

ADNI Phenotypes

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SCHOOL OF MEDICINE

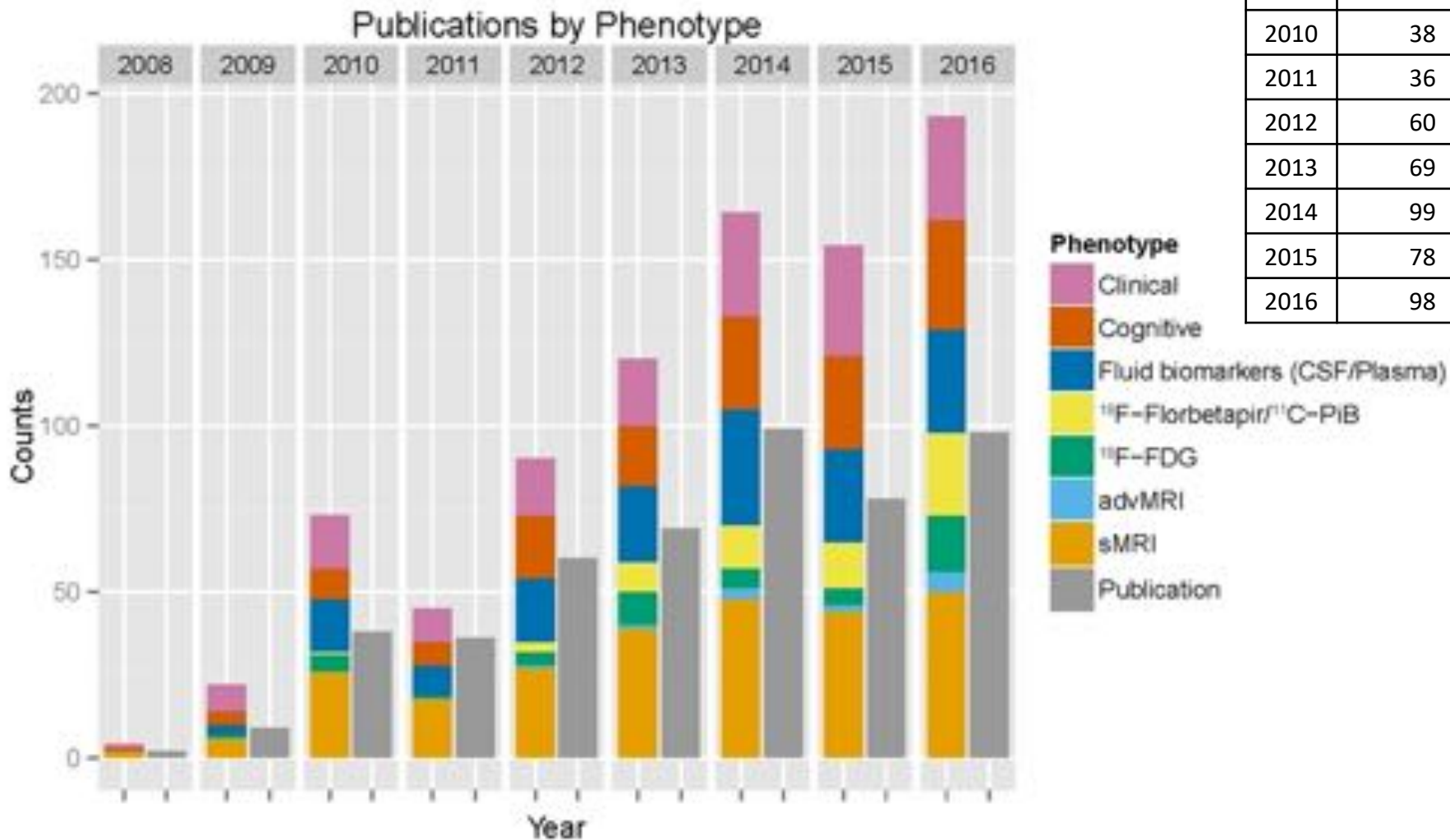


Introduction

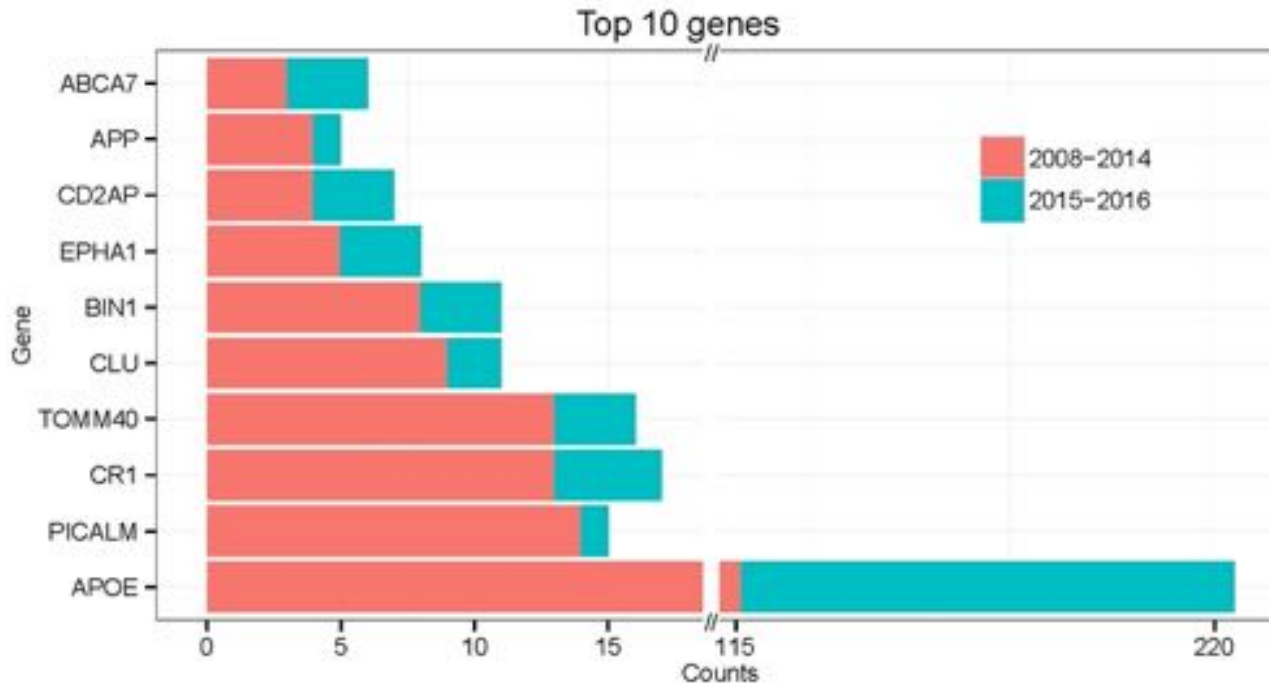
- ADNI provides numerous phenotypes to evaluate with genetic analysis, both with genome-wide and targeted analyses (i.e., pathway, gene-based)
- As a longitudinal study, many phenotypes are available both on a cross-sectional basis and a longitudinal basis
- The majority of phenotypes are available starting at the baseline visit, while some were only added at later timepoints



Introduction



Introduction



Common reported genes in manuscripts using ADNI genetic data (2008–2016)

Goals

- Describe ADNI visits and collection
- Describe ADNI clinical/cognitive phenotypes
- Describe ADNI fluid phenotypes
- Describe ADNI imaging phenotypes
- Briefly describe genomic analyses with ADNI phenotypes to date



ADNI Phenotypes

- ADNI is broadly divided into four phases
 - ADNI-1: Started enrolling in 2005
 - ADNI-GO: 200 early mild cognitive impairment (EMCI) patients enrolled starting in 2010
 - ADNI-2: Started enrolling in 2011
 - ADNI-3: Started enrolling in January 2017
 - “Roll over” of some participants through stages
- Participants include the following categories: cognitively normal (CN), significant memory concern (SMC; similar to SCD), EMCI, late MCI, and mild AD



ADNI Phenotypes

Study Schedule	ADNI1												ADNI GO: New Participants					ADNI GO: Follow-Up from ADNI1				ADNI2: New Participants										ADNI2: Follow-Up from ADNI1/GO		
	Screen			Baseline			Month 6		Month 12		Month 18		Month 24		Month 30		Month 36		Screen	Baseline	Month 3	Month 6	Month 12	Month 18	Month 24	Ongoing 6 Month Interim (phone)		Ongoing Annual	Initial	Ongoing 6 Month Interim	Ongoing Annual			
	CN	MCI	AD	CN	MCI	AD	CN	MCI	AD	CN	MCI	AD	CN	MCI	AD	CN	MCI	AD	EMCI	EMCI	EMCI	EMCI	EMCI	EMCI/LMC I	EMCI/LMC I	EMCI/LMC I	EMCI/LMC I	EMCI/LMC I	EMCI/LMC I	EMCI/LMC I	EMCI/LMC I	EMCI/LMC I	EMCI/LMC I	EMCI/LMC I
Explant Study	x	x	x															x																
Obtain Consent	x	x	x															x																
Demographics, Family History, Inclusion and Exclusion Criteria	x	x	x															x																
Medical History, Physical Exam, Neurological Exam, Hachinski	x	x	x															x																
Vital Signs	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x																
Height	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x																	
Screening Labs	x	x	x															x																
APOE	x	x	x															x																
DNA Sample Collection for APOE Genotyping and GWAS																		x																
Cell Immortalization Sample Collection																		x																
American National Adult Reading Test				x	x	x												x																
Mini Mental State Examination	x	x	x															x																
Logical Memory I and II	x	x	x															x																
Everyday Cognition (Ecog)																		x																
Montreal Cognitive Assessment (MoCA)																		x																
Digit Span				x	x	x	x	x	x	x	x	x	x	x	x	x	x	x																
Category Fluency				x	x	x	x	x	x	x	x	x	x	x	x	x	x	x																
Category Fluency (Animals)				x	x	x	x	x	x	x	x	x	x	x	x	x	x	x																
Frails A & B				x	x	x	x	x	x	x	x	x	x	x	x	x	x	x																
Digit Symbol				x	x	x	x	x	x	x	x	x	x	x	x	x	x	x																
Boxton Naming Test				x	x	x	x	x	x	x	x	x	x	x	x	x	x	x																
Auditory Verbal Learning Test				x	x	x	x	x	x	x	x	x	x	x	x	x	x	x																
Geriatric Depression Scale	x	x	x															x																
Clock Drawing				x	x	x	x	x	x	x	x	x	x	x	x	x	x	x																
Neuropsychiatric Inventory				x	x	x	x	x	x	x	x	x	x	x	x	x	x	x																
Neuropsychiatric Inventory Q				x	x	x	x	x	x	x	x	x	x	x	x	x	x	x																
ADAS-Cog				x	x	x	x	x	x	x	x	x	x	x	x	x	x	x																
ADAS-Cog 13 (with Delayed Word Recall and Number Cancellation)				x	x	x	x	x	x	x	x	x	x	x	x	x	x	x																
Clinical Dementia Rating Scale	x	x	x															x																
Activities of Daily Living (FAQ)				x	x	x	x	x	x	x	x	x	x	x	x	x	x	x																
Plasma and Serum Biomarker Collection																		x																
RNA Sample Collection																		x																
Collect and Process Biomarkers				x	x	x	x	x	x	x	x	x	x	x	x	x	x	x																
Concomitant Medications	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x																
Subject Payments	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x																
Phone Contact																		x																
Adverse Events	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x																
Diagnostic Summary				x	x	x	x	x	x	x	x	x	x	x	x	x	x	x																
MRI (1.5 T) (100%)	x	x	x															x																
MRI (3 T) (25%)				x	x	x	x	x	x	x	x	x	x	x	x	x	x	x																
MRI (3 T) (100%)																		x																
PET (50%)				x	x	x	x	x	x	x	x	x	x	x	x	x	x	x																
18F-AV-45 Amyloid Imaging (100%)																		x																
FDG-PET Imaging (100%)																		x																
LP (minimum of 20%)				x	x	x												x																
CSF Collection by Lumbar Puncture (100%)																		x																

