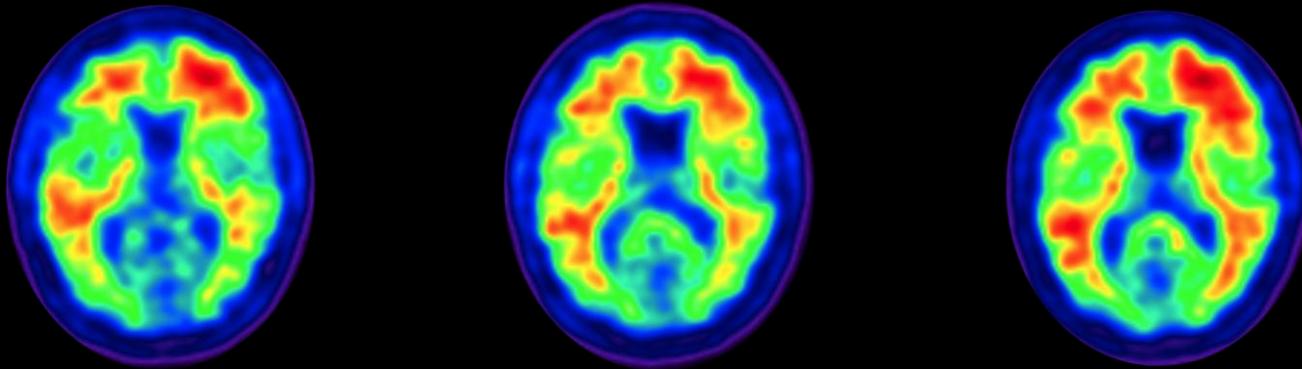


Amyloid, Glucose Metabolism, and Longitudinal Change

Susan Landau



Helen Wills Neuroscience Institute
University of California, Berkeley

Lawrence Berkeley National Lab

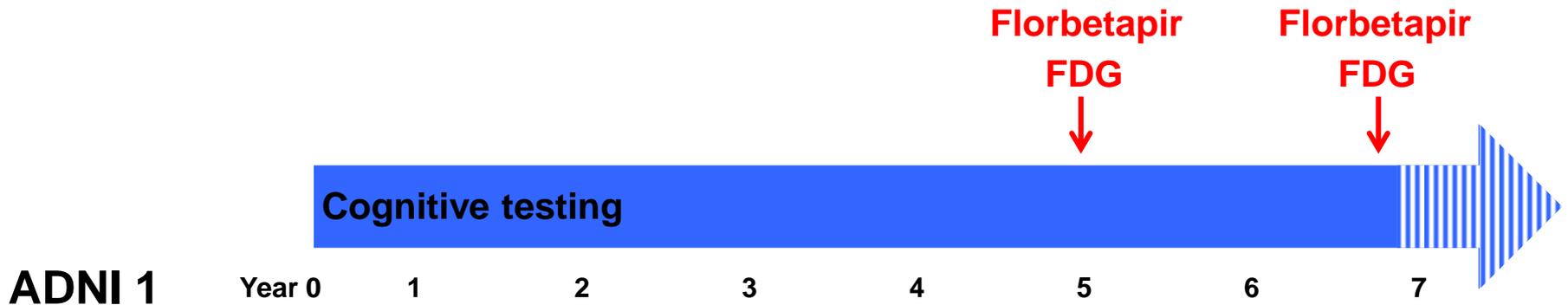


Disclosures

Biogen

Synarc

ADNI timeline



How are florbetapir & FDG status related to longitudinal cognitive decline?



What is the relationship between longitudinal florbetapir and FDG measurements?

Methods

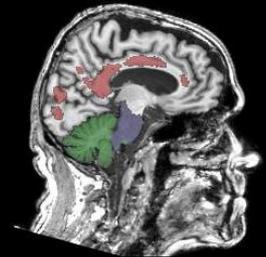
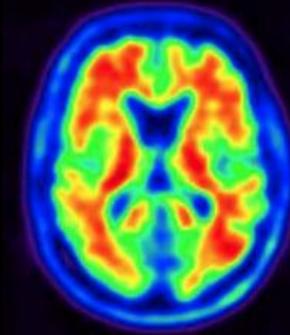
ADNI 1/GO/2 subjects (Normal, Early MCI, Late MCI, AD)

ADNI 1: Up to 9 years of cognitive followup, concurrent FDG & florbetapir

ADNI GO/2: Baseline and 2-year florbetapir & FDG scans

Florbetapir

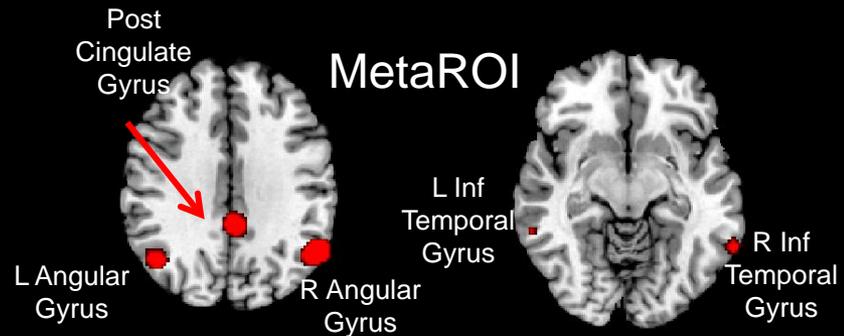
Cortical retention across Freesurfer-defined temporal, parietal, cingulate, frontal regions (composite reference)



composite reference region

FDG

AD-specific MetaROI (pons/vermis reference)



