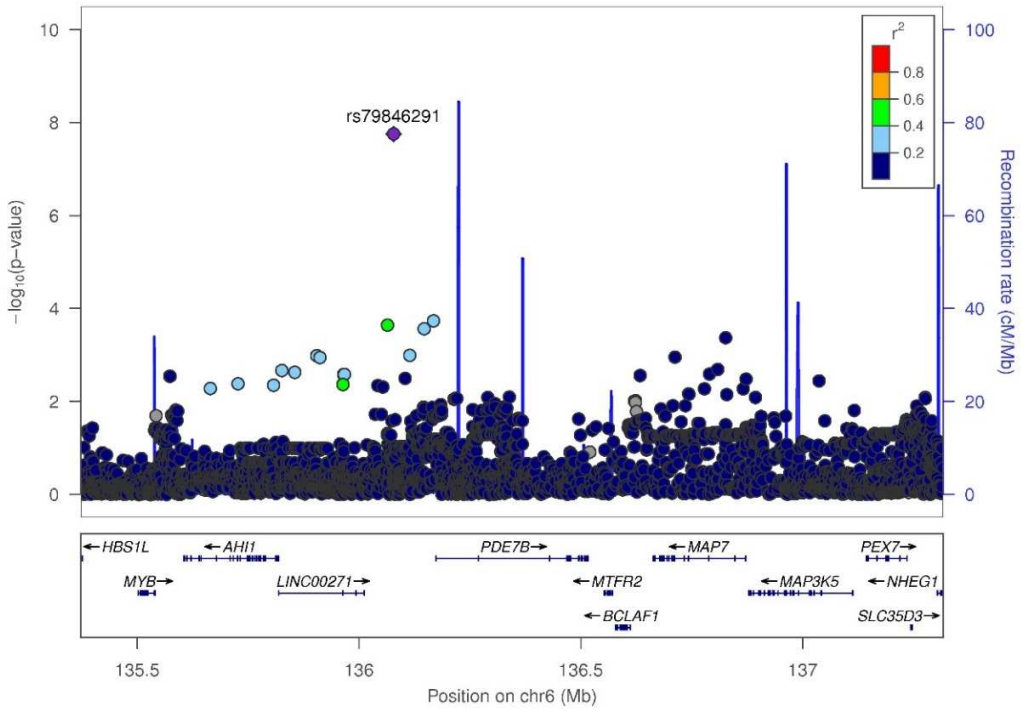


Supplementary Figure 12. Manhattan plot showing the meta-analyzed results of logical memory test (LMT)-delayed recall from all the subjects and three subgroups (CN: clinically normal and MCI: mild cognitive impairment). Blue dot line represents the genome-wide significance threshold of $P<5.0\times10^{-8}$, and the red dot line indicates study-wide significant threshold of $P<8.33\times10^{-9}$. Loci achieving study-wide significance are highlighted in red, and loci at genome-wide significance are in blue.

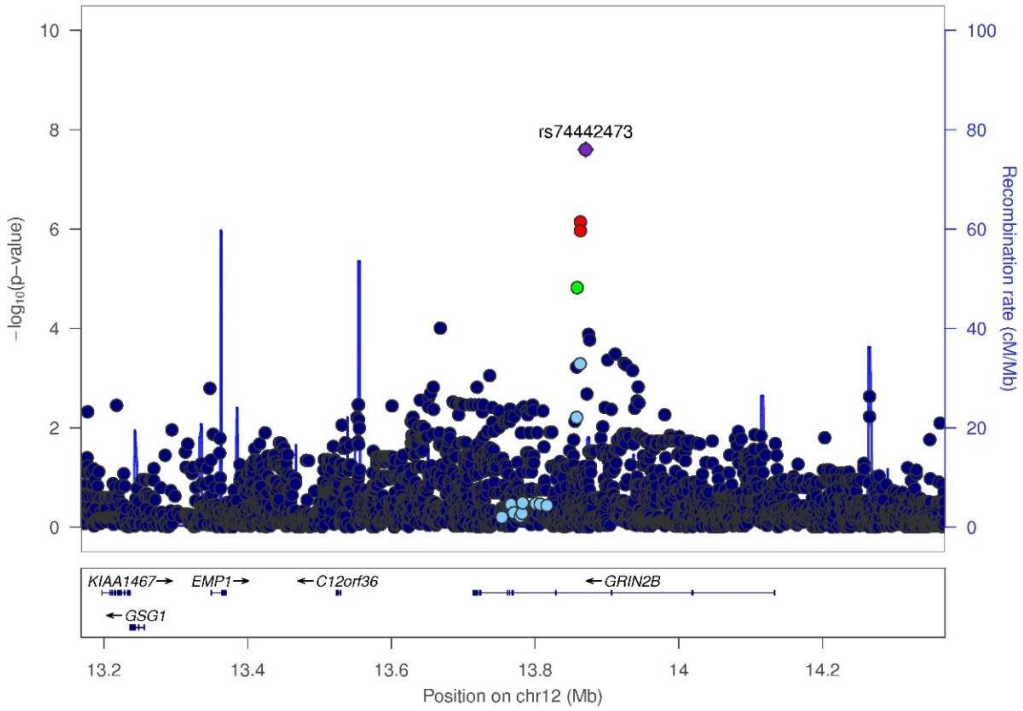


Supplementary Figure 13. Regional association plots of **(A)** *PDE7B* from association test with hippocampal volume in AD subjects, **(B)** *GRIN2B* from association test with CSF $A\beta_{42}$ in CN subjects, **(C)** *NRG1* from logical memory test immediate recall in MCI subjects, **(D)** *AKAP9* from CSF phosphorylated Tau in the MCI subjects, and **(E)** *BDNF* from CSF phosphorylated Tau using CN subjects