ADNI General Phenotypes

	ADNI-1			ADNI-GO	ADNI-1 roll over	ADNI-2					ADNI-1/GO roll over
	Screen/BL			Screen/BL	Visit 1	Screen/Baseline					Initial
	CN	MCI	AD	EMCI	CN/MCI	CN	EMCI	LMCI	AD	SMC	CN/EMCI/LMCI
Approximate n	200	400	200	200	n/a	150	150	150	150	100	n/a
Explain Study	x	x	x	x	x	x	x	x	x	x	x
Obtain Consent	x	x	x	x	x	x	x	x	x	x	x
Demographics, Family History, Inclusion and Exclusion Criteria	x	x	x	x		x	x	x	x	x	
Medical History, Physical Exam, Neurological Exam, Hachinski	x	x	x	x	x	x	x	x	x	x	x



ADNI Clinical Phenotypes

	ADNI-1			ADNI-1 roll over	ADNI-GO/ADNI-2				ADNI-1/GO roll over
	SC/BL	M6	Annual	Annual	SC/BL	M3	M6	Annual	Annual
	All	All	All	CN/MCI	All	All	All	All	CN/EMCI/LMCI
Height	x	x	x		x	x	x	x	
DNA Sample for APOE and GWAS	x	x	x	x	x	x	x	x	x
Cell Immortalization Sample Collection					x	x	x	x	
Vital Signs (HR, BP, temp, weight)	x	x	x	x	x	x	x	x	x
Medications	x	x	x	x	x	x	x	x	x
Adverse Events	x	x	x	x	x	x	x	x	x
Diagnosis	x	x	x	x	x	x	x	x	x



ADNI Clinical/Cognitive Phenotypes

	ADNI-1			ADNI-1 roll over	ADNI-GO/2								ADNI-1/GO roll over
	SC/BL	M6	Annual	Annual	SC/BL		M3		M6		Annual		Annual
	All	All	All	CN/MCI	CN E/LMCI AD	SMC	CN E/LMCI AD	SMC	CN E/LMCI AD	SMC	CN E/LMCI AD	SMC	CN E/LMCI
American National Adult Reading Test	X				X	X							
CDR	X	X	X	X	X	X			X	X	X	X	X
FAQ	X	X	X	X	X	X			X	X	X	X	X
GDS	X	X	X	X	X	X			X	X	X	X	X
NPI/NPI-Q	X	X	X	X	X	X			X	X	X	X	X
ADAS-Cog	X	X	X	X	X	X			X	X	X	X	X
Neuropsych Battery	X	X	X	X	X	X			X	X	X	X	X
MoCA				X	X	X			X	X	X	X	X
ECog (Self & Informant)				X	X	X			X	X	X	X	X
CCI-20 (Self)					X	X							



ADNI Clinical/Cognitive Phenotypes

ADNI-1/GO/2 Battery

AMNART (Baseline only)
ADAS-Cog
MMSE
Weschler's Logical Memory I & II
Rey Auditory Verbal Learning Test
Clock Drawing
Trail Making A & B
Animal Fluency
Boston Naming Test

ADNI-1 only

Vegetable Fluency
Digit Symbol
Digit Span

ADNI-GO/2 only

MoCA
ECog
CCI-20 (SMC only)



ADNI Fluid Phenotypes

	ADNI-1			ADNI-1 roll over		ADNI-GO/2				ADNI-1/GO roll over
	SC/BL	M6	Annual	Visit 1	Annual	SC/BL	M3	M6	Annual	Annual
	All	All	All	CN/MCI	CN/MCI	All	All	All	All	CN/EMCI/ LMCI
Screening Labs	X					X				
Plasma and Serum Collection				X	X	X		X	X	X
RNA Collection				X	X	X			X	X
	ADNI-1			ADNI-1 roll over		ADNI-GO/2				ADNI-1/GO roll over
	SC/BL	M6	Annual	Visit 1	Every 2 years	SC/BL	M3	M6	Every 2 years	Every 2 years
	50%	50%	50%	CN/MCI	CN/MCI	All	All	All	All	CN/EMCI/ LMCI
CSF Collection	X	X	X	X	X	X			X	X



ADNI Imaging Phenotypes

	ADNI-1			ADNI-1 roll over		ADNI-GO/2				ADNI-1/GO roll over	
	SC/BL	M6	Annual	Visit 1	Annual	SC/BL	M3	M6	Annual	Initial	Annual
	1.5T - All 3T-25%	1.5T - All 3T-25%	1.5T - All 3T-25%	1.5T - CN/MCI 3T-25%	1.5T - CN/MCI 3T-25%	All	All	All	All	CN E/LMCI	CN E/LMCI
1.5T sMRI Scans	X	X	X	X	X						
3T sMRI Scans	X	X	X	X	X	X	X	X	X	X	X
	ADNI-1			ADNI-1 roll over		ADNI-GO/2				ADNI-1/GO roll over	
	SC/BL	M6	Annual	Visit 1	Every 2 years	SC/BL	M3	M6	Every 2 years	Every 2 years	
	50%	50%	50%	CN/MCI	CN/MCI	All	All	All	All	CN E/LMCI	
[¹⁸ F]FDG PET	X	X	X	X	X	X			X	X	
[¹¹ C]PiB PET	Selected people, various visits										
[¹⁸ F]Florbetapir (AV-45) PET				X	X	X			X	X	
[¹⁸ F]Flortaucipir (AV-1451) PET						Selected people, various visits (earliest 24m FU)					



ADNI Imaging Phenotypes

ADNI-1 Sequence

2 MPRAGEs – brain structure
PD/T2 – WM hyperintensities

ADNI-1 Roll Over Sequence

1 MPRAGE/SPGR
1 Accelerated MPRAGE/SPGR
2D FLAIR - WM hyperintensities
T2* - cerebral microbleeds

ADNI-GO/2 Sequence

1 MPRAGE/SPGR
1 Accelerated MPRAGE/SPGR
2D FLAIR
T2*
~1/3 of sample (each):
Diffusion Tensor Imaging (DTI) – WM integrity, structural connectivity
Arterial Spin Labeling (ASL) – brain perfusion
Resting-state fMRI – functional connectivity



Important Things to Know

RID: Unique Subject ID – most phenotypes coded by this ID

PTID: Full ID (Site ID _S_ Subject ID) – MRI and PET images and genetics are coded by this ID

VISCODE = Visit at which the data was collected

ADNI MERGE has many target variables but may not encompass all of the variables you are looking for...

Other Important Sheets: Neuropsychological battery (NEUROBAT), patient demographics (PTDEMOG), family history (FHQ, RECFHQ), CSF (UPENNBIOMK_MASTER), MRI (UCSFFSX51_08_01_16), Tau (UCBERKELEYAV1451), AV-45 (UCBERKELEYAV45), FDG (UCBERKELEYFDG), medications (RECCMEDS), medical history (MEDHIST), vital signs (VITALS), data dictionary (DATADIC), ADNI merge dictionary (ADNIMERG_DICT)



Important Things to Know

The screenshot shows the ADNI (Alzheimer's Disease Neuroimaging Initiative) website. At the top, there is a navigation bar with the ADNI logo and the University of Southern California logo. Below this is a search bar and a navigation menu with options: HOME, ADNI GUIDE, DOWNLOAD, SEARCH, PROJECTS, SUPPORT. A secondary menu below that includes Study Data, Image Collections, and Biomarkers Data. On the left side, there is a green sidebar menu with categories: Assessments, Demographics, Enrollment, Genetics, Imaging, Medical History, Study Info, Subject Characteristics, Test Data, and Active. The main content area displays a search bar with the text 'ADNI' and a list of data files under the heading 'ASSESSMENTS'. The list includes sub-sections for 'All Diagnostics' and 'All Neuropsychology', each containing numerous file names with their respective formats and versions.



Important Things to Know

The screenshot displays the ADNI (Alzheimer's Disease Neuroimaging Initiative) website search interface. At the top, the ADNI logo is prominent, along with navigation links for HOME, ADNI GUIDE, DOWNLOAD, SEARCH, PROJECTS, and SUPPORT. Below these are links for Study Data, Image Collections, and Biomarker Data. The main search area is titled 'Search' and includes tabs for 'Advanced Search Portal' and 'Data Collections'. On the left, there are 'Search Options' and 'Display Options' sections. The 'Search Options' section includes checkboxes for 'Include Previous Downloads', 'Project Phase', 'Subject', 'Subject Specific Information', 'Assessments', 'Study Visit', 'Image', 'Imaging Protocol', 'Image Status', 'Image Processing', and 'Image Type' (with 'Original' selected). The 'Display Options' section includes 'Order by' (set to 'Subject ID'), 'and' (set to 'AND'), and 'and' (set to '1'). The 'Search Criteria' section on the right contains a search bar and a list of criteria with checkboxes, including 'ADNI', 'ADNI1', 'ADNI2', 'ADNI3', 'ADNI4', 'ADNI5', 'ADNI6', 'ADNI7', 'ADNI8', 'ADNI9', 'ADNI10', 'ADNI11', 'ADNI12', 'ADNI13', 'ADNI14', 'ADNI15', 'ADNI16', 'ADNI17', 'ADNI18', 'ADNI19', 'ADNI20', 'ADNI21', 'ADNI22', 'ADNI23', 'ADNI24', 'ADNI25', 'ADNI26', 'ADNI27', 'ADNI28', 'ADNI29', 'ADNI30', 'ADNI31', 'ADNI32', 'ADNI33', 'ADNI34', 'ADNI35', 'ADNI36', 'ADNI37', 'ADNI38', 'ADNI39', 'ADNI40', 'ADNI41', 'ADNI42', 'ADNI43', 'ADNI44', 'ADNI45', 'ADNI46', 'ADNI47', 'ADNI48', 'ADNI49', 'ADNI50', 'ADNI51', 'ADNI52', 'ADNI53', 'ADNI54', 'ADNI55', 'ADNI56', 'ADNI57', 'ADNI58', 'ADNI59', 'ADNI60', 'ADNI61', 'ADNI62', 'ADNI63', 'ADNI64', 'ADNI65', 'ADNI66', 'ADNI67', 'ADNI68', 'ADNI69', 'ADNI70', 'ADNI71', 'ADNI72', 'ADNI73', 'ADNI74', 'ADNI75', 'ADNI76', 'ADNI77', 'ADNI78', 'ADNI79', 'ADNI80', 'ADNI81', 'ADNI82', 'ADNI83', 'ADNI84', 'ADNI85', 'ADNI86', 'ADNI87', 'ADNI88', 'ADNI89', 'ADNI90', 'ADNI91', 'ADNI92', 'ADNI93', 'ADNI94', 'ADNI95', 'ADNI96', 'ADNI97', 'ADNI98', 'ADNI99', 'ADNI100'. The 'ADNI' criteria are currently selected.

Important Things to Know

The screenshot shows the ADNI website interface. At the top, there are logos for SIDA and USC University of Southern California. The main navigation bar includes links for HOME, ADNI GUIDE, DOWNLOAD, SEARCH, PROJECTS, and SUPPORT. Below this, there are sub-links for Study Data, Image Collections, and Genetic Data. A green sidebar on the left lists various data types: ADNI WGS + Omni1.0M, ADNI OMNI, ADNI WGS + Omni1.0M, ADNI Core Expression, ADNI T1w Data, and DNA Methylation Profiling. The main content area is titled 'ADNI WGS + Omni1.0M' and contains a description of the data: 'ADNI WGS+ Omni1.0M samples whole-genome sequenced (WGS) at high coverage, and genotyped using the Illumina Omni 2.5M BeadChip. WGS data were generated using two different pipelines: 1) Broad best practices (BWA & GATK HaplotypeCaller) and 2) CASAVA-1.8.2a1_1108080.8'. Below the description is a table listing data releases.