Landau et al. Neurobiol of Aging 2009

Cognitive

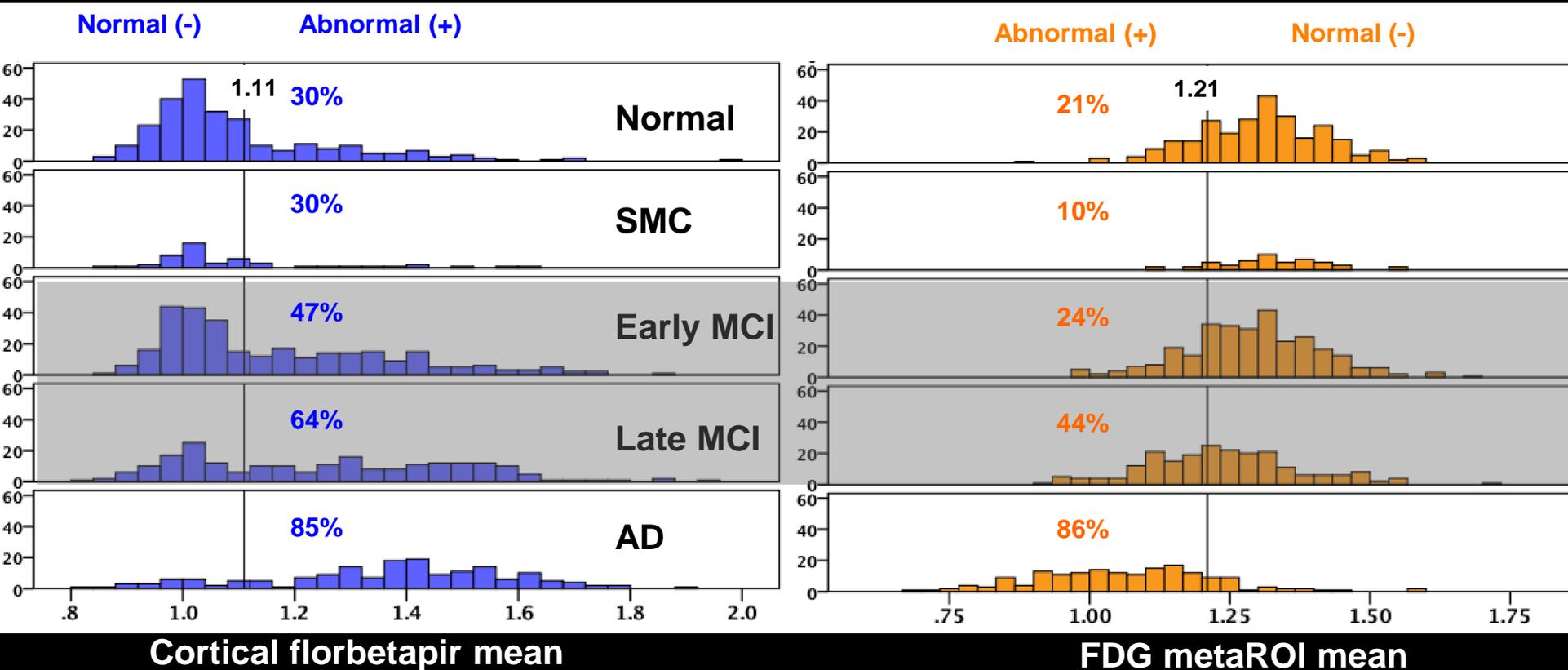
ADAS-cog, AVLT free recall

Longitudinal associations: Mixed effects regression

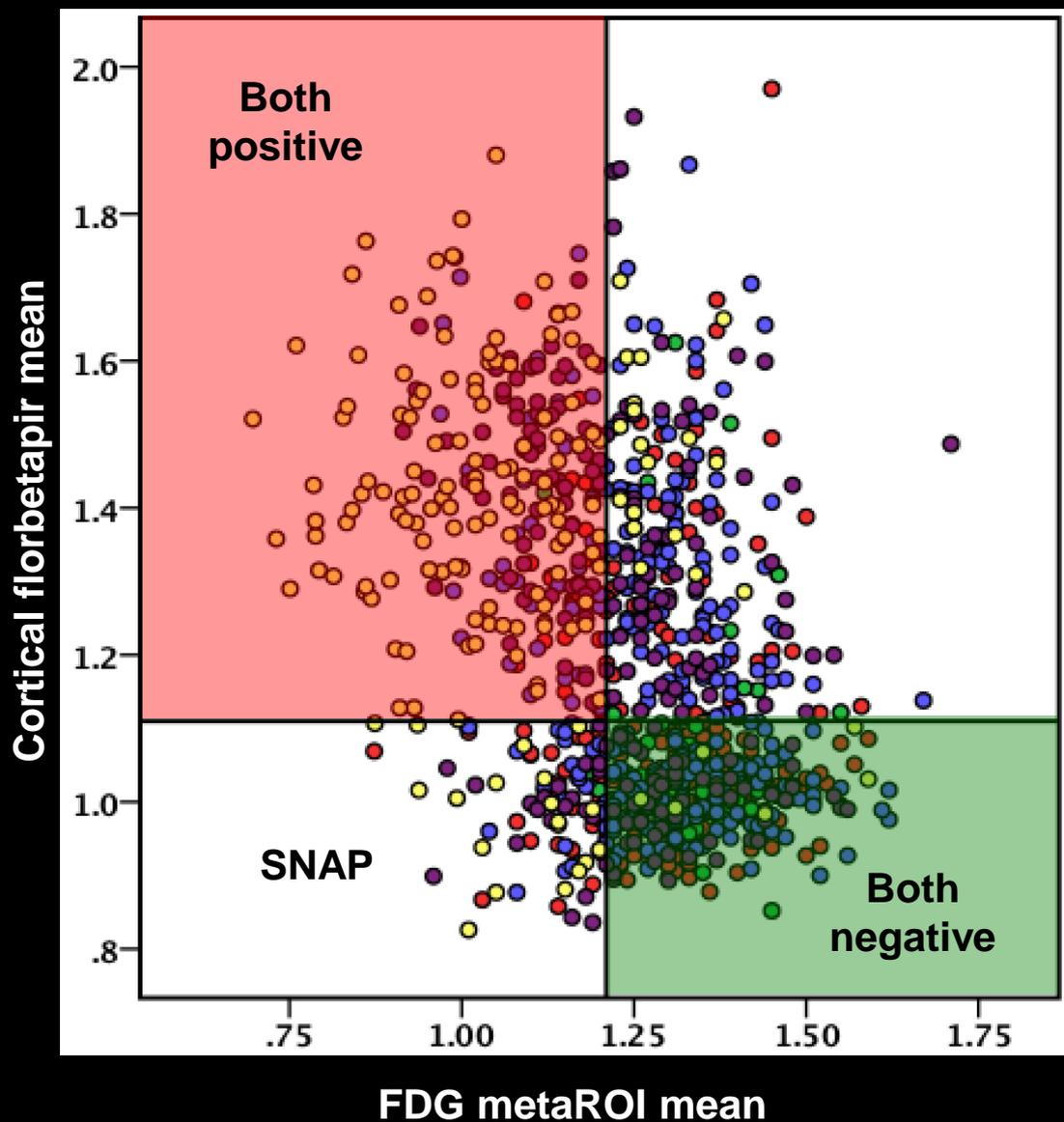
Amyloid and hypometabolism in ADNI

Florbetapir

FDG

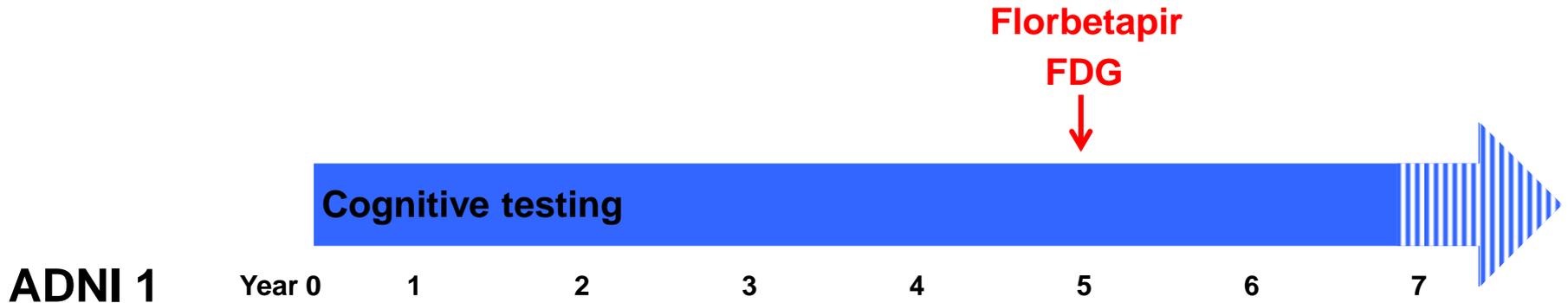


Agreement between florbetapir and FDG



	N	p-value
Normal	265	0.05
Subj Mem Compl	50	ns
Early MCI	299	0.003
Late MCI	217	<0.001
AD	171	ns
Total	1002	

ADNI timeline



ADNI 1

Year 0

1

2

3

4

5

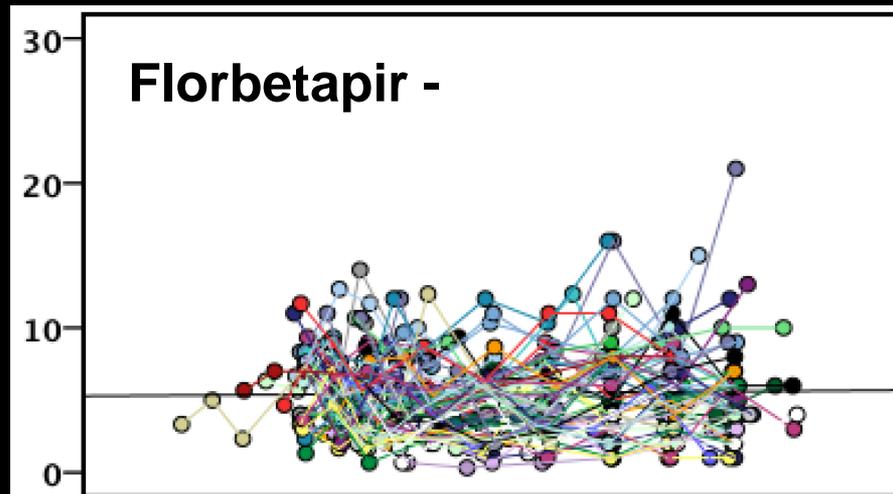
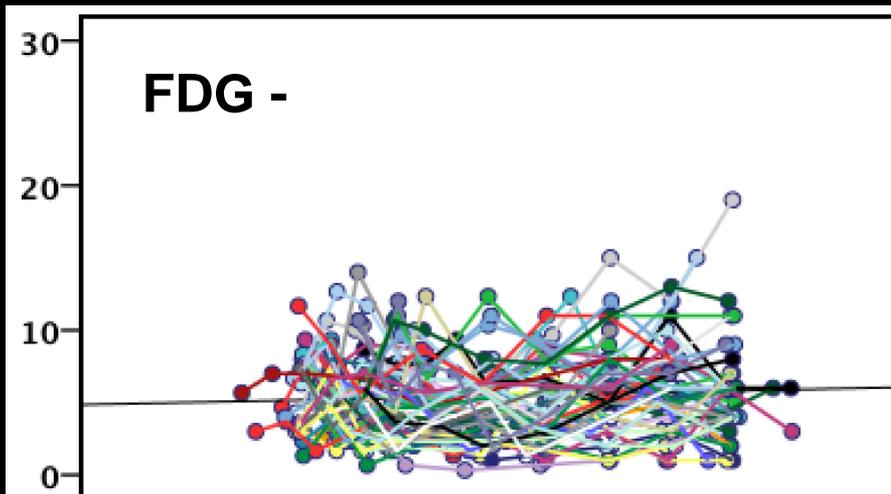
6