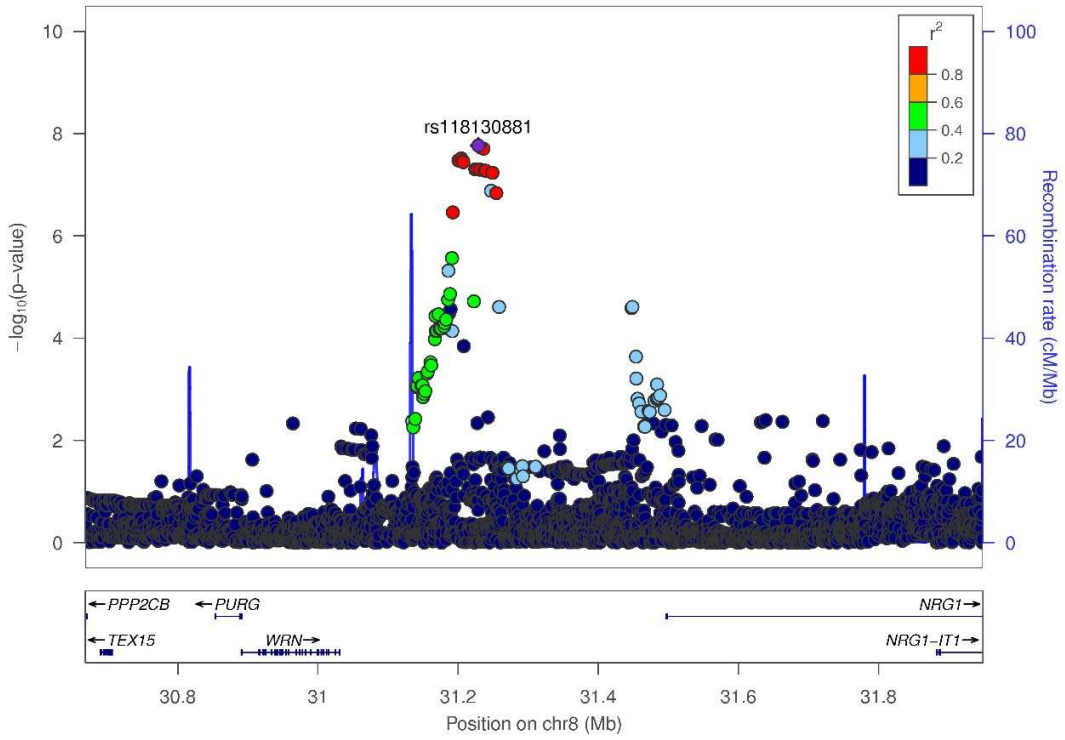
A.



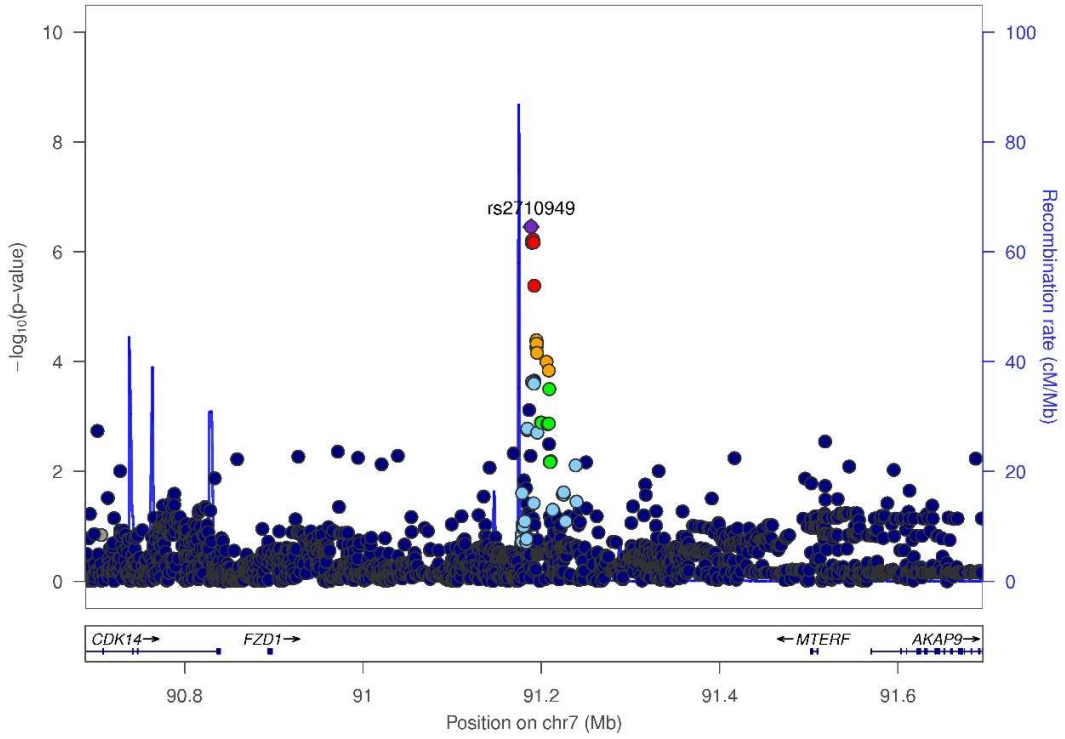
B.



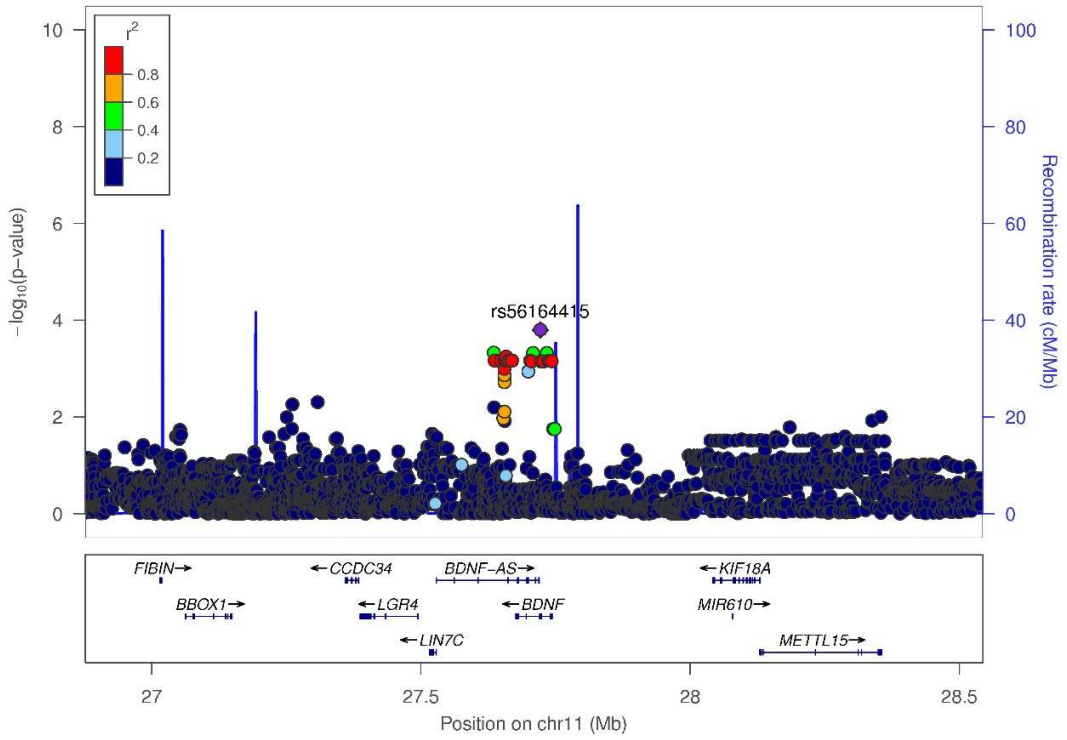
C.


rs118130881
r²
0.8
0.6
0.4
0.2
−log10(p−value)
Recombination rate (cM/Mb)
PPP2CB
PURG
NRG1
TEX15
WRN
NRG1−IT1
Position on chr8 (Mb)

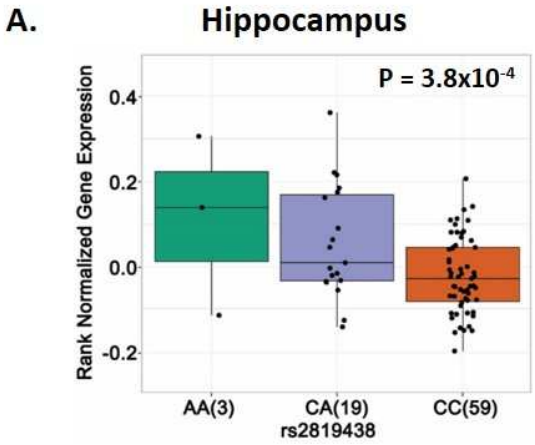
D.