ALL WGS (CASAVA 1.8.2a1) + WGS (GATK 1.8.2a1) + Omni1.0M SNP 422K	Version	File Format
ADNI WGS Data - CASAVA 1.8.2a1 141.34.01.01	Version 2013.08.24	VCF format
ADNI WGS Data - CASAVA 1.8.2a1 141.34.02.01	Version 2013.08.27	VCF format
ADNI WGS Data - CASAVA 1.8.2a1 141.34.03.01	Version 2013.08.27	VCF format
ADNI WGS Data - CASAVA 1.8.2a1 141.34.04.01	Version 2013.08.27	VCF format
ADNI WGS Data - CASAVA 1.8.2a1 141.34.05.01	Version 2013.08.27	VCF format
ADNI WGS Data - CASAVA 1.8.2a1 141.34.06.01	Version 2013.08.27	VCF format
ADNI WGS Data - CASAVA 1.8.2a1 141.34.07.01	Version 2013.08.27	VCF format
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ADNI WGS Data - CASAVA 1.8.2a1 141.34.11.01	Version 2013.08.27	VCF format
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ADNI WGS Data - CASAVA 1.8.2a1 141.34.28.01	Version 2013.08.27	VCF format
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ADNI WGS Data - CASAVA 1.8.2a1 141.34.30.01	Version 2013.08.27	VCF format
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ADNI WGS Data - CASAVA 1.8.2a1 141.34.95.01	Version 2013.08.27	VCF format
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ADNI WGS Data - CASAVA 1.8.2a1 141.34.97.01	Version 2013.08.27	VCF format
ADNI WGS Data - CASAVA 1.8.2a1 141.34.98.01	Version 2013.08.27	VCF format
ADNI WGS Data - CASAVA 1.8.2a1 141.34.99.01	Version 2013.08.27	VCF format
ADNI WGS Data - CASAVA 1.8.2a1 141.34.100.01	Version 2013.08.27	VCF format

Important Things to Know

The screenshot shows the Microsoft Excel interface with the ribbon set to 'HOME'. The active cell is E1, containing the text 'COLPROT'. The data table below is as follows:

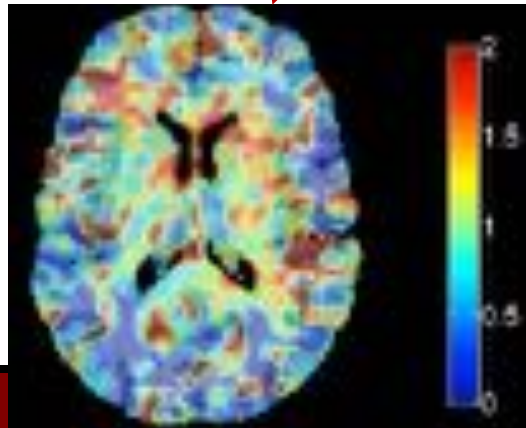
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O
1	RID	PTID	VISCODE	SITE	COLPROT	ORIGPROTEXAMDATE	DX_BI	AGE	PTGENDEF	PTEDUCA1	PTETHCAT	PTRACCA1	PTMARRY	APOE4	
2		2 011_5_0002	bl	11	ADN11	ADN11									
3			m06												
4			m36												
5			m60												
6			m66												
7			m126												
8			m120												
9			m108												
10			m102												
11			m96												
12			m90												
13			m84												
14			m78												
15			m72												

MR Imaging Phenotypes

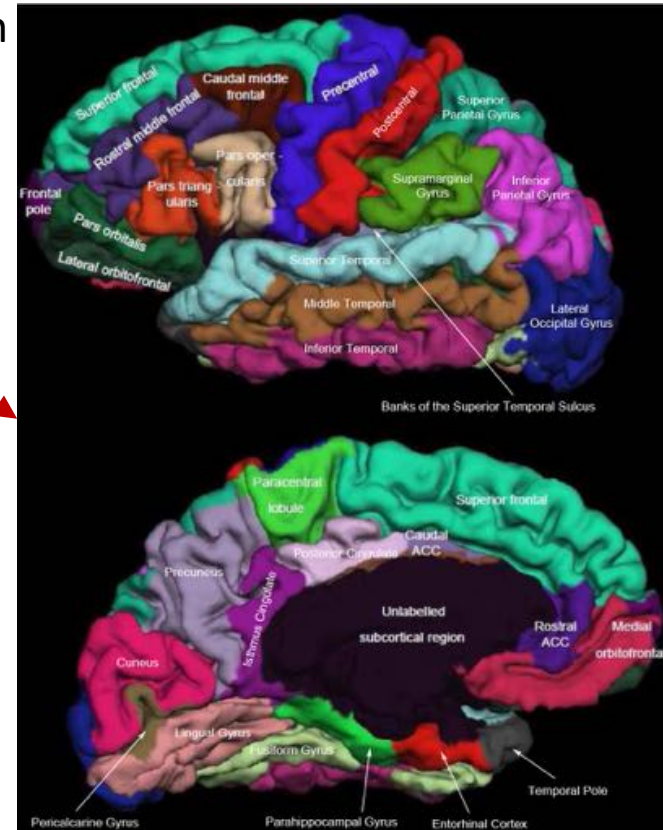
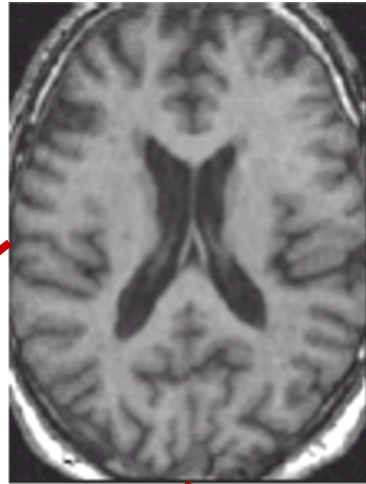
Voxel-Based Morphometry



Tensor-Based Morphometry



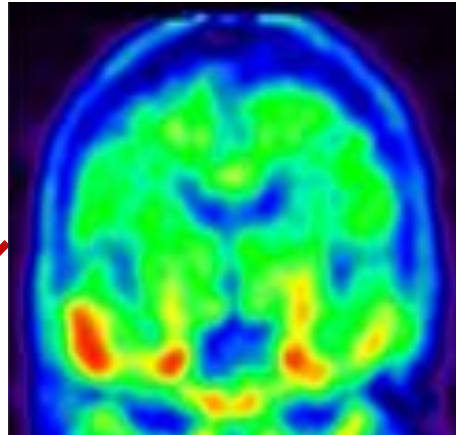
Segmentation & Parcellation



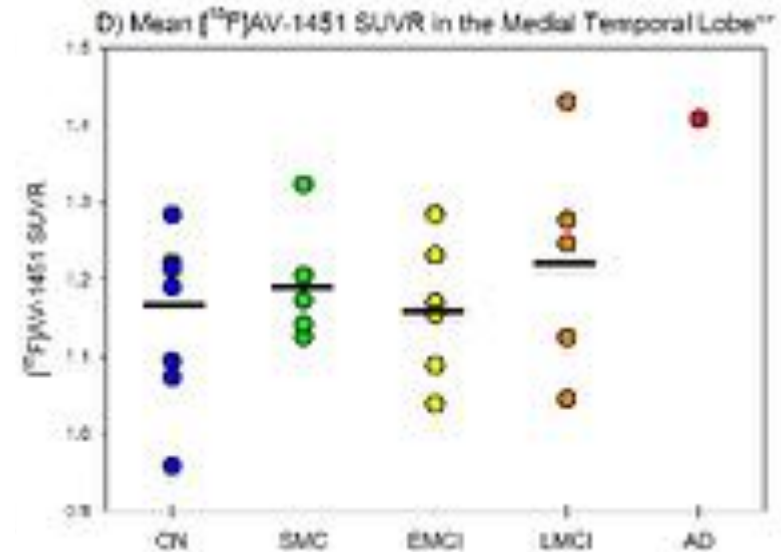
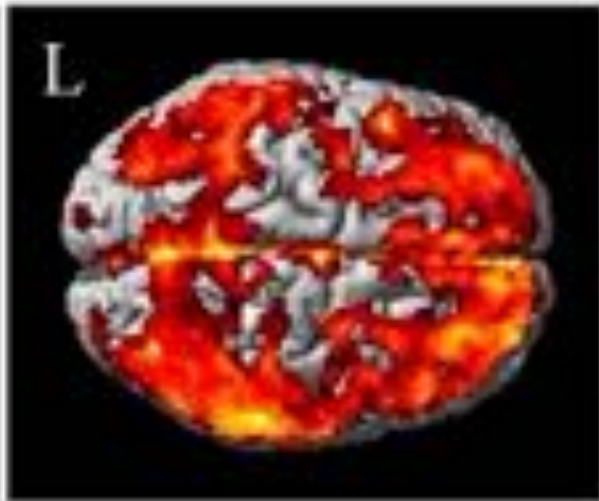
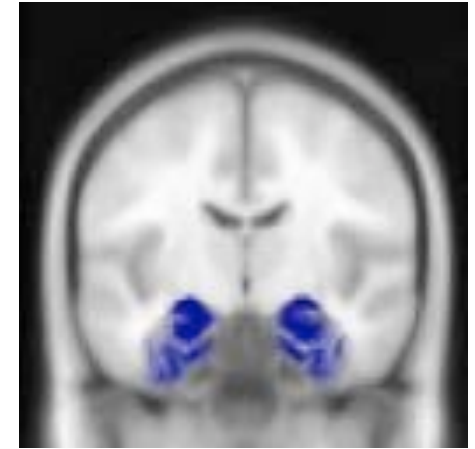
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ADNI Imaging Phenotypes

Voxel-Based Analysis

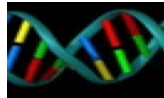


ROI-based analysis

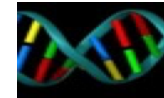


Brain-Genome Association Strategies

Candidate Gene/SNP

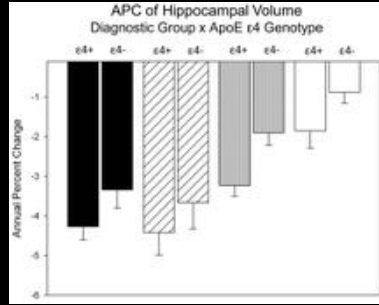


Biological Pathway

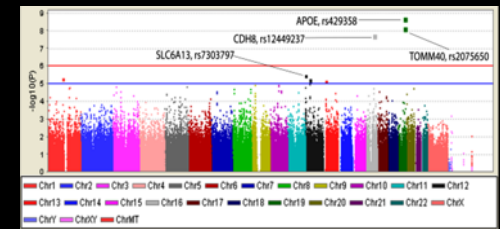
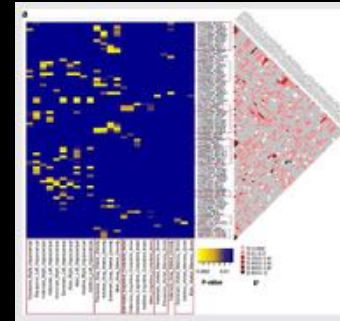


Genome-wide Analysis

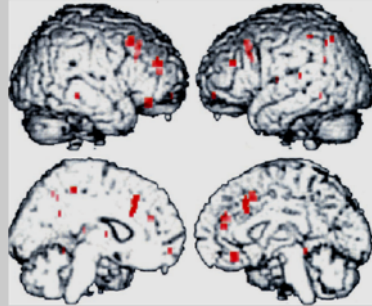
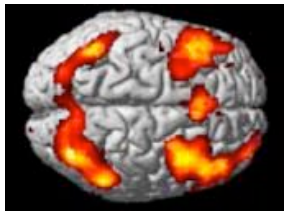
ROI