7

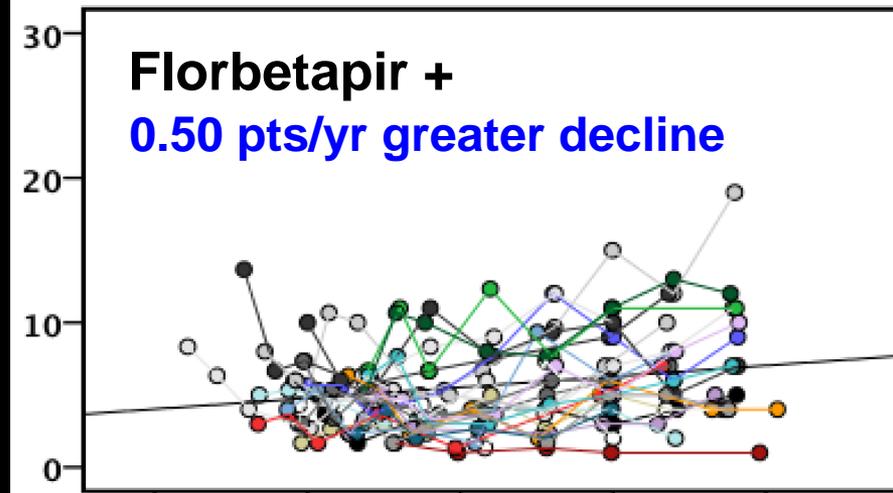
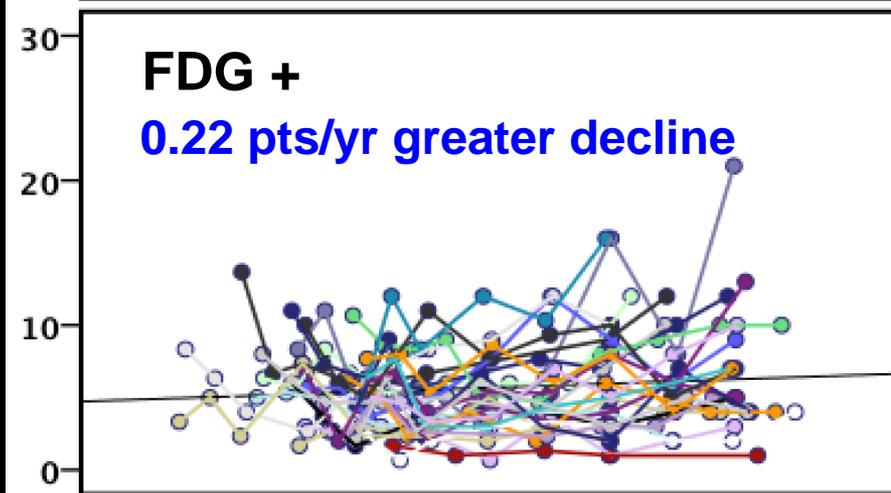
How are florbetapir & FDG status related to longitudinal cognitive decline?

Normals N=90

ADAS-cog



ADAS-cog

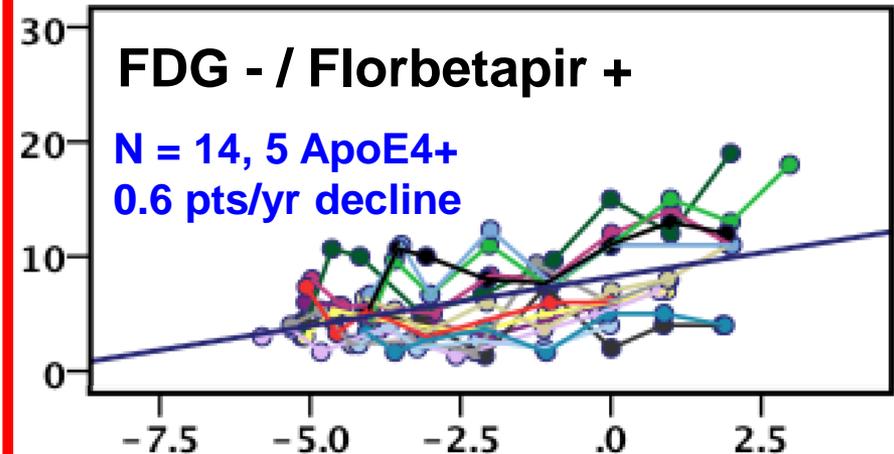
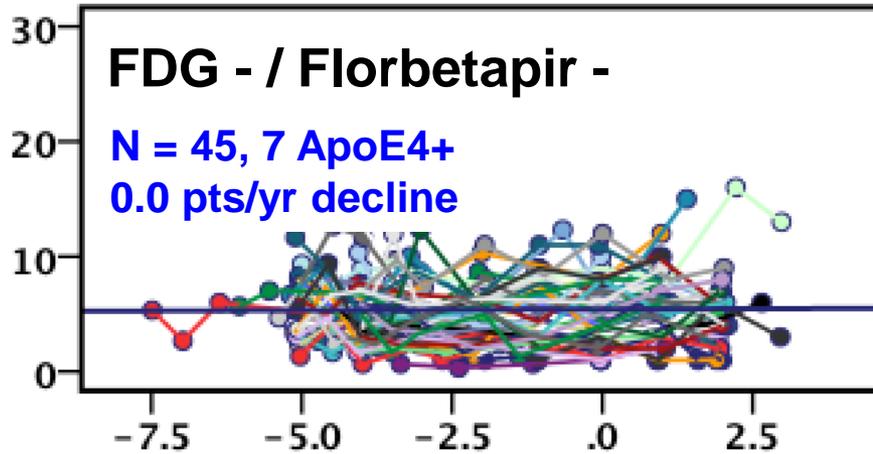


Time (yrs) relative to scan

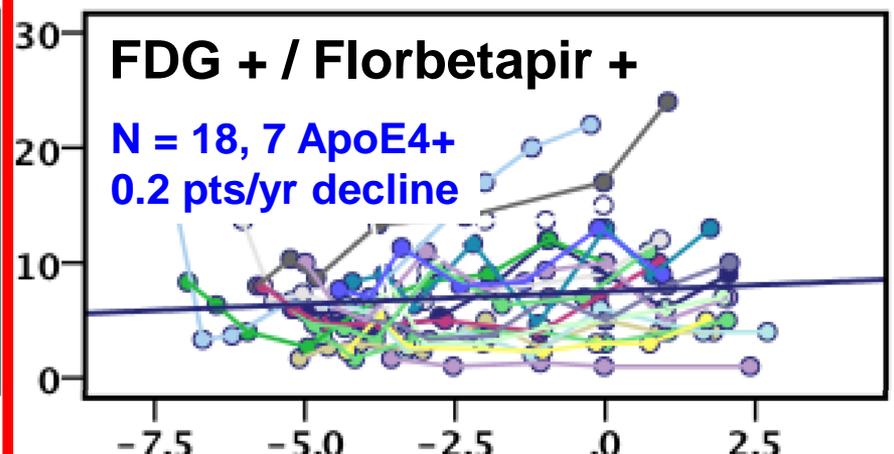
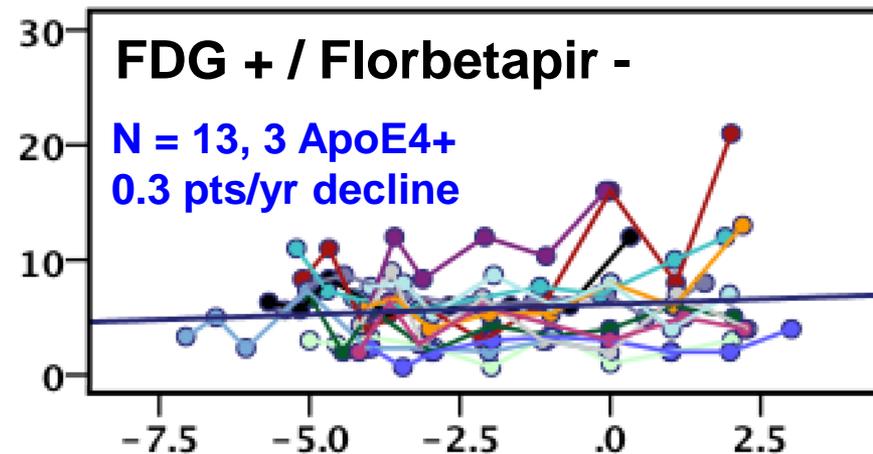
Time (yrs) relative to scan