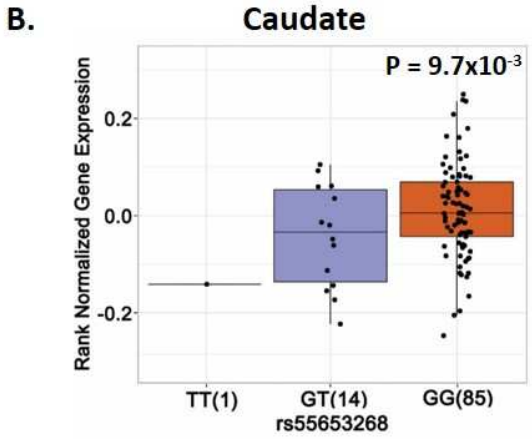

rs2710949
−log10(p−value)
Recombination rate (cM/Mb)
CDK14
FZD1
MTERF
AKAP9
Position on chr7 (Mb)

E.


r2
0.8
0.6
0.4
0.2
rs56164415
−log10(p−value)
Recombination rate (cM/Mb)
FIBIN
CCDC34
BDNF−AS
KIF18A
BBOX1
LGR4
BDNF
MIR610
LIN7C
METTL15
Position on chr11 (Mb)

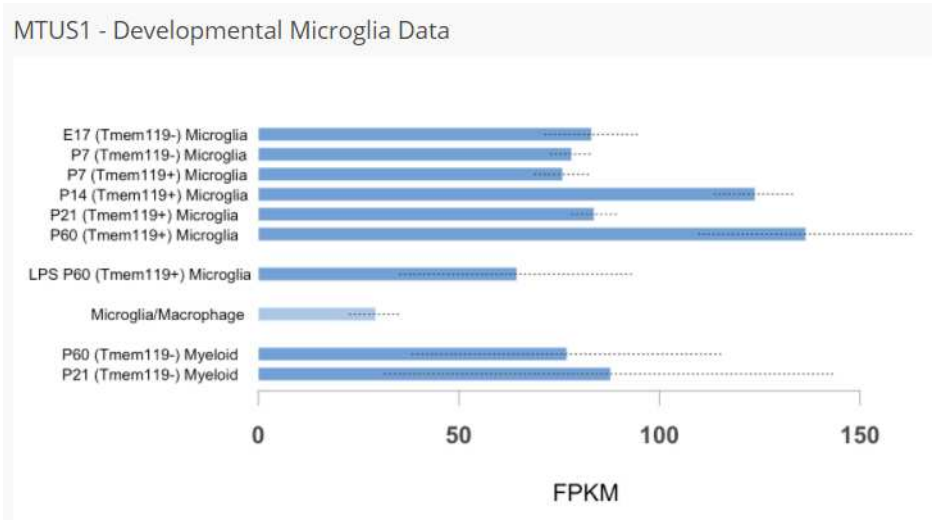
Supplementary Figure 14. Association between gene expression levels in brains from the GTEx Portal database and SNPs. **A**. *C14orf79* in hippocampus and rs2819438. **B**. *MTUS1* in caudate and rs55653268.



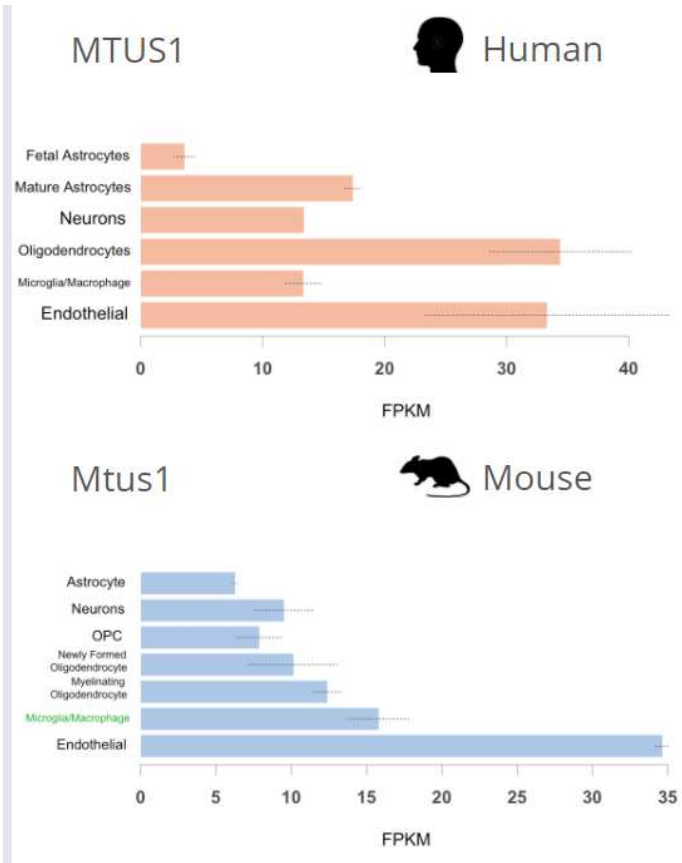


Supplementary Figure 15. Expression of *MTUS1* in mouse and human brain. (A) Expression profiles in murine myeloid cells. (B) Cell type specific expression in human and mouse. Data were obtained from: http://web.stanford.edu/group/barres_lab/brainseqMariko/brainseq2.html.

A.



B.



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Supplementary Table 1. Association *P* -values of Alzheimer disease loci previously established by GWAS with CSF biomarkers of Aß42, total and phosphorylated tau, MRI hippocampal volume, and test scores for immediate and delayed recall in normal, mild cognitively impaired, and AD subjects.