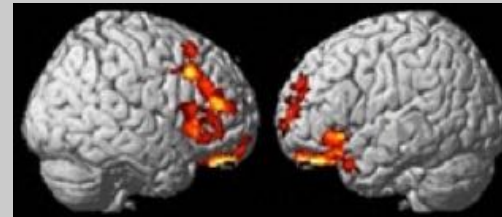
Risacher et al 2010



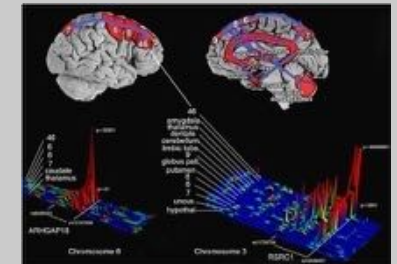
Circuit



Egan et al 2001 COMT

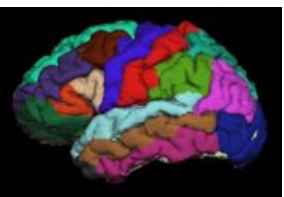


Swaminathan et al 2010 PiB ROIs & amyloid pathway

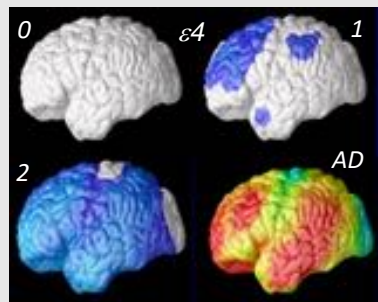


Potkin et al 2009 Mol Psych schizophrenia study

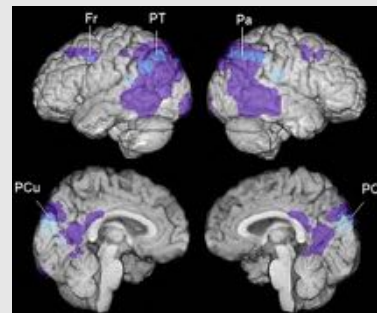
Whole Brain



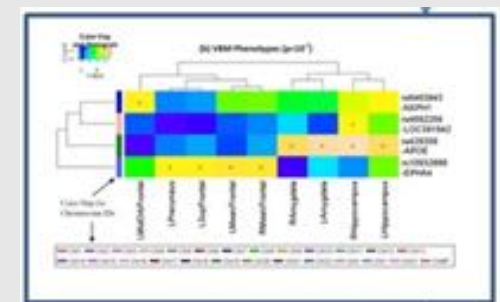
Saykin, 2011



Reiman et al PNAS 2009; Also Ho et al 2010 FTO



Reiman et al 2008 cholesterol pathway genes



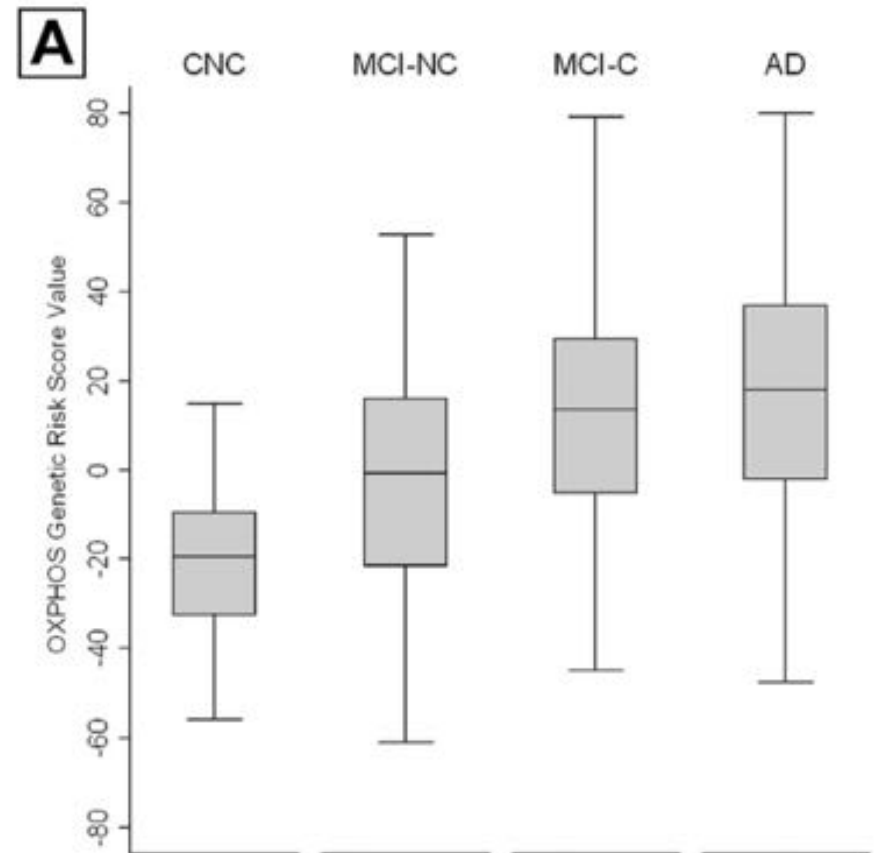
Shen et al 2010 ROIs; Stein et al 2010 voxels

ADNI Genetic Studies: Case/Control

Table 1 Association of *ABCA7* variants with Alzheimer's disease in studied groups based on Fisher's association test, including age, gender, and PC as covariates. Gene-based analysis was conducted with CMC collapsing method

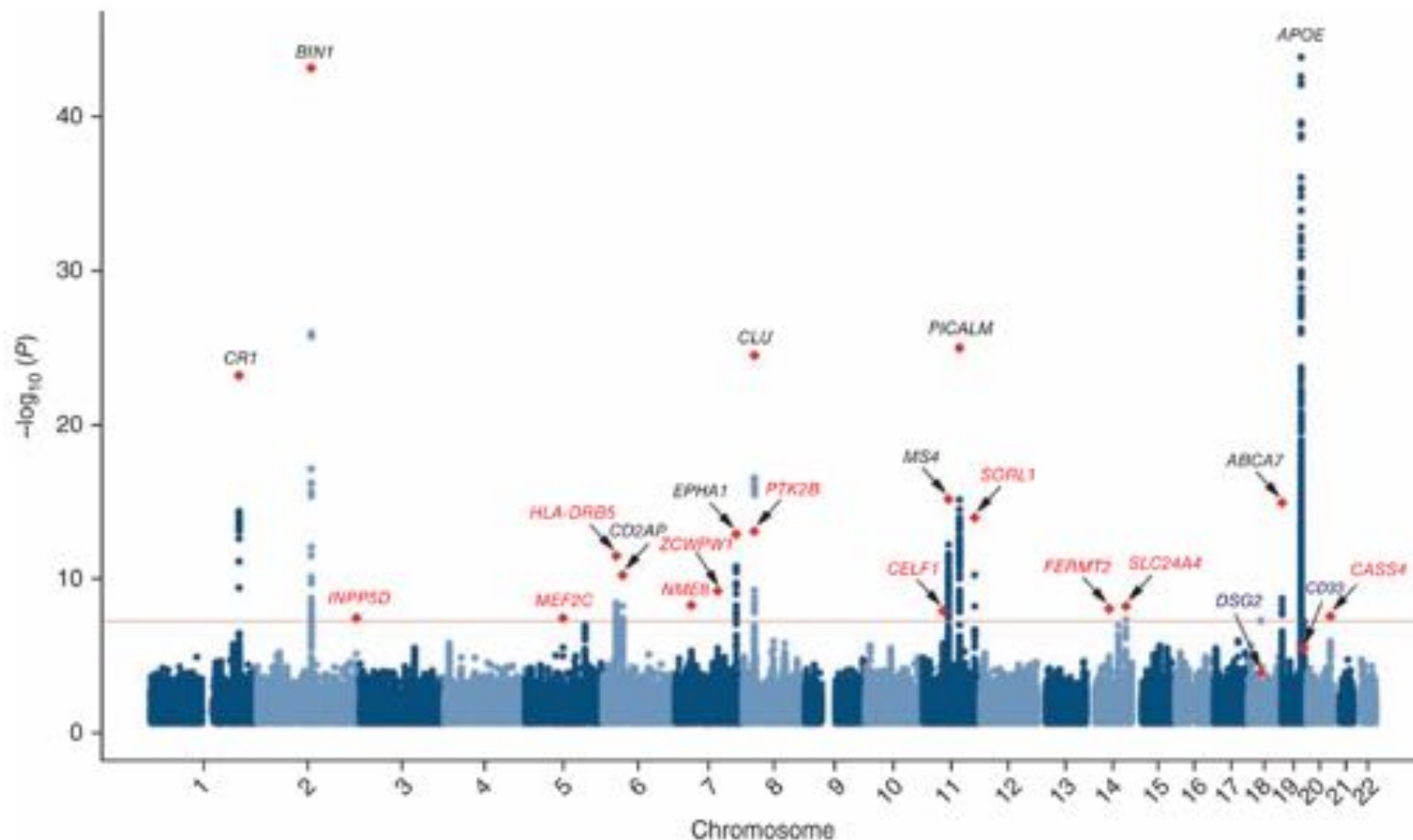
rsID/position ^a	MAF		OR (95 % CI)	P
	Cases	Controls		
rs4147929 (GWAS SNP)	0.179	0.1581	1.162 (1.02–1.31)	0.022
19:998507 ^a	0.006	0.0037	1.735 (0.54–3.04)	0.121
p.Glu709AlafsX86				
19:1006907 ^a	0.003	0.0027	1.285 (0.76–3.21)	0.569
p.Leu1403ArgfsX7				
rs113809142	0.002	0.0012	1.695 (0.34–5.91)	0.451
c.4416+2T>G				
rs200538373	0.009	0.0076	1.231 (0.68–2.61)	0.476
c.5570+5G>C				
Loss-of-function (All low frequency variants)	0.016	0.0107	1.549 (1.02–2.34)	0.038

Single gene – *ABCA7*



Pathway/Network based
(oxidative phosphorylation genes)

ADNI Genetic Studies: Case/Control



GWAS



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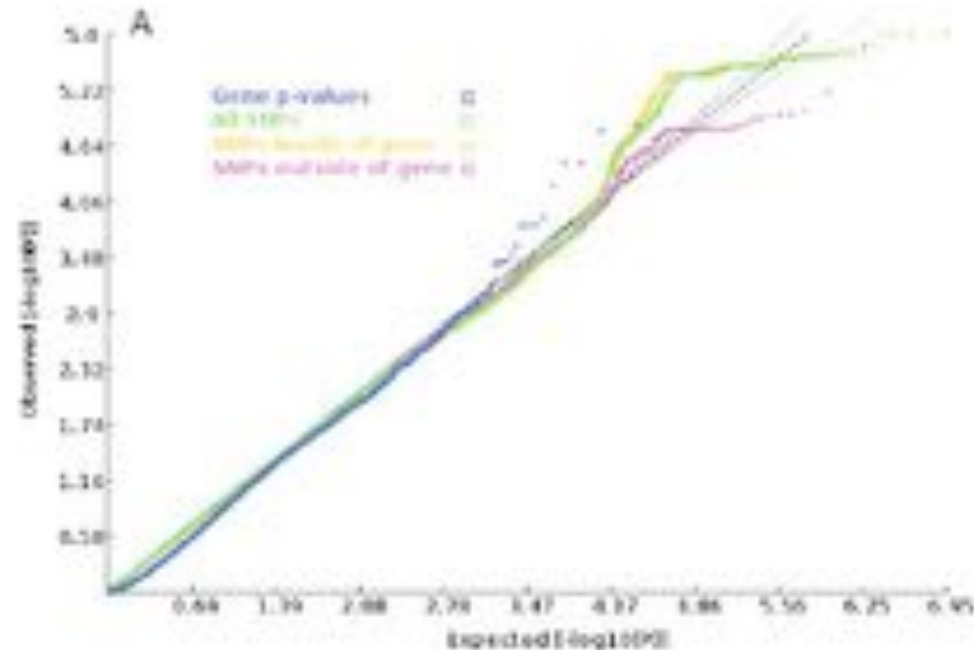
Lambert et al. (2013) *Nat Genetics*

ADNI Genetic Studies: Clinical Status

FAQ values for $\epsilon 2$ and non- $\epsilon 2$ groups at

	$\epsilon 2$ M (SD)	non- $\epsilon 2$ M (SD)
Baseline	2.83 (6.4)	5.13 (6.6)
12 Months ^{1,2}	3.53 (6.7)	6.90 (8.2)
24 Months ^{3,4,5}	3.29 (6.8)	8.66 (9.5)