Normals N=90

ADAS-cog



ADAS-cog

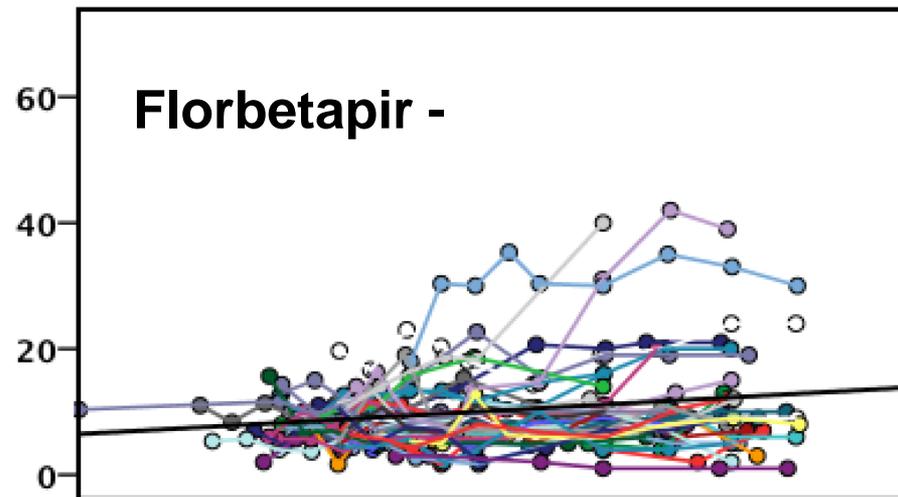
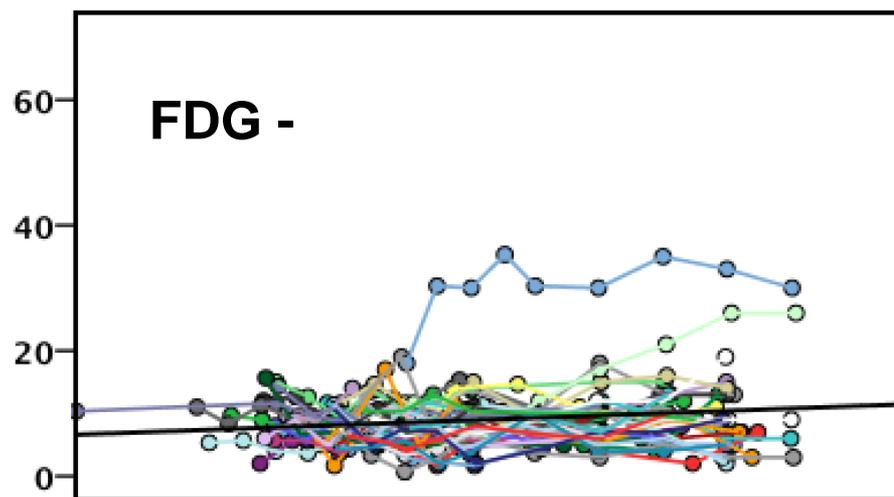


Time (yrs) relative to scan

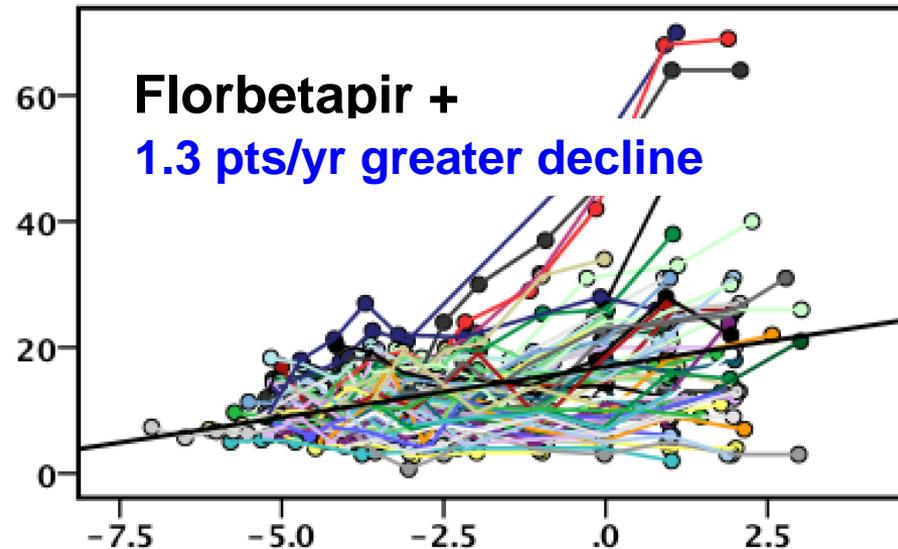
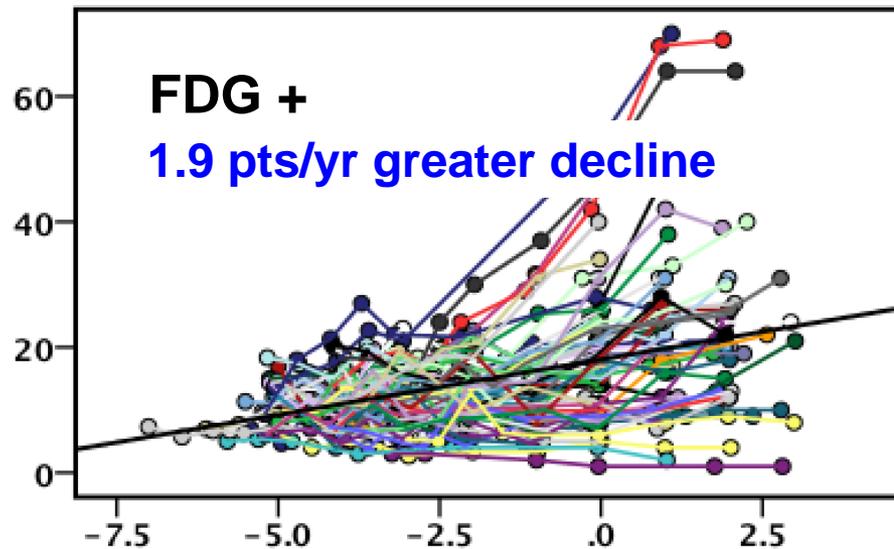
Time (yrs) relative to scan

MCI N=99

ADAS-cog



ADAS-cog

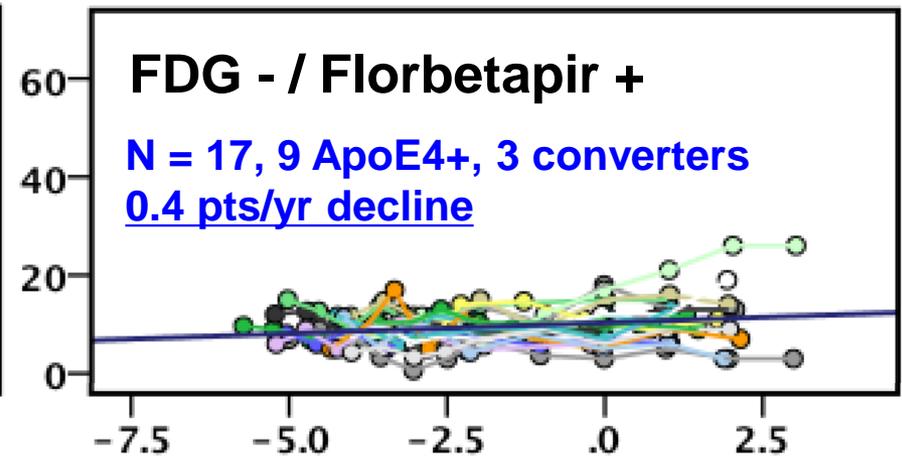
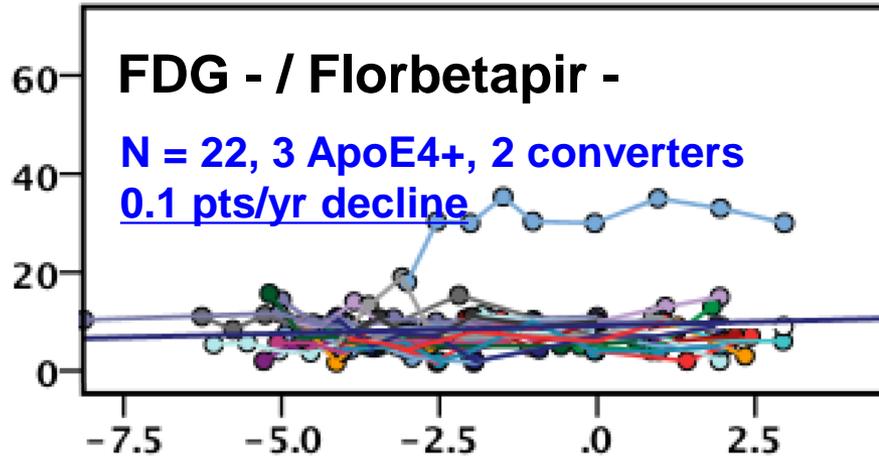