				CSF $A\beta_{42}$											
				ALL			CN			MCI			AD		
CHR	BP	SNP	Gene	Beta	SE	P	Beta	SE	P	Beta	SE	P	Beta	SE	P
1	207692049	rs6656401	*CR1*	-0.12	0.07	0.11	-0.06	0.15	0.67	-0.09	0.10	0.35	-0.01	0.13	0.97
2	127892810	rs6733839	*BIN1*	-0.06	0.06	0.26	-0.11	0.10	0.26	-0.03	0.08	0.71	-0.06	0.12	0.60
2	234068476	rs35349669	*INPP5D*	-0.10	0.05	0.07	-0.15	0.10	0.13	-0.05	0.07	0.48	0.23	0.12	0.05
5	88223420	rs190982	*MEF2C*	-0.05	0.06	0.41	0.00	0.10	0.99	-0.11	0.08	0.18	-0.21	0.13	0.12
5	139707439	rs11168036	*HBEGF*	0.01	0.06	0.84	0.00	0.10	0.98	0.08	0.08	0.33	-0.15	0.11	0.20
6	32578530	rs9271192	*HLA region*	0.02	0.06	0.75	0.26	0.11	0.02	-0.04	0.09	0.64	0.13	0.12	0.30
6	47487762	rs10948363	*CD2AP*	0.06	0.06	0.33	-0.10	0.12	0.41	0.00	0.08	0.98	0.34	0.12	4.15E-03
7	37841534	rs2718058	*NME8*	-0.02	0.06	0.71	-0.06	0.11	0.57	0.01	0.07	0.90	0.11	0.12	0.36
7	100004446	rs1476679	*ZCWPW1*	-0.09	0.06	0.16	-0.09	0.11	0.43	-0.07	0.08	0.37	0.02	0.13	0.90
7	143110762	rs11771145	*EPHA1*	0.05	0.06	0.41	0.09	0.10	0.39	0.09	0.08	0.28	-0.10	0.12	0.41
8	27195121	rs28834970	*PTK2B*	0.06	0.06	0.26	0.14	0.10	0.17	0.04	0.08	0.64	-0.04	0.12	0.73
8	27467686	rs9331896	*CLU*	-0.07	0.06	0.27	-0.05	0.10	0.59	-0.05	0.08	0.57	0.01	0.12	0.96
10	11720308	rs7920721	*USP6NL*	-0.07	0.06	0.21	-0.25	0.10	0.01	-0.03	0.07	0.69	0.05	0.11	0.63
11	47557871	rs10838725	*CELF1*	0.08	0.06	0.17	0.15	0.11	0.15	0.08	0.08	0.29	0.12	0.14	0.37
11	59923508	rs983392	*MS4A region*	0.00	0.05	0.94	0.12	0.09	0.20	-0.03	0.08	0.68	0.01	0.12	0.93
11	85867875	rs10792832	*PICALM*	0.06	0.06	0.26	0.08	0.10	0.43	0.06	0.08	0.40	-0.12	0.12	0.34
11	121435587	rs11218343	*SORL1*	-0.23	0.15	0.11	-0.40	0.27	0.14	-0.12	0.18	0.51	-0.27	0.49	0.59
14	53400629	rs17125944	*FERMT2*	0.20	0.09	0.04	0.14	0.18	0.44	0.20	0.13	0.13	0.09	0.18	0.62
14	92926952	rs10498633	*SLC24A4*	-0.14	0.07	0.03	-0.32	0.12	5.93E-03	-0.05	0.09	0.54	-0.04	0.14	0.77
17	44353222	rs2732703	*KANSL1*	-0.15	0.10	0.12	-0.02	0.20	0.93	-0.28	0.13	0.03	0.15	0.21	0.48
17	56409089	rs2632516	*BZRAP1*	-0.05	0.05	0.38	-0.08	0.10	0.42	-0.10	0.07	0.17	-0.01	0.12	0.91
19	3405592	rs9749589	*NFIC*	-0.05	0.08	0.56	-0.26	0.15	0.08	0.03	0.11	0.81	0.07	0.18	0.72
19	1063443	rs4147929	*ABCA7*	-0.08	0.07	0.22	0.20	0.15	0.18	-0.15	0.09	0.08	0.07	0.14	0.63
19	51727962	rs3865444	*CD33*	-0.01	0.06	0.87	-0.18	0.11	0.09	0.03	0.08	0.72	-0.07	0.12	0.55
20	55018260	rs7274581	*CASS4*	0.02	0.09	0.80	0.36	0.16	0.03	-0.13	0.12	0.28	0.40	0.21	0.06

		CSF t-Tau											
		ALL			CN			MCI			AD		
SNP	Gene	Beta	SE	P	Beta	SE	P	Beta	SE	P	Beta	SE	P
rs6656401	*CR1*	0.08	0.08	0.30	0.10	0.13	0.44	0.04	0.10	0.69	-0.04	0.15	0.77
rs6733839	*BIN1*	0.02	0.06	0.74	-0.02	0.09	0.87	0.00	0.08	1.00	-0.04	0.14	0.77
rs35349669	*INPP5D*	0.07	0.06	0.22	-0.01	0.09	0.93	0.09	0.07	0.19	-0.19	0.13	0.16
rs190982	*MEF2C*	0.22	0.06	1.94E-04	0.06	0.09	0.55	0.31	0.08	1.03E-04	-0.10	0.15	0.52
rs11168036	*HBEGF*	-0.01	0.06	0.89	0.08	0.09	0.37	-0.07	0.08	0.38	0.10	0.13	0.46
rs9271192	*HLA region*	-0.02	0.07	0.81	-0.02	0.10	0.84	-0.06	0.09	0.50	-0.09	0.14	0.52
rs10948363	*CD2AP*	-0.05	0.06	0.44	-0.04	0.11	0.71	-0.03	0.08	0.73	-0.10	0.14	0.45
rs2718058	*NME8*	0.07	0.06	0.21	0.01	0.10	0.95	0.06	0.07	0.44	0.10	0.14	0.45
rs1476679	*ZCWPW1*	0.10	0.06	0.10	0.08	0.10	0.43	0.05	0.08	0.58	-0.32	0.15	0.03
rs11771145	*EPHA1*	0.11	0.06	0.06	0.04	0.09	0.68	0.04	0.08	0.62	-0.28	0.13	0.04
rs28834970	*PTK2B*	-0.06	0.06	0.29	-0.04	0.09	0.64	-0.06	0.08	0.44	-0.01	0.14	0.96
rs9331896	*CLU*	0.03	0.06	0.57	-0.01	0.09	0.96	0.07	0.08	0.37	0.17	0.14	0.23
rs7920721	*USP6NL*	-0.01	0.06	0.87	0.04	0.09	0.64	-0.01	0.07	0.95	-0.07	0.13	0.57
rs10838725	*CELF1*	0.00	0.06	0.98	-0.14	0.09	0.13	0.01	0.08	0.90	0.06	0.16	0.70
rs983392	*MS4A region*	0.10	0.06	0.07	0.10	0.08	0.25	0.03	0.08	0.65	0.17	0.13	0.22
rs10792832	*PICALM*	-0.11	0.06	0.06	0.10	0.09	0.29	-0.20	0.08	0.01	-0.02	0.14	0.89
rs11218343	*SORL1*	0.10	0.15	0.52	0.17	0.24	0.47	0.05	0.19	0.79	-0.32	0.57	0.57
rs17125944	*FERMT2*	0.03	0.10	0.78	-0.02	0.17	0.92	0.09	0.13	0.46	0.12	0.21	0.58
rs10498633	*SLC24A4*	0.07	0.07	0.31	0.12	0.11	0.26	0.04	0.09	0.67	0.04	0.16	0.79
rs2732703	*KANSL1*	0.02	0.10	0.85	-0.13	0.18	0.46	0.12	0.13	0.38	-0.40	0.24	0.09
rs2632516	*BZRAP1*	-0.10	0.05	0.07	-0.15	0.09	0.08	-0.04	0.07	0.60	0.07	0.14	0.64
rs9749589	*NFIC*	-0.04	0.08	0.62	0.20	0.13	0.13	-0.07	0.11	0.53	0.11	0.21	0.59
rs4147929	*ABCA7*	0.12	0.07	0.09	0.01	0.14	0.93	0.08	0.09	0.39	0.11	0.16	0.50
rs3865444	*CD33*	0.01	0.06	0.89	-0.09	0.10	0.35	0.03	0.08	0.68	-0.11	0.14	0.43
rs7274581	*CASS4*	0.24	0.09	0.01	-0.04	0.15	0.80	0.33	0.12	6.40E-03	-0.13	0.24	0.59