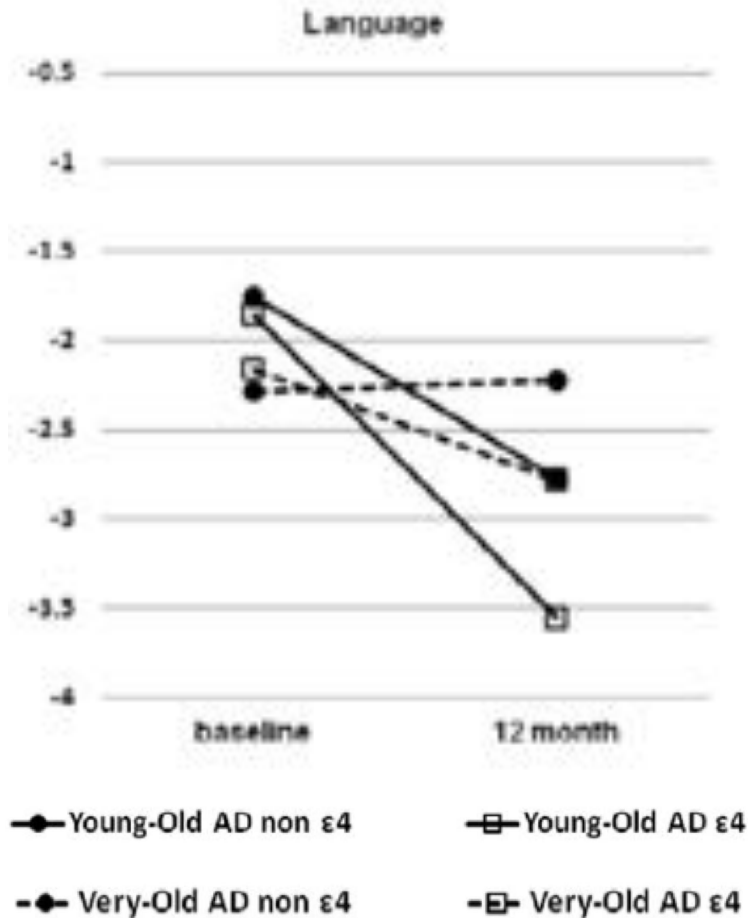
Single gene - APOE



Depressive Symptoms - GWAS



ADNI Genetic Studies: Cognition

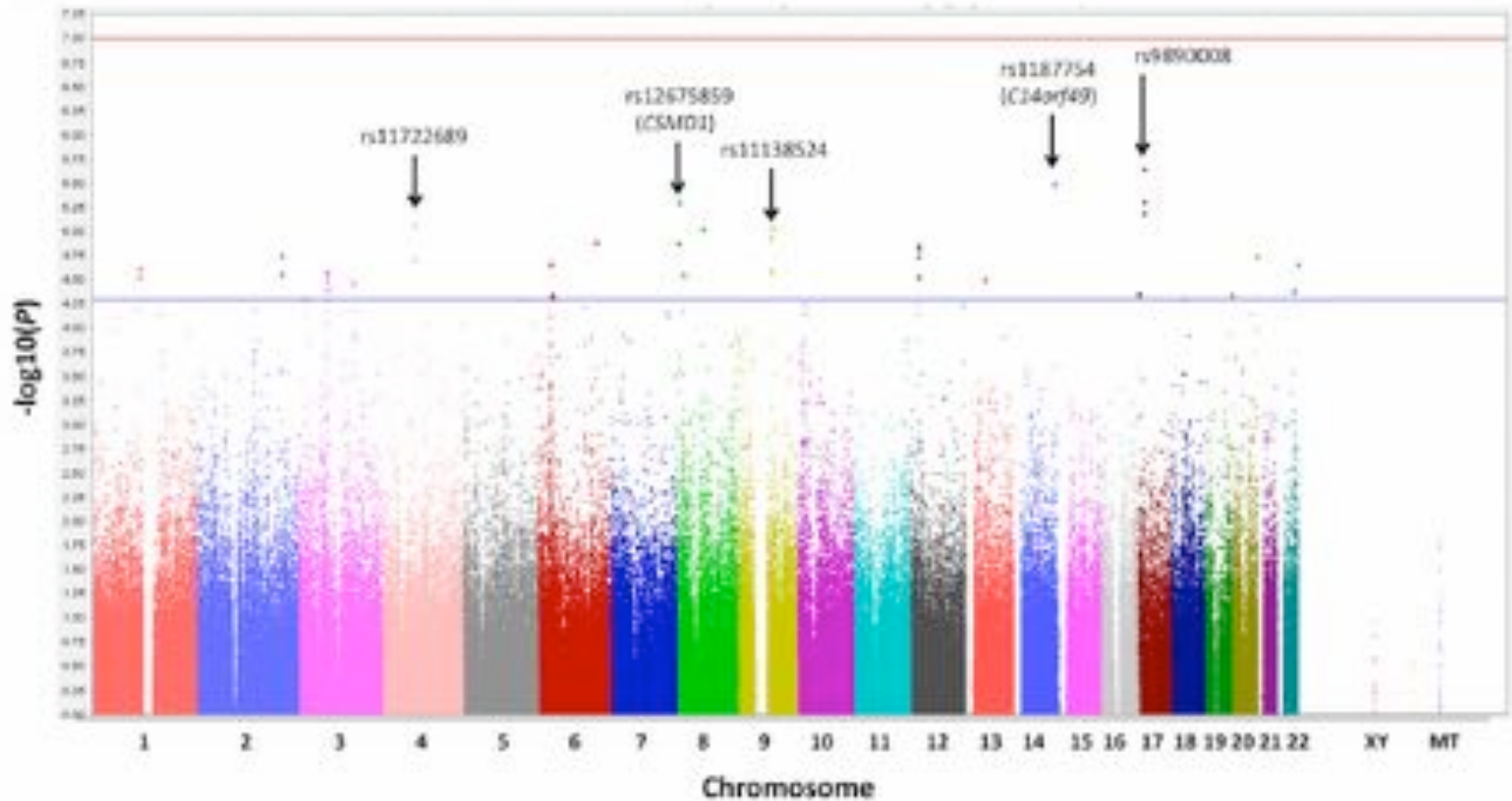


Single gene - APOE

	Conservative PGRS (IGAP loci only)
Analyses within older participants without dementia (ADNI)	
Baseline memory	-0.069 [0.027]; $p = 0.01^*$
Longitudinal memory	-0.002 [0.007]; $p = 0.71$
Baseline executive function	-0.029 [0.033]; $p = 0.37$
Longitudinal executive function	0.005 [0.008]; $p = 0.53$