Time (yrs) relative to scan

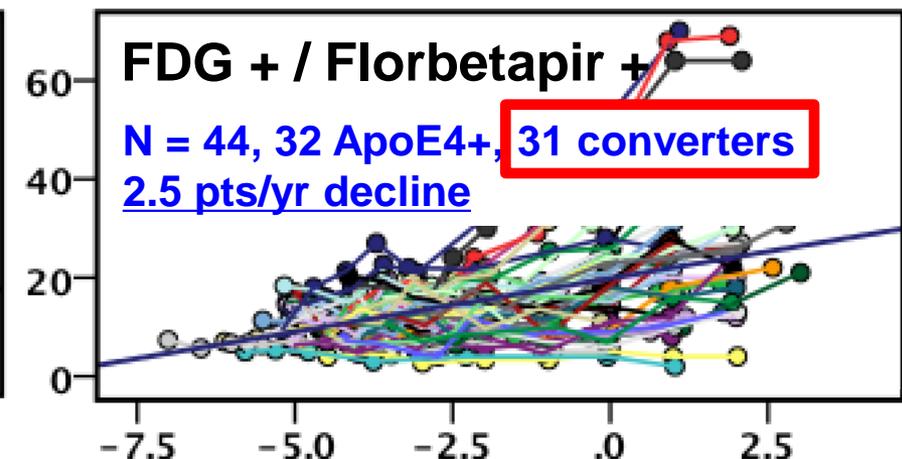
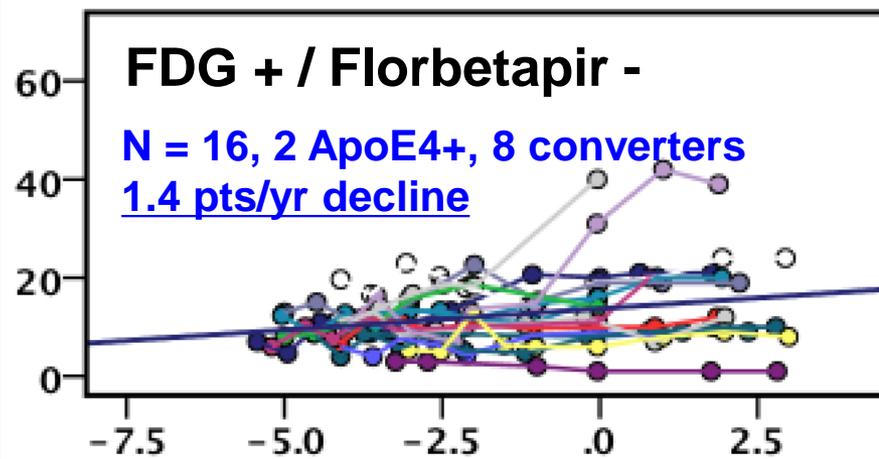
Time (yrs) relative to scan

MCI N=99

ADAS-cog



ADAS-cog



Time (yrs) relative to scan

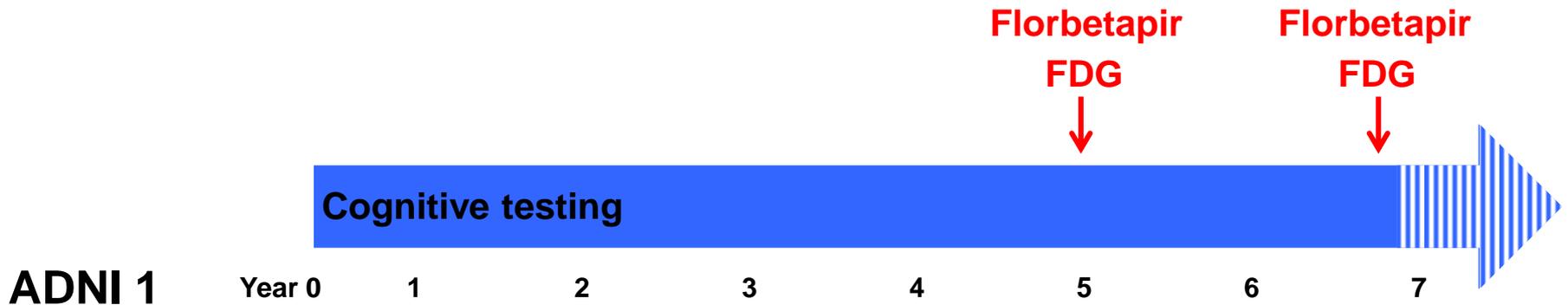
Time (yrs) relative to scan

So far

Normal aging → Amyloid+ status linked to decline
MCI → FDG+ status linked to decline

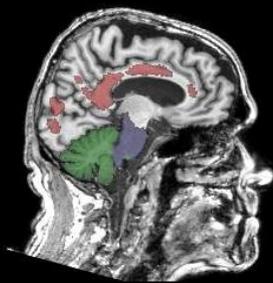
In MCI, combining amyloid and FDG tells us more about progression than either marker individually

ADNI timeline

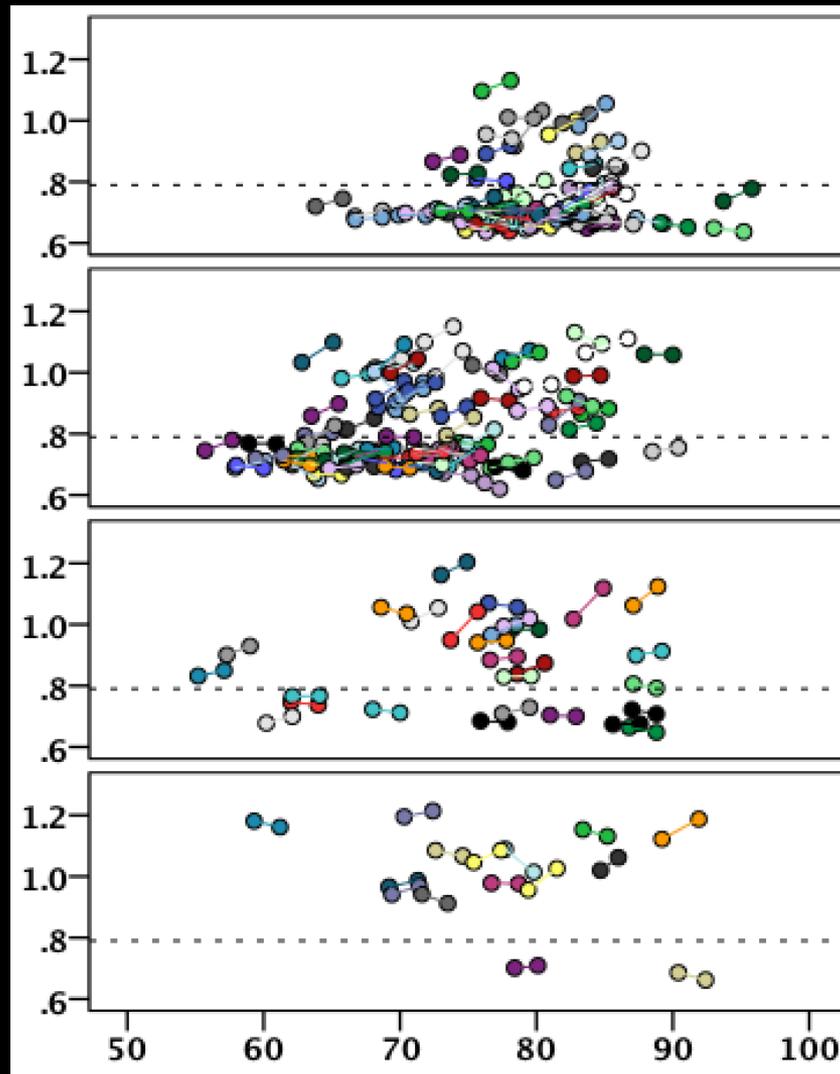


What is the relationship between longitudinal florbetapir and FDG measurements?