		CSF p-Tau											
		ALL			CN			MCI			AD		
SNP	Gene	Beta	SE	P	Beta	SE	P	Beta	SE	P	Beta	SE	P
rs6656401	*CR1*	0.07	0.07	0.33	0.01	0.14	0.93	0.05	0.10	0.63	-0.01	0.14	0.96
rs6733839	*BIN1*	0.04	0.06	0.53	-0.01	0.09	0.89	0.01	0.08	0.89	-0.09	0.13	0.49
rs35349669	*INPP5D*	0.09	0.05	0.10	-0.02	0.10	0.82	0.13	0.07	0.08	-0.21	0.13	0.10
rs190982	*MEF2C*	0.13	0.06	0.03	0.07	0.10	0.49	0.18	0.08	0.02	0.03	0.15	0.84
rs11168036	*HBEGF*	0.01	0.06	0.90	0.23	0.09	0.02	-0.12	0.08	0.12	0.13	0.13	0.30
rs9271192	*HLA region*	0.02	0.06	0.82	-0.07	0.11	0.51	0.01	0.09	0.87	-0.11	0.14	0.41
rs10948363	*CD2AP*	-0.07	0.06	0.27	0.05	0.12	0.65	-0.04	0.08	0.59	-0.23	0.13	0.08
rs2718058	*NME8*	0.03	0.06	0.64	-0.02	0.10	0.82	0.02	0.07	0.81	-0.05	0.13	0.68
rs1476679	*ZCWPW1*	0.15	0.06	0.02	0.19	0.10	0.06	0.09	0.08	0.28	-0.26	0.15	0.07
rs11771145	*EPHA1*	0.07	0.06	0.20	-0.01	0.10	0.94	-0.01	0.08	0.94	-0.30	0.13	0.02
rs28834970	*PTK2B*	-0.01	0.06	0.90	-0.03	0.10	0.75	0.03	0.08	0.73	0.01	0.13	0.95
rs9331896	*CLU*	0.05	0.06	0.42	0.07	0.10	0.46	0.07	0.08	0.41	0.16	0.13	0.25
rs7920721	*USP6NL*	-0.01	0.06	0.89	0.07	0.10	0.48	0.00	0.07	0.97	-0.15	0.12	0.23
rs10838725	*CELF1*	-0.07	0.06	0.23	-0.19	0.10	0.05	-0.11	0.08	0.17	0.19	0.15	0.22
rs983392	*MS4A region*	0.08	0.06	0.16	0.06	0.09	0.47	0.04	0.08	0.59	0.09	0.13	0.50
rs10792832	*PICALM*	-0.11	0.06	0.06	0.08	0.10	0.43	-0.22	0.08	5.55E-03	0.08	0.13	0.53
rs11218343	*SORL1*	0.11	0.15	0.47	0.32	0.25	0.21	0.00	0.18	0.99	-0.08	0.55	0.88
rs17125944	*FERMT2*	-0.04	0.10	0.65	0.01	0.17	0.93	-0.04	0.13	0.78	0.07	0.20	0.73
rs10498633	*SLC24A4*	0.12	0.07	0.08	0.20	0.11	0.07	0.05	0.09	0.59	-0.06	0.15	0.71
rs2732703	*KANSL1*	-0.06	0.10	0.57	0.10	0.18	0.57	-0.01	0.13	0.97	-0.61	0.22	0.01
rs2632516	*BZRAP1*	-0.07	0.05	0.19	-0.10	0.09	0.26	-0.03	0.07	0.66	-0.01	0.13	0.94
rs9749589	*NFIC*	0.00	0.08	0.97	0.14	0.14	0.32	-0.03	0.11	0.77	-0.09	0.20	0.67
rs4147929	*ABCA7*	0.11	0.07	0.10	0.11	0.14	0.45	0.08	0.09	0.35	0.05	0.15	0.76
rs3865444	*CD33*	-0.04	0.06	0.51	-0.13	0.10	0.20	-0.04	0.08	0.59	-0.10	0.14	0.48
rs7274581	*CASS4*	0.15	0.09	0.10	-0.32	0.16	0.04	0.30	0.12	0.01	-0.02	0.23	0.94