AD risk genes -
Pathway/Network based

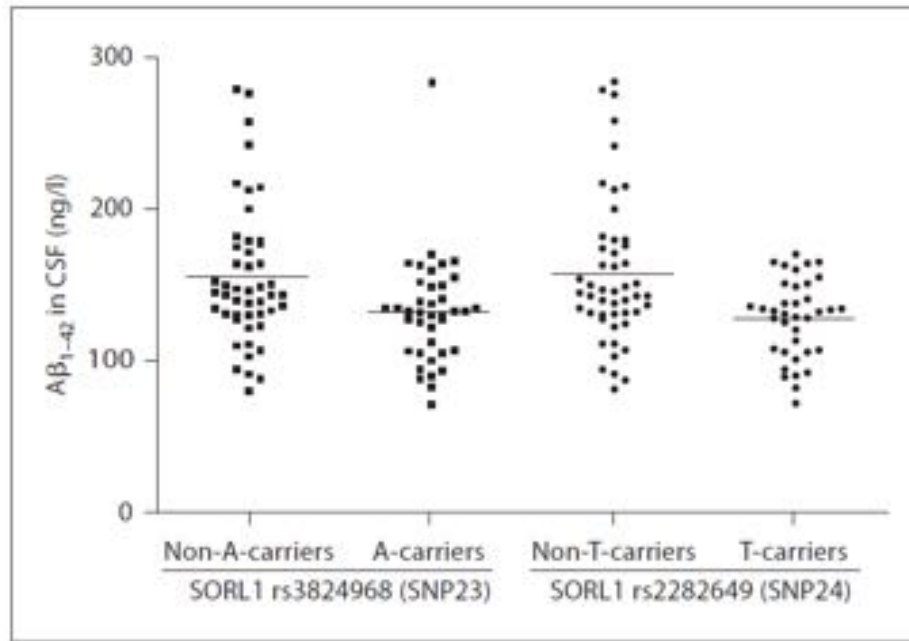
ADNI Genetic Studies: Cognition



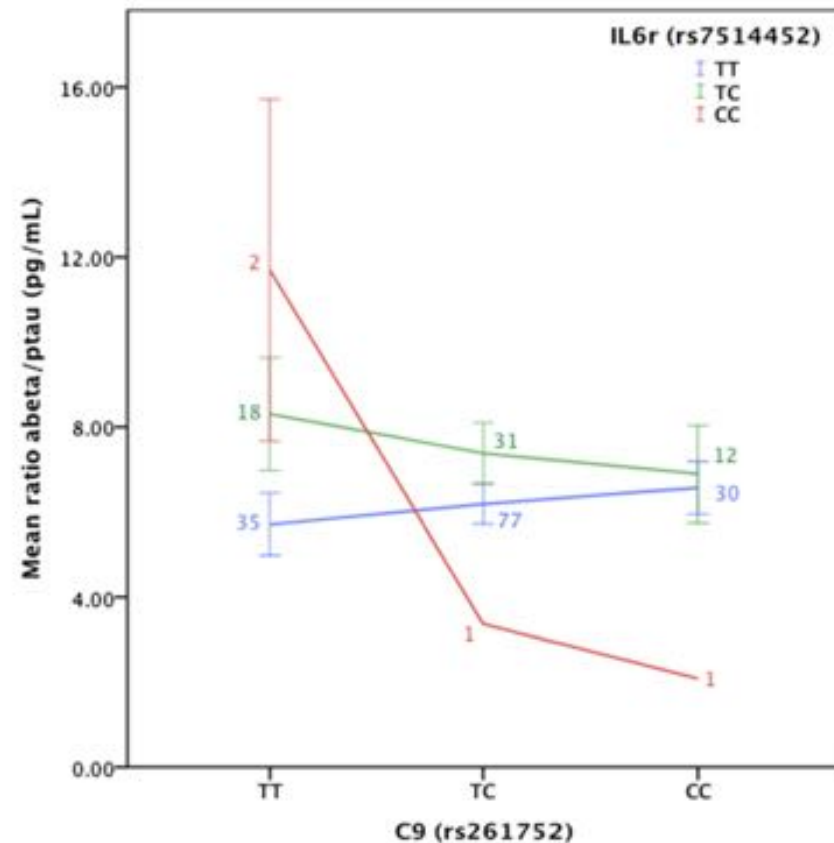
GWAS – episodic memory



ADNI Genetic Studies: CSF



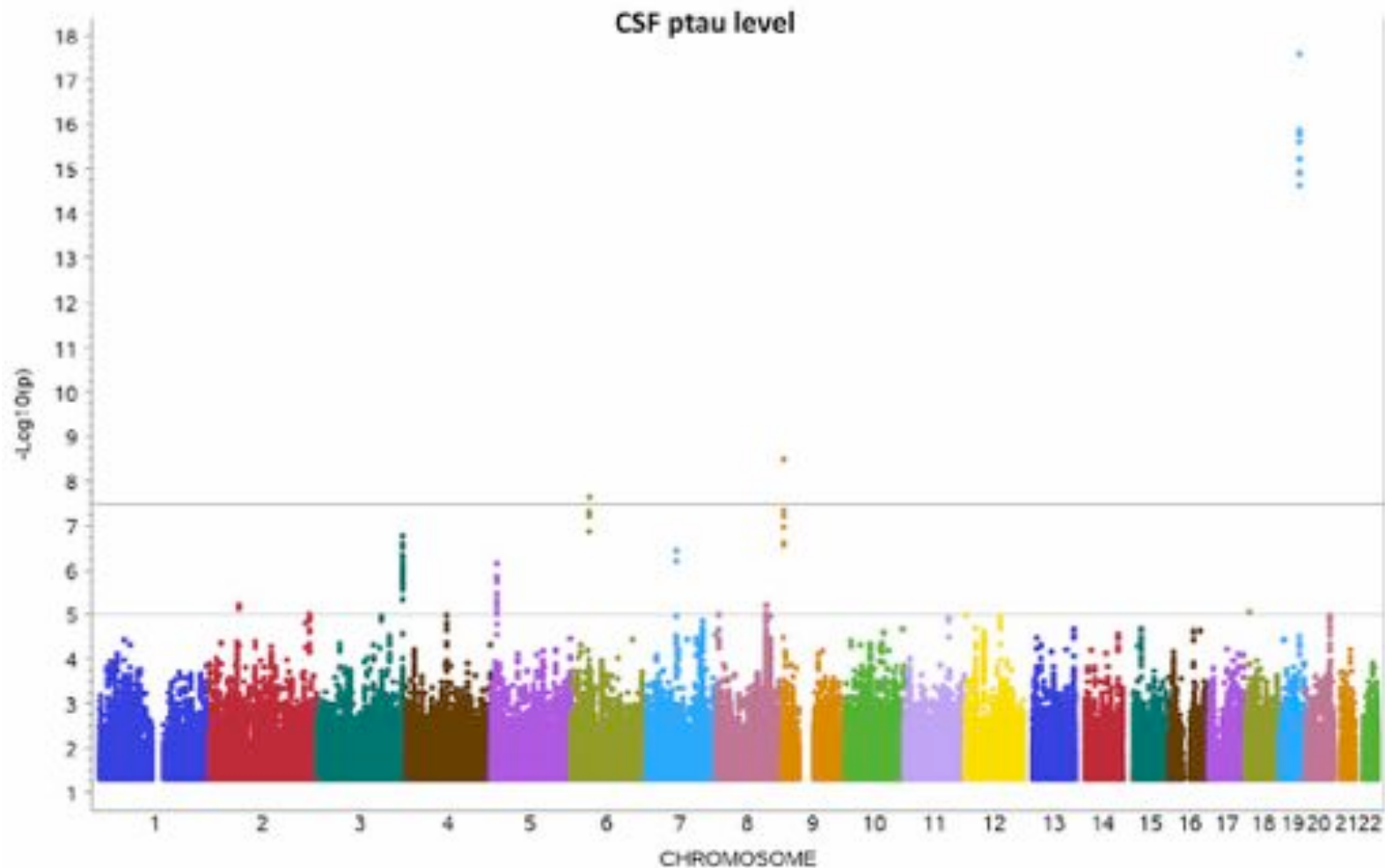
Single gene – *SORL1*
(on CSF Aβ₁₋₄₂ level)



Pathway/Network based
(immune pathway; Aβ/p-tau)

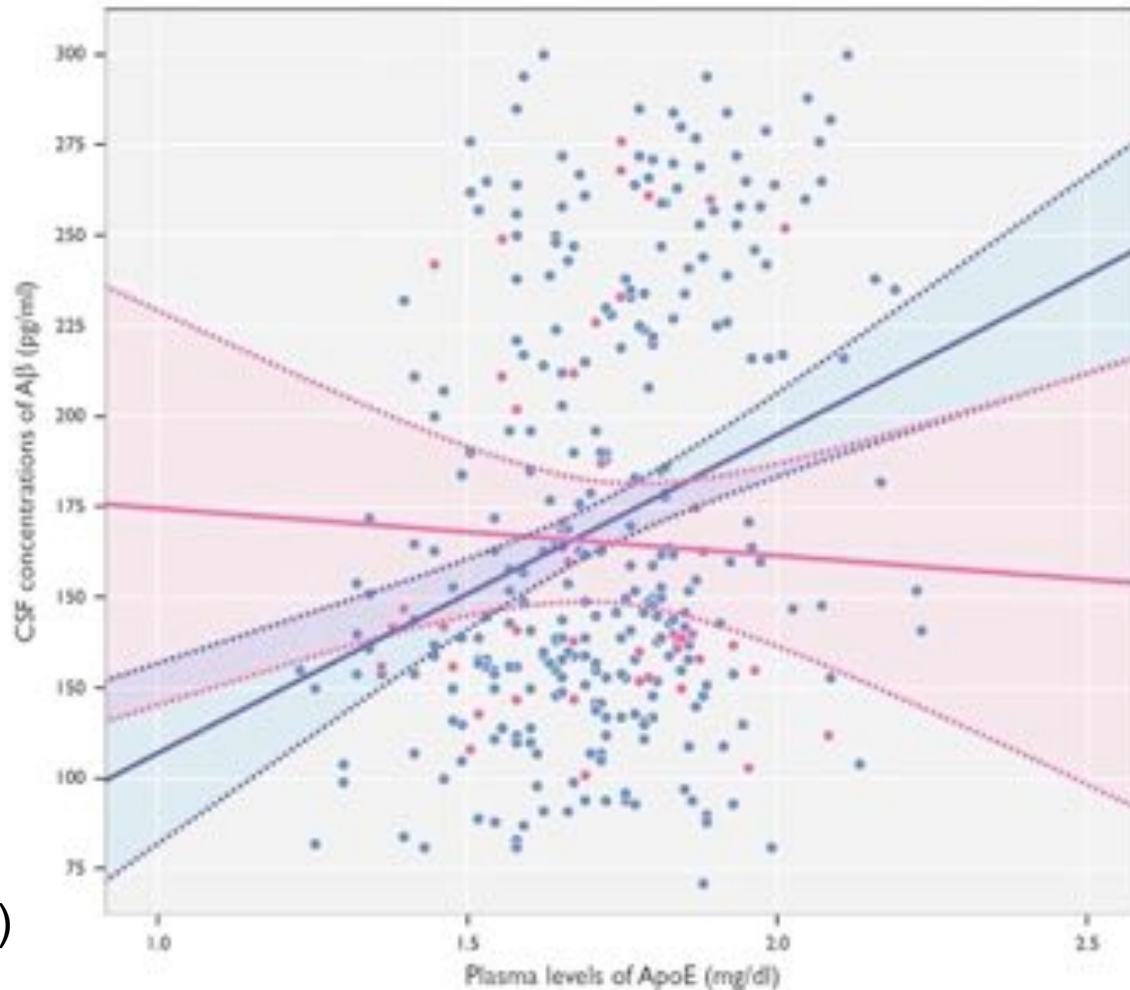


ADNI Genetic Studies: CSF



GWAS – CSF p-tau

ADNI Genetic Studies: Blood

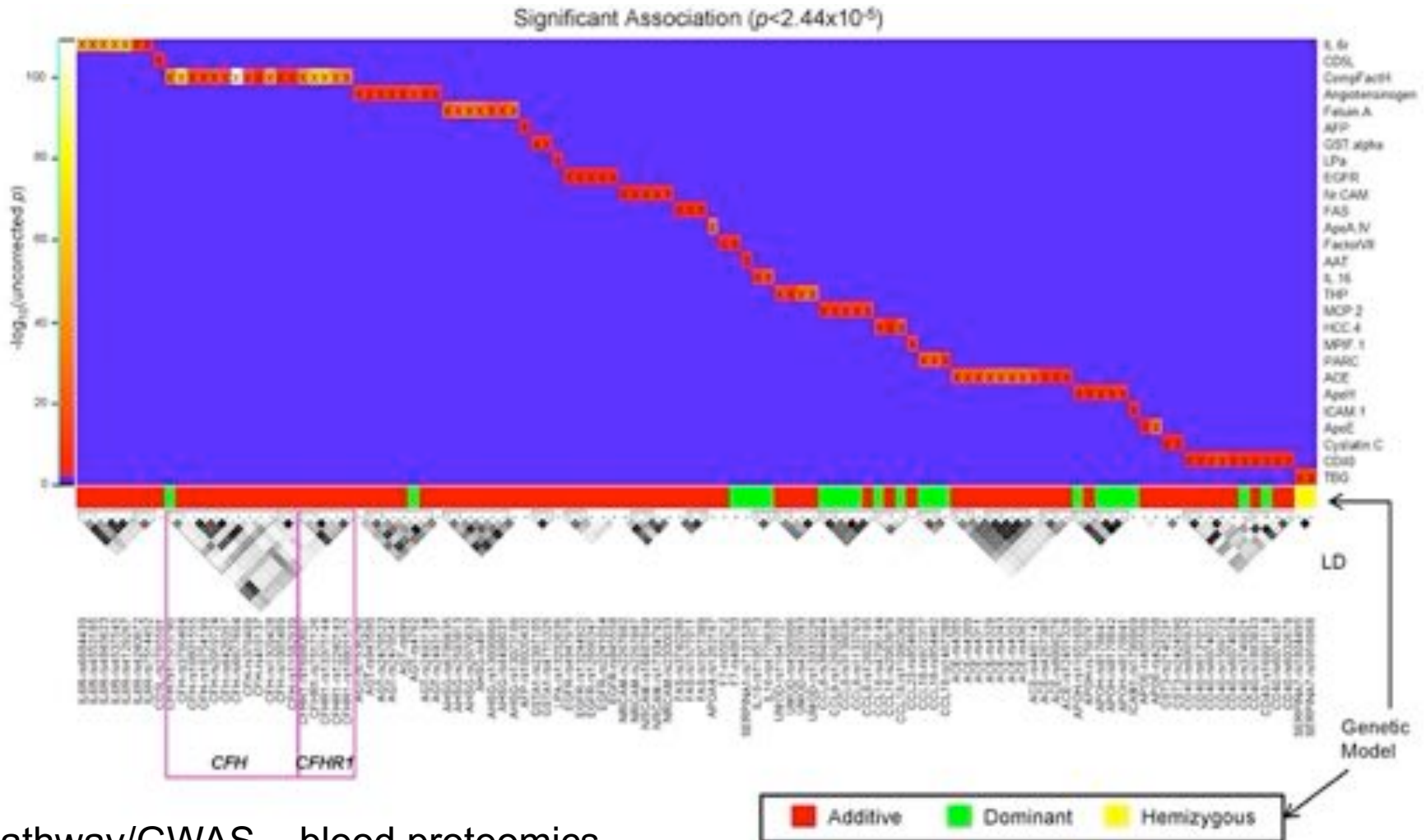


Single gene
(Plasma APOE
by *MTHFR* gene)

Higher plasma ApoE levels are associated with increased CSF Aβ₁₋₄₂ concentrations in C-allele carriers (blue), but not in T-homozygotes (pink).