Florbetapir change over 2 years



Cortical SUVR
(composite ref)



Normal
N=68

Early MCI
N=84

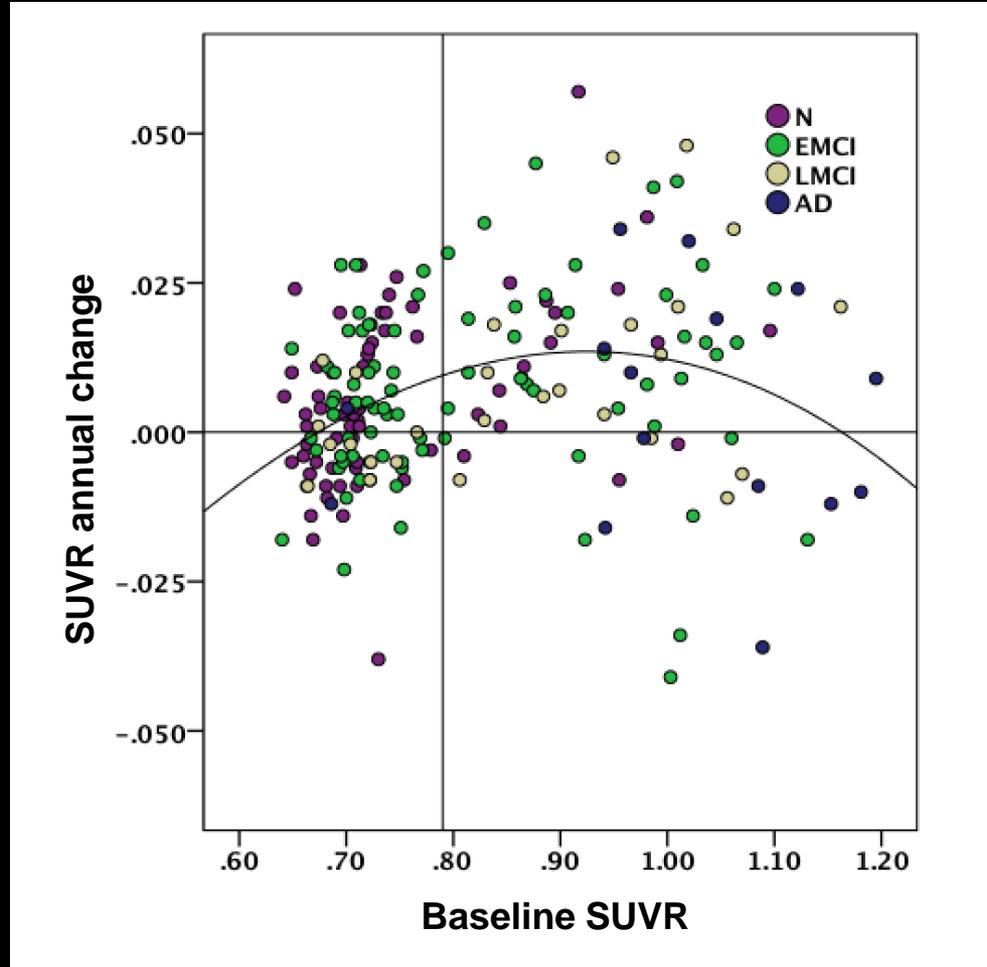
Late MCI
N=28

AD
N=15

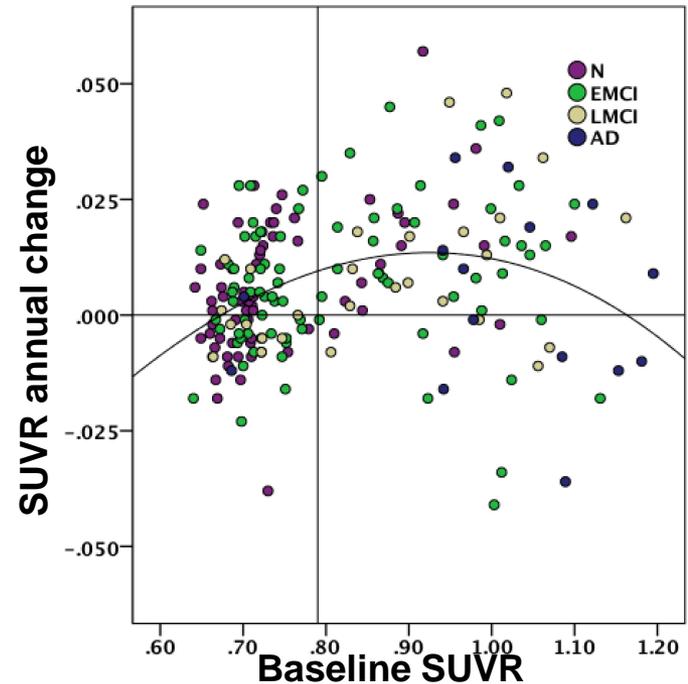
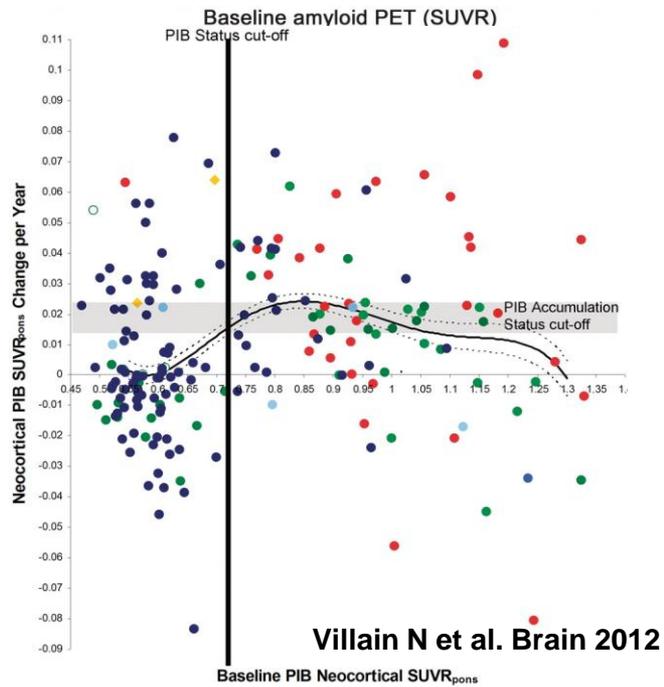
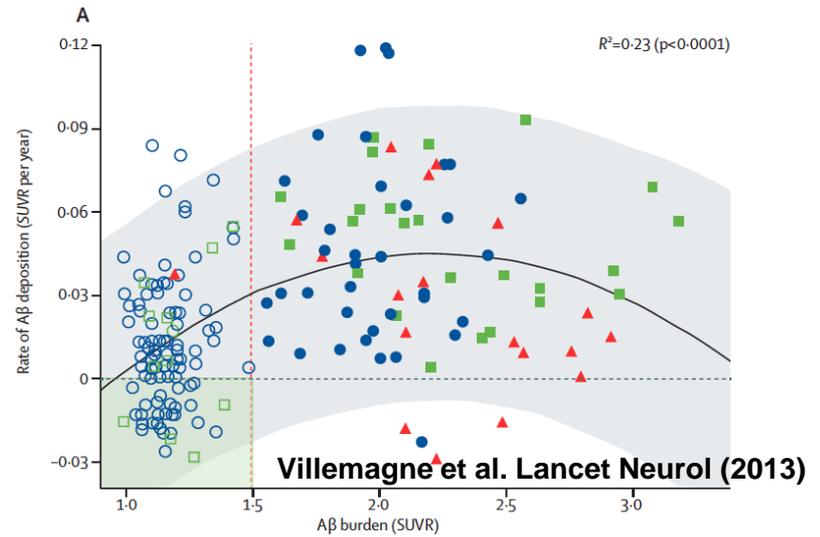
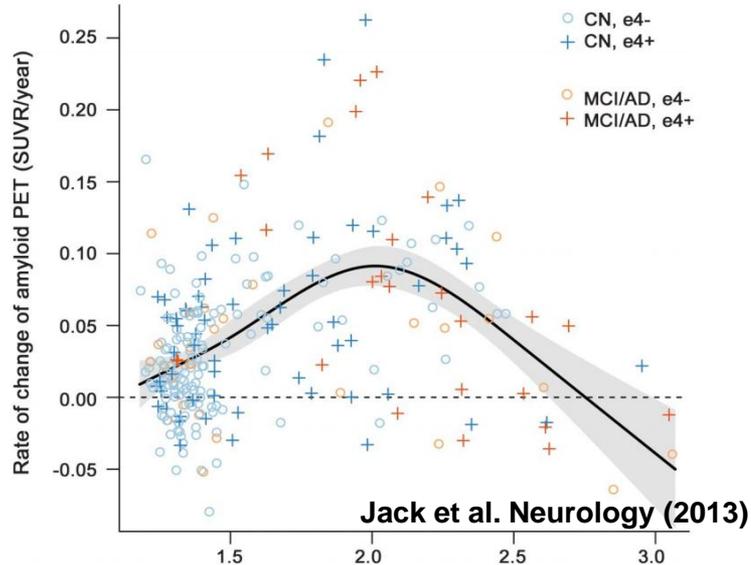
Total N = 195