		HPV											
		ALL			CN			MCI			AD		
SNP	Gene	Beta	SE	P	Beta	SE	P	Beta	SE	P	Beta	SE	P
rs6656401	*CR1*	-0.02	0.06	0.74	0.12	0.10	0.25	0.08	0.08	0.31	0.02	0.12	0.88
rs6733839	*BIN1*	-0.02	0.05	0.64	0.03	0.07	0.70	-0.06	0.07	0.38	-0.11	0.10	0.26
rs35349669	*INPP5D*	-0.08	0.05	0.12	-0.05	0.07	0.52	-0.05	0.06	0.42	0.07	0.11	0.55
rs190982	*MEF2C*	-0.02	0.05	0.75	0.07	0.07	0.31	-0.01	0.07	0.84	-0.07	0.12	0.59
rs11168036	*HBEGF*	-0.02	0.05	0.68	-0.02	0.07	0.80	-0.02	0.06	0.79	0.19	0.10	0.06
rs9271192	*HLA region*	0.05	0.06	0.39	0.03	0.08	0.72	0.06	0.07	0.39	-0.09	0.11	0.43
rs10948363	*CD2AP*	0.01	0.05	0.82	0.10	0.08	0.22	-0.11	0.07	0.11	-0.10	0.11	0.34
rs2718058	*NME8*	-0.07	0.05	0.13	0.00	0.07	0.96	-0.11	0.06	0.06	0.13	0.10	0.23
rs1476679	*ZCWPW1*	-0.04	0.05	0.43	-0.01	0.07	0.88	0.04	0.07	0.56	.	.	.
rs11771145	*EPHA1*	-0.09	0.05	0.08	-0.03	0.07	0.68	-0.09	0.06	0.14	0.04	0.11	0.70
rs28834970	*PTK2B*	0.03	0.05	0.61	-0.01	0.07	0.91	0.01	0.06	0.81	.	.	.
rs9331896	*CLU*	-0.05	0.05	0.36	-0.06	0.07	0.42	-0.05	0.07	0.48	.	.	.
rs7920721	*USP6NL*	0.06	0.05	0.25	0.03	0.07	0.69	0.09	0.06	0.14	-0.10	0.09	0.29
rs10838725	*CELF1*	-0.01	0.05	0.81	0.06	0.07	0.39	0.02	0.06	0.75	-0.24	0.12	0.05
rs983392	*MS4A region*	-0.10	0.05	0.05	0.01	0.07	0.83	-0.06	0.06	0.33	-0.13	0.11	0.24
rs10792832	*PICALM*	0.13	0.05	0.01	0.11	0.07	0.13	0.13	0.06	0.05	0.06	0.11	0.55
rs11218343	*SORL1*	-0.26	0.12	0.03	-0.25	0.16	0.13	-0.16	0.16	0.31	-0.38	0.27	0.17
rs17125944	*FERMT2*	0.10	0.09	0.27	-0.15	0.13	0.24	0.07	0.11	0.52	0.22	0.17	0.19
rs10498633	*SLC24A4*	0.04	0.06	0.44	0.08	0.08	0.37	0.02	0.07	0.74	-0.15	0.11	0.20
rs2732703	*KANSL1*	-0.05	0.09	0.60	0.10	0.12	0.41	-0.09	0.11	0.42	0.11	0.19	0.56
rs2632516	*BZRAP1*	0.01	0.05	0.76	0.01	0.07	0.85	0.02	0.06	0.69	0.10	0.11	0.34
rs9749589	*NFIC*	0.06	0.07	0.41	-0.12	0.10	0.24	0.05	0.09	0.61	0.02	0.16	0.91
rs4147929	*ABCA7*	-0.03	0.06	0.57	0.02	0.10	0.84	-0.10	0.07	0.20	0.24	0.13	0.06
rs3865444	*CD33*	0.04	0.05	0.41	0.07	0.07	0.30	0.01	0.07	0.86	0.07	0.11	0.56
rs7274581	*CASS4*	-0.05	0.08	0.55	0.02	0.11	0.88	-0.07	0.11	0.50	0.19	0.18	0.29

		LMiT											
		ALL			CN			MCI			AD		
SNP	Gene	Beta	SE	P	Beta	SE	P	Beta	SE	P	Beta	SE	P
rs6656401	*CR1*	-0.14	0.06	0.02	-0.20	0.08	0.01	0.01	0.06	0.93	0.06	0.10	0.58
rs6733839	*BIN1*	-0.03	0.05	0.46	-0.01	0.06	0.93	-0.04	0.05	0.44	-0.03	0.08	0.68
rs35349669	*INPP5D*	-0.08	0.04	0.06	0.04	0.06	0.51	-0.10	0.04	0.02	-0.06	0.09	0.49
rs190982	*MEF2C*	-0.03	0.05	0.58	0.03	0.06	0.64	-0.07	0.05	0.13	-0.25	0.09	9.30E-03
rs11168036	*HBEGF*	0.03	0.05	0.54	-0.04	0.06	0.49	0.09	0.05	0.04	0.04	0.08	0.59
rs9271192	*HLA region*	0.05	0.05	0.31	0.08	0.06	0.23	0.07	0.05	0.19	0.12	0.09	0.18
rs10948363	*CD2AP*	0.04	0.05	0.40	-0.02	0.07	0.76	0.00	0.05	0.98	-0.02	0.09	0.82
rs2718058	*NME8*	-0.04	0.04	0.39	0.03	0.06	0.65	-0.02	0.04	0.59	0.00	0.09	0.97
rs1476679	*ZCWPW1*	-0.12	0.05	0.01	-0.03	0.06	0.64	-0.10	0.05	0.05	.	.	.
rs11771145	*EPHA1*	0.00	0.05	0.96	0.03	0.06	0.60	-0.02	0.05	0.62	-0.13	0.09	0.16
rs28834970	*PTK2B*	0.03	0.05	0.56	0.11	0.06	0.06	-0.03	0.04	0.49	-0.03	0.09	0.74
rs9331896	*CLU*	0.01	0.05	0.89	0.02	0.06	0.76	0.06	0.05	0.18	-0.02	0.09	0.85
rs7920721	*USP6NL*	0.08	0.05	0.07	0.05	0.06	0.38	0.10	0.04	0.02	0.09	0.08	0.24
rs10838725	*CELF1*	0.01	0.05	0.84	0.10	0.06	0.09	-0.03	0.05	0.55	0.02	0.09	0.80
rs983392	*MS4A region*	-0.08	0.05	0.09	-0.04	0.05	0.50	-0.02	0.05	0.75	0.04	0.09	0.63
rs10792832	*PICALM*	0.07	0.05	0.11	-0.02	0.06	0.79	0.08	0.05	0.08	0.10	0.09	0.25
rs11218343	*SORL1*	-0.14	0.12	0.22	-0.18	0.14	0.19	-0.09	0.12	0.44	0.10	0.22	0.66
rs17125944	*FERMT2*	0.10	0.08	0.22	0.05	0.11	0.66	0.01	0.08	0.87	-0.02	0.13	0.88
rs10498633	*SLC24A4*	0.03	0.05	0.59	-0.07	0.07	0.28	0.06	0.05	0.28	-0.11	0.10	0.25
rs2732703	*KANSL1*	-0.05	0.08	0.55	0.05	0.10	0.60	-0.12	0.08	0.13	0.14	0.15	0.38
rs2632516	*BZRAP1*	0.09	0.04	0.03	0.03	0.05	0.61	0.07	0.04	0.10	-0.04	0.08	0.65
rs9749589	*NFIC*	0.08	0.07	0.21	-0.08	0.08	0.35	-0.01	0.07	0.87	-0.20	0.12	0.11
rs4147929	*ABCA7*	-0.04	0.06	0.45	-0.07	0.08	0.35	0.00	0.05	0.99	0.12	0.10	0.24
rs3865444	*CD33*	0.06	0.05	0.23	0.03	0.06	0.63	0.07	0.05	0.16	-0.02	0.09	0.82
rs7274581	*CASS4*	-0.06	0.07	0.40	0.16	0.09	0.06	-0.07	0.08	0.40	0.10	0.15	0.48