ADNI Genetic Studies: Blood

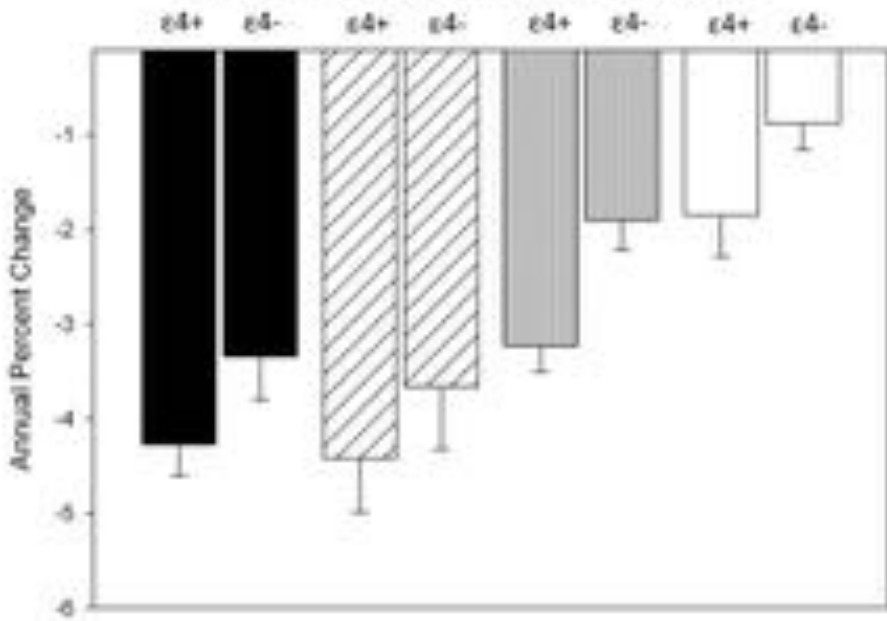


Pathway/GWAS – blood proteomics



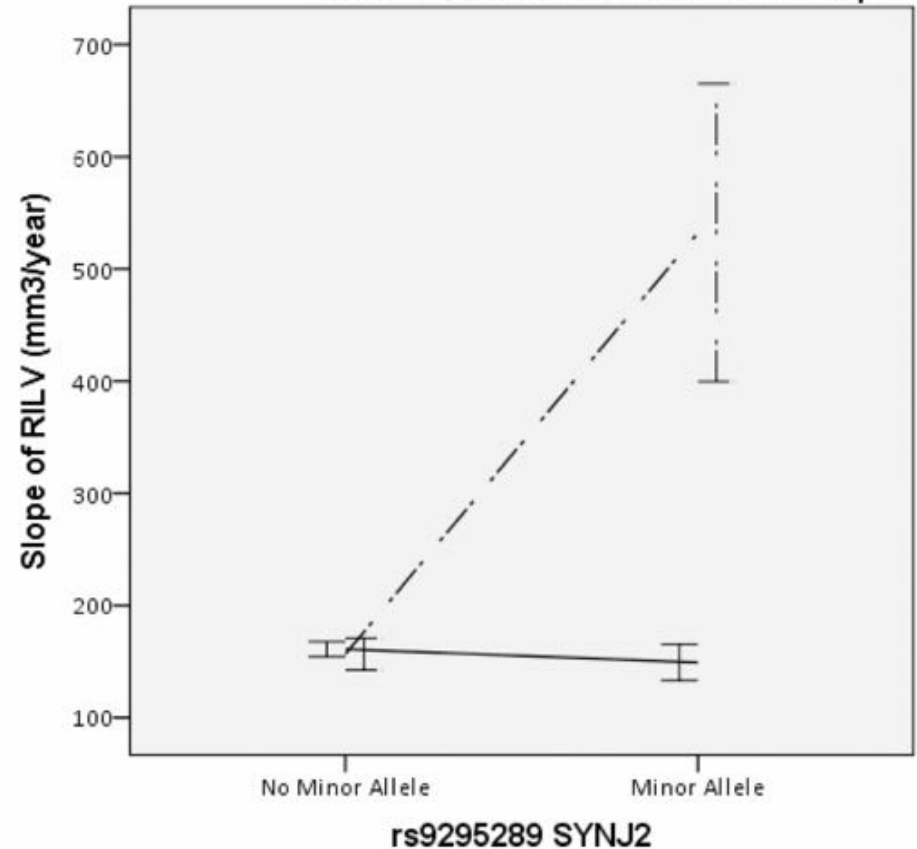
ADNI Genetic Studies: MRI

APC of Hippocampal Volume
Diagnostic Group x ApoE ϵ 4 Genotype



Single gene (APOE)

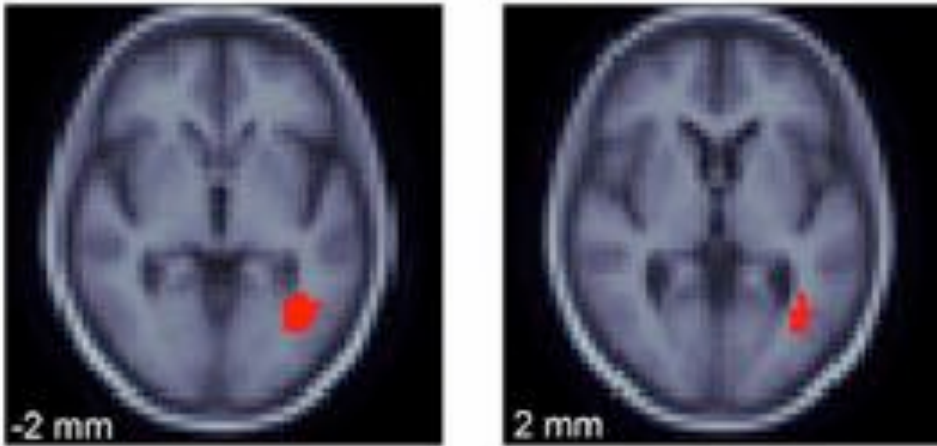
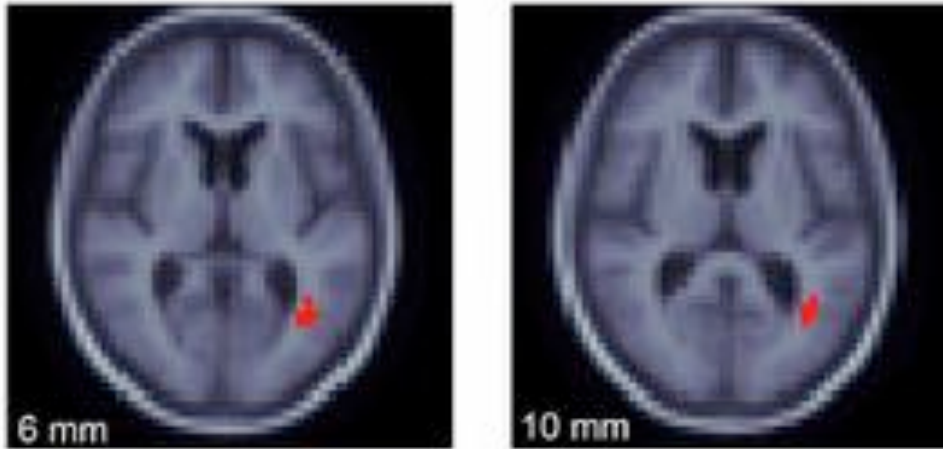
SYNJ2-PI4KA Interaction & RILV Slope



Pathway/Network based
(Ventricle by Inositol-related genes)



ADNI Genetic Studies: MRI



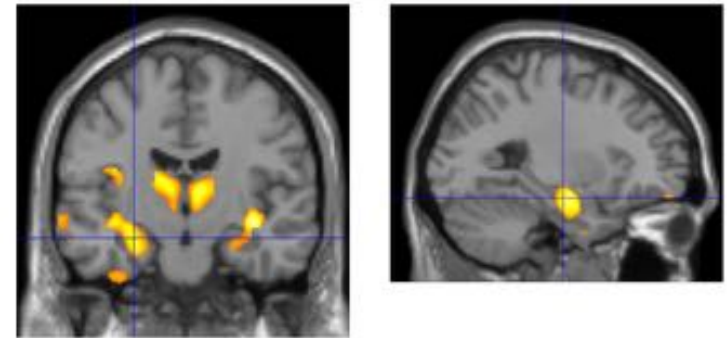
Voxel-wise GWAS

rs713155

rs9610775 (*CARD10*)



A. SurfStat

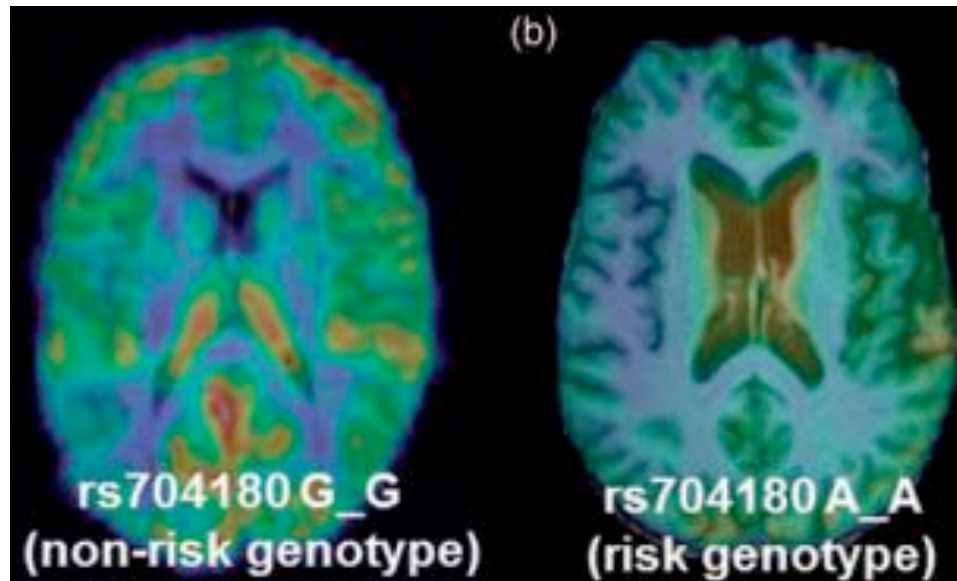


B. VBM

WES in extreme phenotype



ADNI Genetic Studies: Advanced MRI



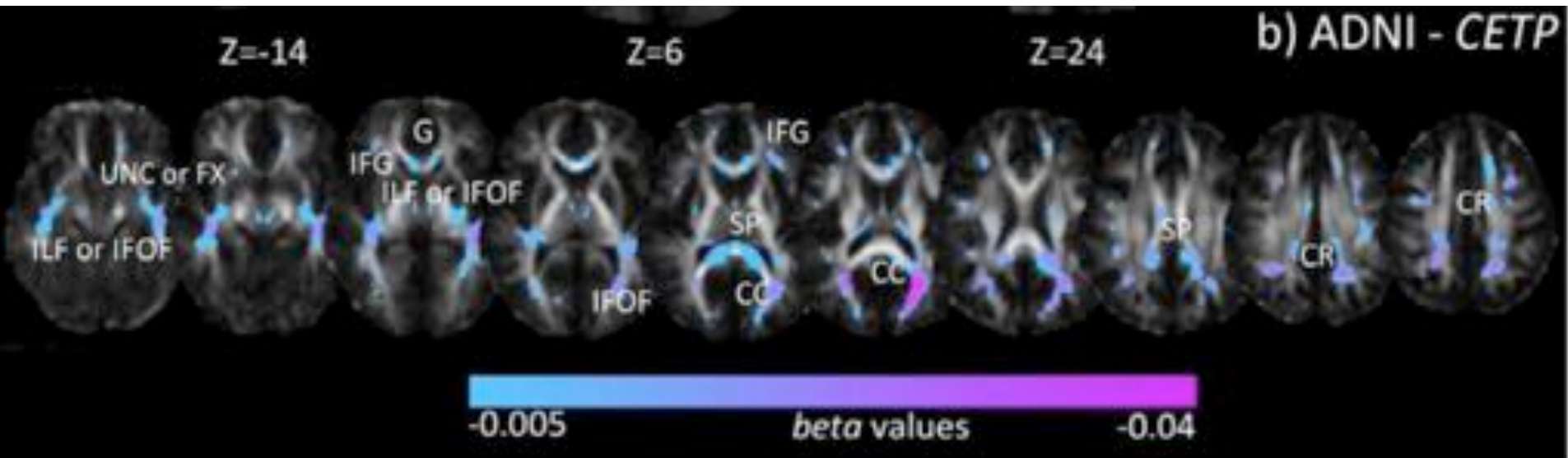
Arteriolo sclerosis gene (ABCC9) - ASL



APOE ϵ 4 carriers – rsfMRI
(\uparrow connectivity of left hippocampus)