Age

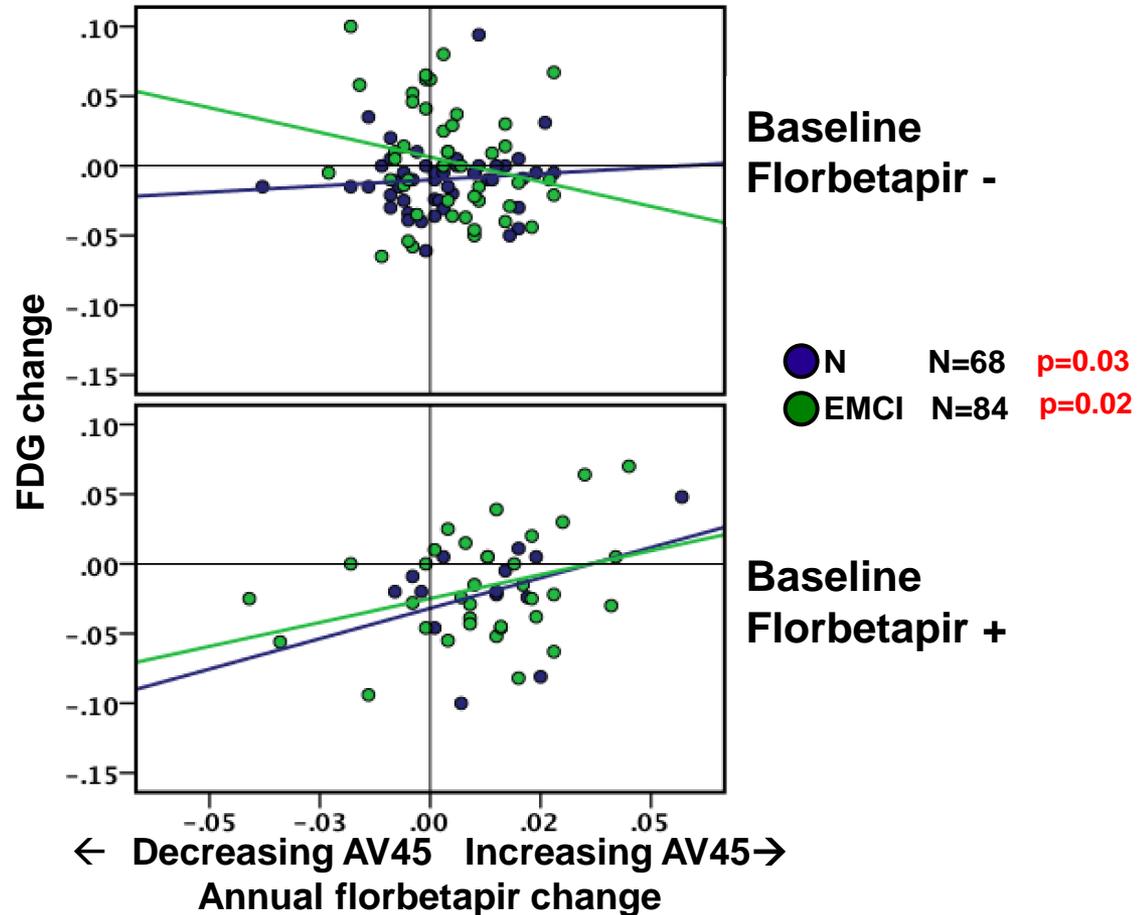
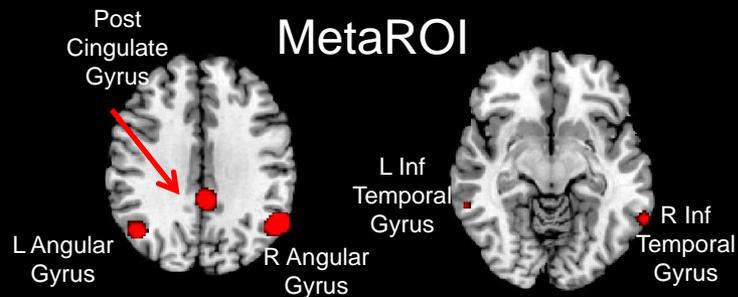
Amyloid change N=195



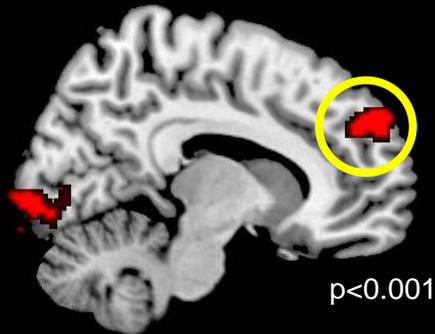
Amyloid change



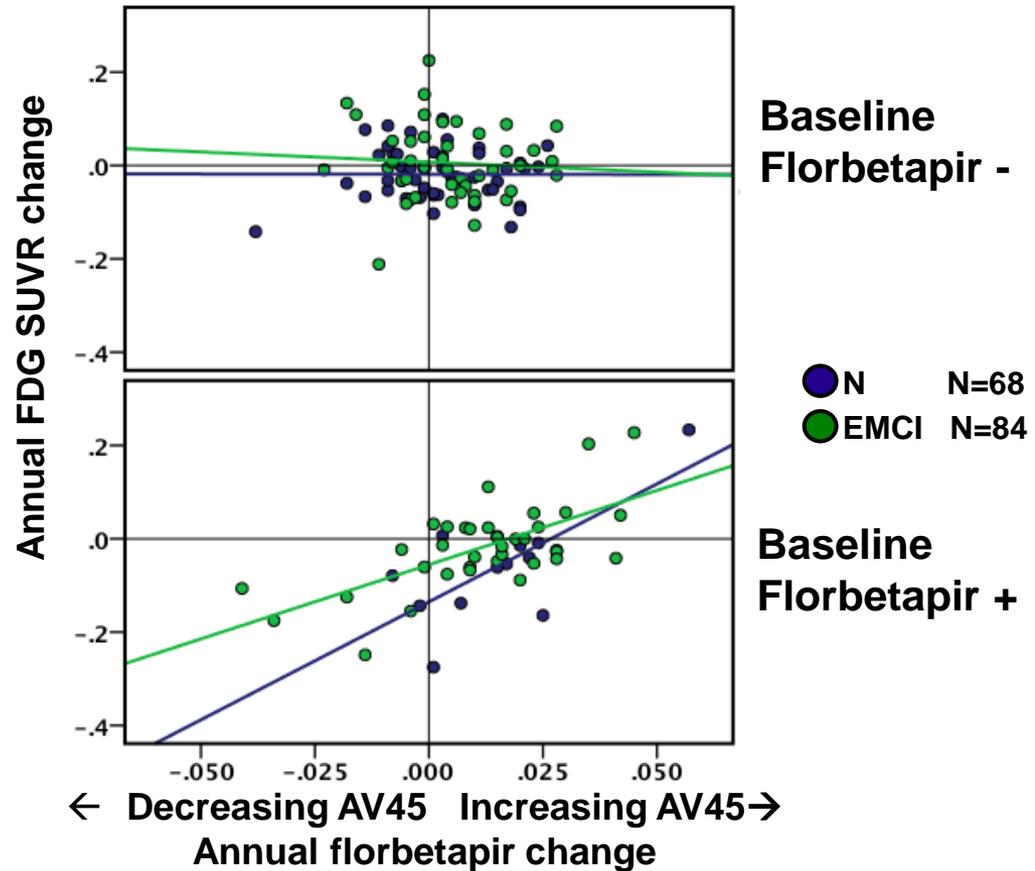
Longitudinal florbetapir and glucose metabolism