		LMdT											
		ALL			CN			MCI			AD		
SNP	Gene	Beta	SE	P	Beta	SE	P	Beta	SE	P	Beta	SE	P
rs6656401	*CR1*	-0.14	0.06	0.02	-0.13	0.07	0.07	-0.01	0.06	0.90	0.05	0.08	0.53
rs6733839	*BIN1*	-0.01	0.05	0.80	-0.01	0.05	0.90	0.00	0.05	0.93	-0.05	0.06	0.43
rs35349669	*INPP5D*	-0.05	0.04	0.22	0.01	0.05	0.79	-0.06	0.04	0.12	-0.15	0.07	0.04
rs190982	*MEF2C*	-0.07	0.05	0.17	0.02	0.05	0.74	-0.11	0.04	0.01	-0.12	0.08	0.10
rs11168036	*HBEGF*	0.01	0.05	0.80	-0.01	0.05	0.77	0.06	0.04	0.19	0.00	0.06	0.96
rs9271192	*HLA region*	0.07	0.05	0.20	0.07	0.05	0.22	0.06	0.05	0.24	0.00	0.07	0.97
rs10948363	*CD2AP*	0.01	0.05	0.91	-0.06	0.06	0.25	-0.06	0.05	0.23	-0.03	0.07	0.69
rs2718058	*NME8*	-0.07	0.04	0.14	-0.06	0.05	0.22	-0.04	0.04	0.38	0.00	0.07	0.97
rs1476679	*ZCWPW1*	-0.10	0.05	0.03	-0.02	0.05	0.62	-0.09	0.05	0.05	.	.	.
rs11771145	*EPHA1*	-0.01	0.05	0.83	0.00	0.05	0.96	0.02	0.04	0.65	-0.04	0.07	0.55
rs28834970	*PTK2B*	0.00	0.05	0.95	0.09	0.05	0.05	-0.07	0.04	0.08	-0.05	0.07	0.51
rs9331896	*CLU*	-0.04	0.05	0.41	-0.06	0.05	0.23	0.02	0.05	0.69	-0.05	0.07	0.44
rs7920721	*USP6NL*	0.01	0.05	0.85	-0.01	0.05	0.85	0.07	0.04	0.08	-0.11	0.06	0.08
rs10838725	*CELF1*	0.02	0.05	0.68	0.10	0.05	0.06	-0.01	0.04	0.87	-0.05	0.08	0.47
rs983392	*MS4A region*	-0.11	0.05	0.02	-0.01	0.05	0.81	-0.04	0.04	0.34	0.00	0.07	1.00
rs10792832	*PICALM*	0.02	0.05	0.61	-0.08	0.05	0.11	0.04	0.04	0.35	0.02	0.07	0.80
rs11218343	*SORL1*	-0.25	0.12	0.03	-0.21	0.12	0.07	-0.20	0.11	0.07	-0.16	0.18	0.37
rs17125944	*FERMT2*	0.13	0.08	0.09	0.10	0.09	0.27	0.03	0.08	0.66	0.09	0.11	0.42
rs10498633	*SLC24A4*	0.02	0.05	0.73	-0.04	0.06	0.46	0.11	0.05	0.02	0.10	0.08	0.20
rs2732703	*KANSL1*	0.00	0.08	0.96	0.03	0.08	0.71	0.03	0.07	0.71	0.13	0.12	0.30
rs2632516	*BZRAP1*	0.06	0.04	0.18	0.02	0.05	0.61	0.02	0.04	0.55	0.01	0.07	0.89
rs9749589	*NFIC*	0.08	0.07	0.20	-0.04	0.07	0.52	-0.01	0.06	0.87	-0.10	0.10	0.31
rs4147929	*ABCA7*	-0.07	0.06	0.20	-0.05	0.06	0.45	-0.04	0.05	0.49	0.11	0.08	0.21
rs3865444	*CD33*	0.02	0.05	0.75	-0.03	0.05	0.50	0.07	0.05	0.12	0.11	0.07	0.13
rs7274581	*CASS4*	-0.12	0.07	0.12	0.16	0.07	0.02	-0.07	0.07	0.35	-0.07	0.12	0.54

Supplementary Table 2. Effect sizes and P-values for additional SNPs that show a suggestive association (P<10-6) across six endophenotypes - CSF biomarkers of Aß42, total and phosphorylated tau, MRI hippocampal volume, and test scores for immediate and delayed recall in normal, mild cognitively impaired, and AD

Supplementary Table 7. Correlation matrix of expressions for the genes which were suggestively associated with at least one of endophenotypes or were previously detected in GWAS of AD risk.