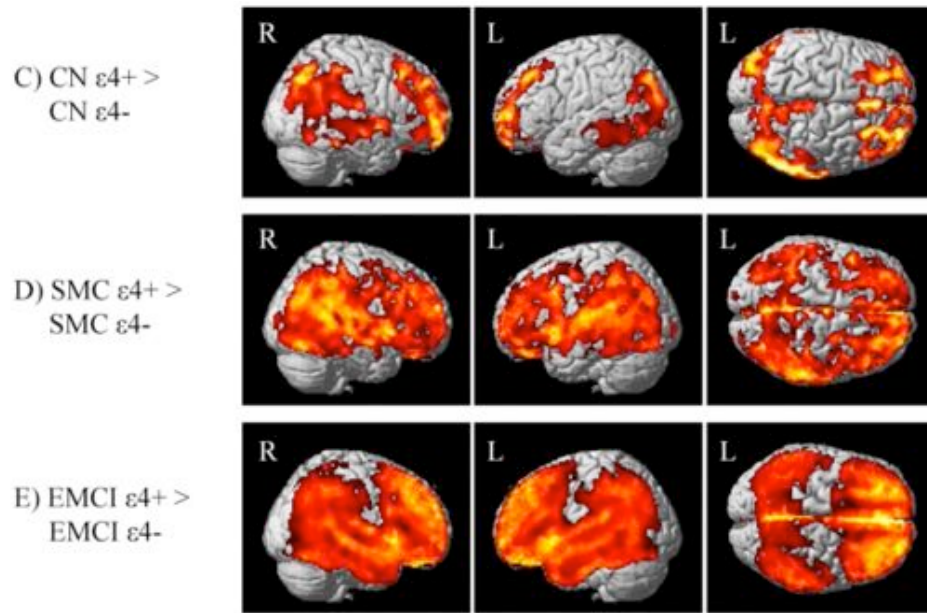
ADNI Genetic Studies: Advanced MRI



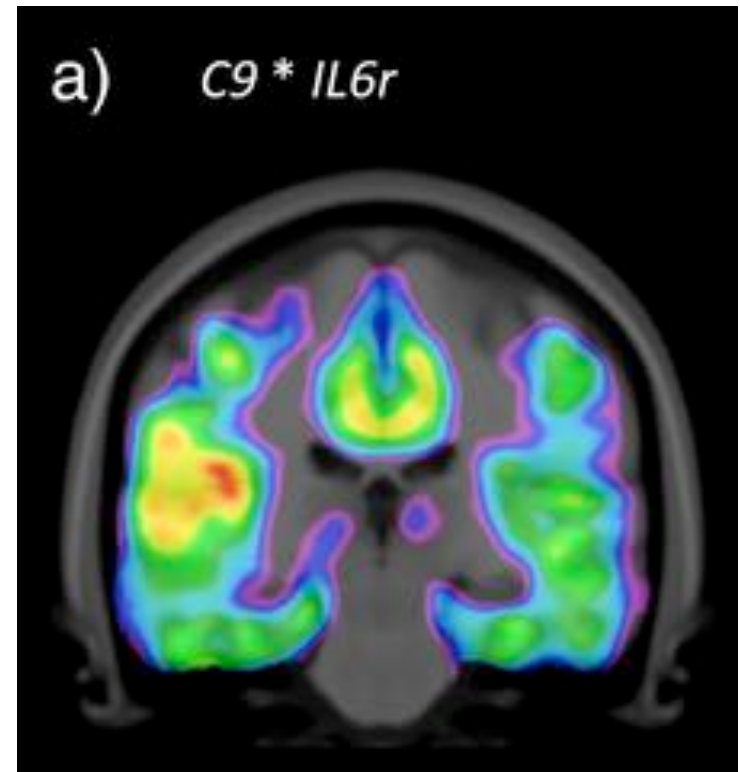
FA on DTI by CETP genotype



ADNI Genetic Studies: Amyloid PET



Single gene – APOE



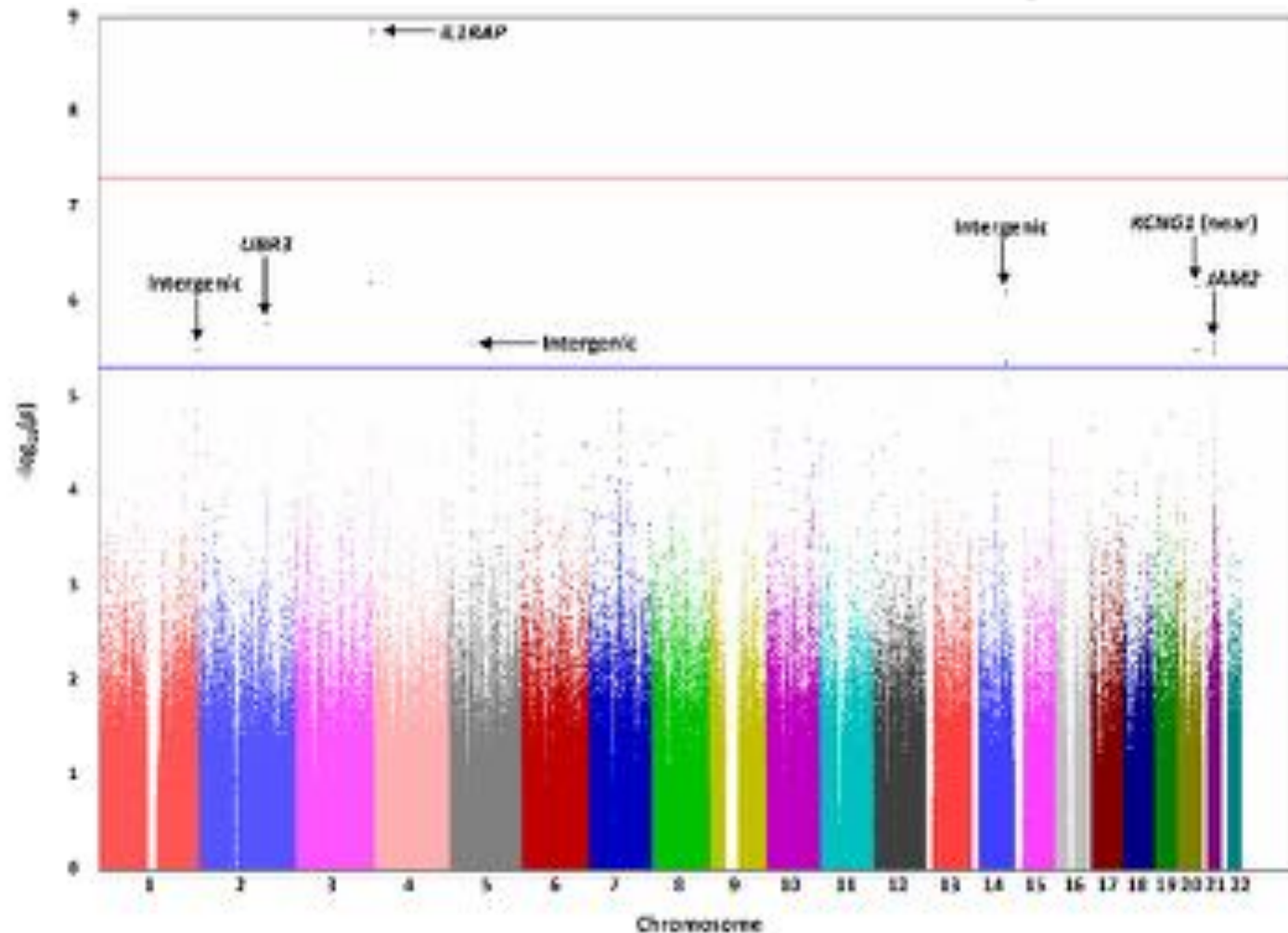
Pathway/Network based
(immune pathway; A β PET)



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Risacher et al. (2015) *Alz & Dementia*
Benedet et al. (2015) *J Neuroinflammation*

ADNI Genetic Studies: Amyloid PET

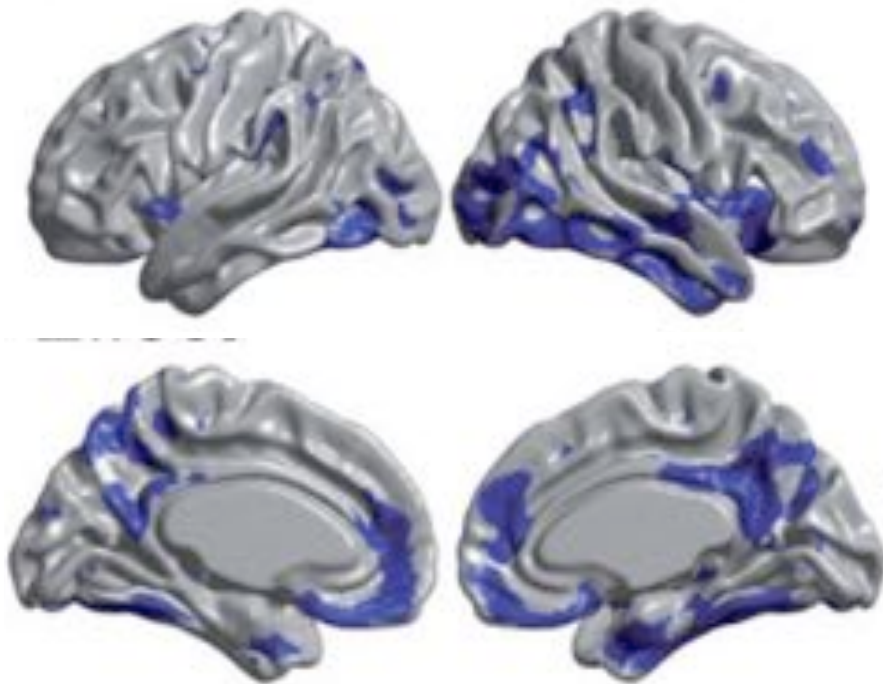


GWAS – longitudinal change in Aβ PET

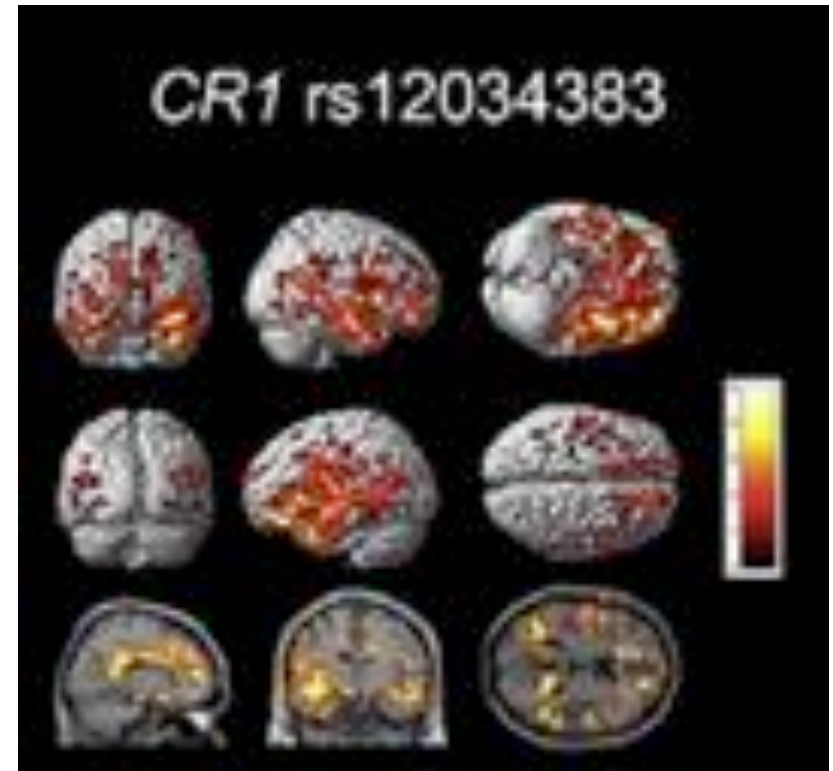


ADNI Genetic Studies: FDG PET

APOE ϵ 4 Effect



Single gene - APOE



AD risk genes -
Pathway/Network based



ADNI Genetic Studies

For more information and a more comprehensive summary of papers see:

Saykin et al. (2015) Genetic Studies of Quantitative MCI and AD Phenotypes in ADNI: Progress, Opportunities, and Plans. *Alzheimer's & Dementia*, 11(7): 792–814.

Shen et al. (2014) Genetic analysis of quantitative phenotypes in AD and MCI: imaging, cognition and biomarkers. *Brain Imaging & Behavior*, 8(2): 183-207.



Summary

- ADNI cross-sectional and longitudinal phenotypes provide an exceptional test-bed for many types of studies
- Numerous genetic studies in the ADNI dataset have been performed to date. However, a number of phenotypes, particularly those released most recently (advanced MRI, tau PET), have yet to be explored.
- More data will soon become available in ADNI-3.



Seeking Computational Neuroscience Post-Docs for Multi-Modality Imaging & Multi-omics Bioinformatics



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