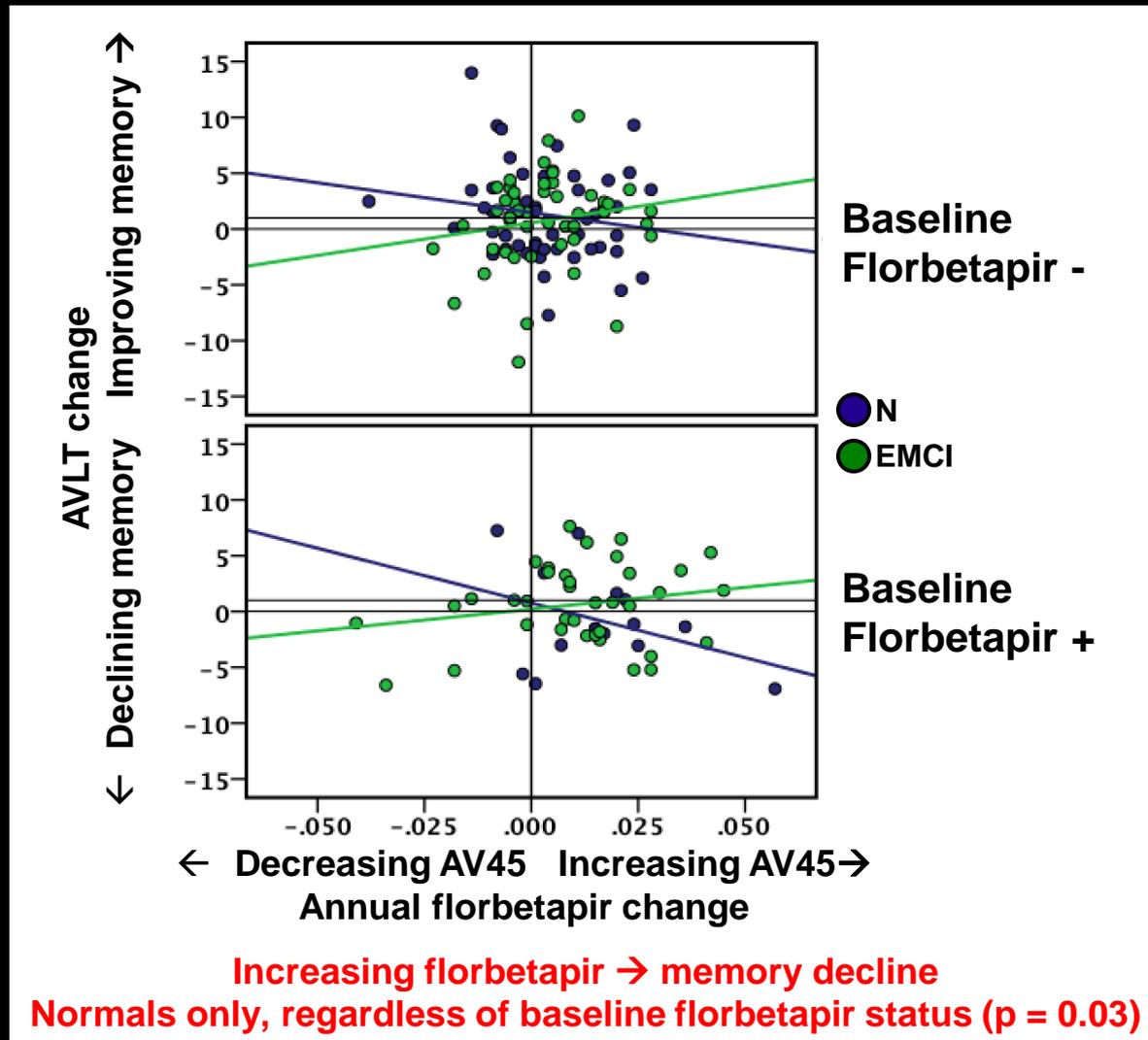
Longitudinal florbetapir and glucose metabolism



Voxelwise SPM analysis:
Baseline florbetapir +/-
X florbetapir change



Longitudinal florbetapir and episodic memory change



Summary

Cognitive decline in normal aging linked to amyloid status, decline in MCI linked to FDG

Increasing florbetapir is related to increasing FDG in normal aging and early MCI; Normals also experience memory decline

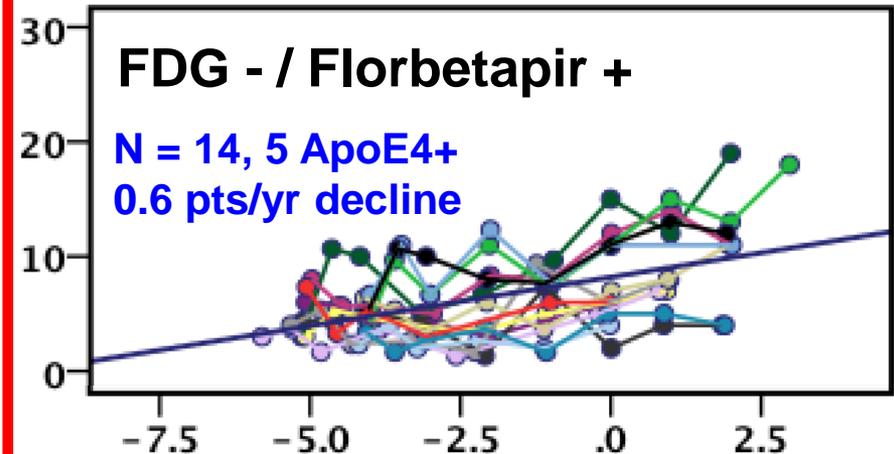
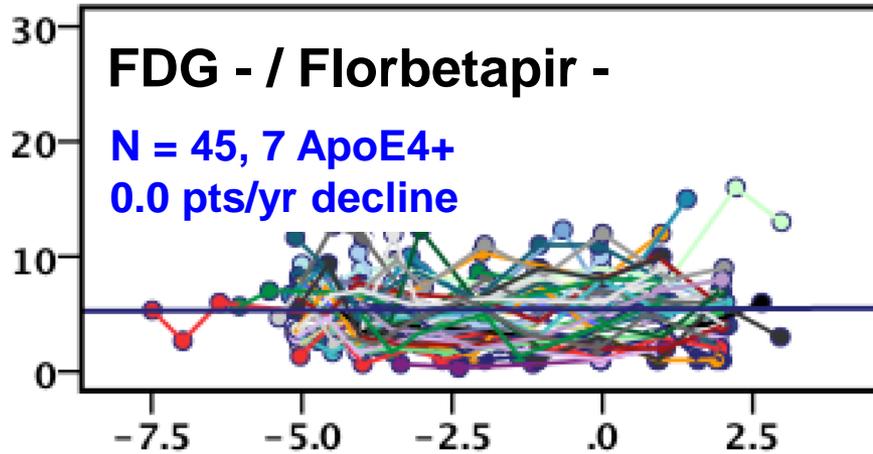
Hypermetabolism related to amyloid and AD development has been reported previously in cross-sectional studies, may be compensatory (Cohen et al 2009, Oh et al 2012, Ossenkoppele et al 2013, Benzinger et al 2013)

Timing of hypermetabolism relative to other biomarker changes is unclear

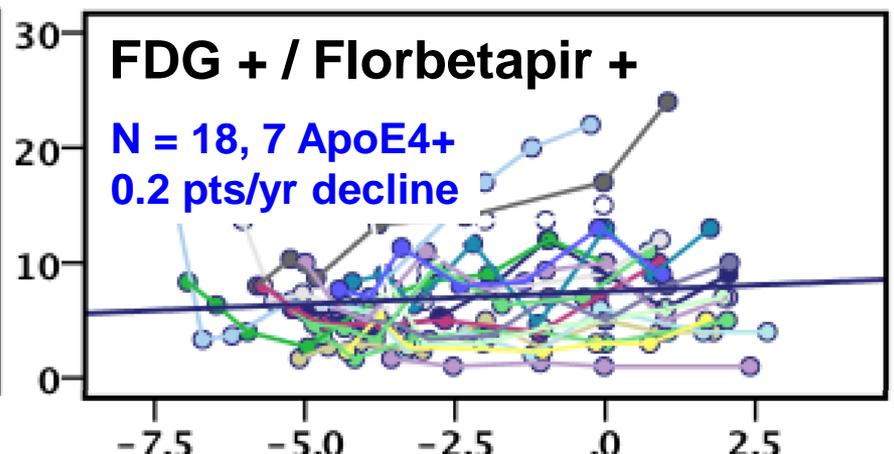
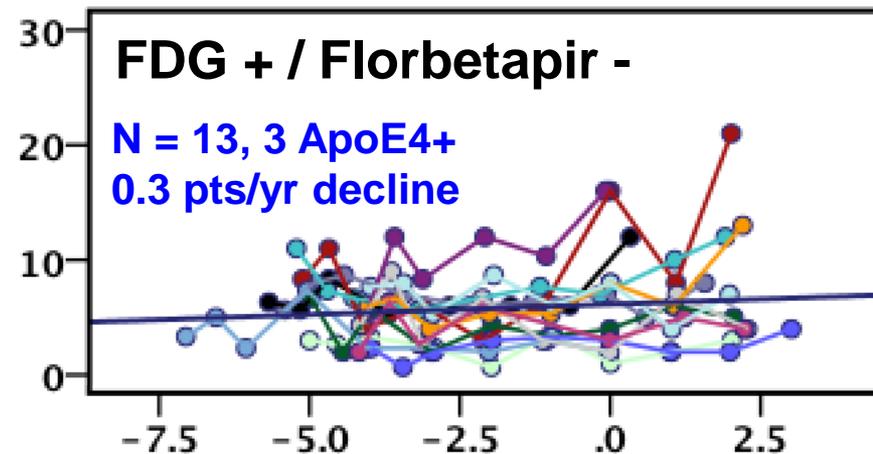
Bidirectional FDG changes may complicate detection of metabolic abnormalities early in disease

Normals N=90

ADAS-cog



ADAS-cog



Time (yrs) relative to scan

Time (yrs) relative to scan

Thank you

ADNI

ADNI participants & staff

Michael Weiner
Bob Koeppe
Eric Reiman
Kewei Chen
Norman Foster
Danielle Harvey
Les Shaw
John Trojanowski
Laurel Beckett
Cliff Jack

Chet Mathis
Andrew Saykin
Ron Petersen
Michael Donohue
Anthony Gamst
Art Toga
Karen Crawford
Paul Aisen

UC Berkeley

Bill Jagust

Suzanne Baker
Allison Fero
Cindee Madison