	ERBIN	MTUS1	BACE1.AS	ZCWPW1	BRIP1	CAMK2B	DAB1	GRIN2B	JPH3	NRG1	SRRM4	ZNF804B	BZRAP1	MAPT	MEF2C	PTK2B	APP	PSEN2	PLXNA4
ERBIN	1.00	0.83	0.53	0.52	-0.34	-0.60	-0.44	-0.68	-0.56	-0.52	-0.68	-0.44	-0.70	-0.50	-0.69	-0.55	-0.62	-0.45	-0.55
MTUS1	0.83	1.00	0.57	0.42	-0.42	-0.54	-0.39	-0.67	-0.50	-0.65	-0.71	-0.48	-0.61	-0.44	-0.73	-0.52	-0.63	-0.60	-0.51
BACE1-AS	0.53	0.57	1.00	0.56	-0.26	-0.58	-0.42	-0.69	-0.40	-0.69	-0.35	-0.21	-0.23	-0.45	-0.35	-0.67	-0.53	-0.49	-0.68
ZCWPW1	0.52	0.42	0.56	1.00	-0.28	-0.53	-0.50	-0.62	-0.38	-0.55	-0.39	-0.21	-0.30	-0.46	-0.47	-0.55	-0.47	-0.46	-0.57
BRIP1	-0.34	-0.42	-0.26	-0.28	1.00	0.33	0.20	0.44	0.09	0.35	0.47	0.47	0.25	0.12	0.60	0.34	0.55	0.36	0.36
CAMK2B	-0.60	-0.54	-0.58	-0.53	0.33	1.00	0.74	0.90	0.78	0.68	0.66	0.34	0.65	0.69	0.40	0.93	0.65	0.59	0.89
DAB1	-0.44	-0.39	-0.42	-0.50	0.20	0.74	1.00	0.81	0.73	0.57	0.52	0.29	0.57	0.50	0.32	0.79	0.60	0.49	0.78
GRIN2B	-0.68	-0.67	-0.69	-0.62	0.44	0.90	0.81	1.00	0.74	0.82	0.72	0.50	0.64	0.70	0.56	0.94	0.83	0.63	0.92
JPH3	-0.56	-0.50	-0.40	-0.38	0.09	0.78	0.73	0.74	1.00	0.55	0.72	0.35	0.75	0.71	0.41	0.75	0.52	0.43	0.66
NRG1	-0.52	-0.65	-0.69	-0.55	0.35	0.68	0.57	0.82	0.55	1.00	0.63	0.48	0.46	0.59	0.49	0.76	0.76	0.52	0.71
SRRM4	-0.68	-0.71	-0.35	-0.39	0.47	0.66	0.52	0.72	0.72	0.63	1.00	0.52	0.80	0.65	0.78	0.64	0.71	0.38	0.54
ZNF804B	-0.44	-0.48	-0.21	-0.21	0.47	0.34	0.29	0.50	0.35	0.48	0.52	1.00	0.38	0.46	0.57	0.30	0.58	0.46	0.30
BZRAP1	-0.70	-0.61	-0.23	-0.30	0.25	0.65	0.57	0.64	0.75	0.46	0.80	0.38	1.00	0.49	0.53	0.57	0.54	0.30	0.49
MAPT	-0.50	-0.44	-0.45	-0.46	0.12	0.69	0.50	0.70	0.71	0.59	0.65	0.46	0.49	1.00	0.46	0.63	0.64	0.49	0.60
MEF2C	-0.69	-0.73	-0.35	-0.47	0.60	0.40	0.32	0.56	0.41	0.49	0.78	0.57	0.53	0.46	1.00	0.39	0.63	0.47	0.41
PTK2B	-0.55	-0.52	-0.67	-0.55	0.34	0.93	0.79	0.94	0.75	0.76	0.64	0.30	0.57	0.63	0.39	1.00	0.67	0.50	0.94
APP	-0.62	-0.63	-0.53	-0.47	0.55	0.65	0.60	0.83	0.52	0.76	0.71	0.58	0.54	0.64	0.63	0.67	1.00	0.54	0.66
PSEN2	-0.45	-0.60	-0.49	-0.46	0.36	0.59	0.49	0.63	0.43	0.52	0.38	0.46	0.30	0.49	0.47	0.50	0.54	1.00	0.52
PLXNA4	-0.55	-0.51	-0.68	-0.57	0.36	0.89	0.78	0.92	0.66	0.71	0.54	0.30	0.49	0.60	0.41	0.94	0.66	0.52	1.00

Supplementary Table 9.

						CSF $A\beta_{42}$												CSF p-Tau												CSF t-Tau											
						ALL				CN				MCI				AD				ALL				CN				MCI				AD			
CHR	BP	SNP	Gene	Deming et al	EA	RA	FREQ	BETA	SE	P	FREQ	BETA	SE	P	FREQ	BETA	SE	P	FREQ	BETA	SE	P	FREQ	BETA	SE	P	FREQ	BETA	SE	P	FREQ	BETA	SE	P	FREQ	BETA	SE	P	FREQ	BETA	SE	P
1	53968219	rs185031519	GLIS1	[illegible]	G	C	0.076	-0.32	0.12	########	0.08	-0.54	0.2	########	0.069	-0.26	0.16	0.12	0.091	-0.13	0.23	0.56	0.075	-0.03	0.12	0.82	0.08	0.03	0.2	0.89	0.069	-0.16	0.17	0.33	0.091	0.23	0.25	0.36	0.076	0.01	0.12	0.95	0.08	0.09	0.19	0.64	0.07	-0.1	0.16	0.56	0.092	0.05	0.26	0.84
6	2838248	rs316341	SERPINB1	[illegible]	G	A	0.29	-0.11	0.06	0.06	0.288	-0.14	0.11	0.23	0.292	-0.12	0.08	0.12	0.295	-0.08	0.12	0.52	0.291	-0.03	0.06	0.65	0.291	-0.02	0.11	0.86	0.292	-0.06	0.08	0.46	0.295	0.1	0.13	0.46	0.291	0.06	0.06	0.33	0.289	0.11	0.1	0.27	0.292	0.03	0.08	0.69	0.297	0.13	0.14	0.33
13	53504675	rs9527039	PCDH8	p-Tau	C	T	0.071	-0.03	0.11	0.77	0.075	-0.38	0.18	########	0.069	0.05	0.15	0.74	0.068	0.27	0.22	0.23	0.071	-0.14	0.11	0.19	0.075	-0.06	0.17	0.73	0.069	-0.23	0.15	0.14	0.068	0.02	0.24	0.93	0.071	-0.1	0.11	0.37	0.074	-0.08	0.17	0.64	0.071	-0.13	0.15	0.38	0.069	0.07	0.25	0.78
18	77381649	rs12961169	CTDP1	p-Tau	T	C	0.189	-0.11	0.07	0.14	0.197	-0.12	0.13	0.37	0.187	-0.1	0.1	0.32	0.185	-0.04	0.14	0.79	0.188	0.22	0.07	########	0.192	0.14	0.13	0.26	0.188	0.23	0.1	########	0.185	0.13	0.16	0.40	0.187	0.11	0.07	0.15	0.19	0.04	0.12	0.72	0.188	0.13	0.1	0.18	0.183	-0.03	0.16	0.84
3	190663557	rs35055419	GMNC	p-Tau or t-Tau	C	T	0.361	-0.1	0.06	0.08	0.31	0.13	0.11	0.24	0.38	-0.1	0.08	0.2	0.389	-0.18	0.12	0.13	0.361	0.21	0.06	########	0.309	0.3	0.1	########	0.381	0.07	0.08	0.37	0.389	0.26	0.13	0.10	0.36	0.27	0.06	########	0.307	0.31	0.1	########	0.379	0.14	0.08	0.08	0.389	0.28	0.13	0.08
9	3929424	rs514716	GLIS3	p-Tau	C	T	0.123	0.03	0.08	0.68	0.149	0.02	0.15	0.89	0.11	0.01	0.11	0.91	0.13	-0.05	0.17	0.78	0.123	-0.24	0.08	########	0.146	-0.18	0.14	0.2	0.111	-0.17	0.11	0.13	0.13	-0.38	0.18	########	0.122	-0.19	0.08	########	0.15	-0.16	0.13	0.24	0.11	-0.08	0.11	0.47	0.126	-0.32	0.19	0.1
19	45410002	rs69449	APOE	All three biomarkers	A	G	0.208	-0.73	0.06	########	0.098	-0.81	0.15	########	0.231	-0.66	0.08	########	0.315	-0.52	0.11	########	0.209	0.47	0.06	########	0.099	0.16	0.15	0.29	0.233	0.5	0.08	########	0.315	0.2	0.13	0.14	0.209	0.48	0.06	########	0.1	0.15	0.14	0.28	0.233	0.48	0.08	########	0.309	0.24	0.14	0.1