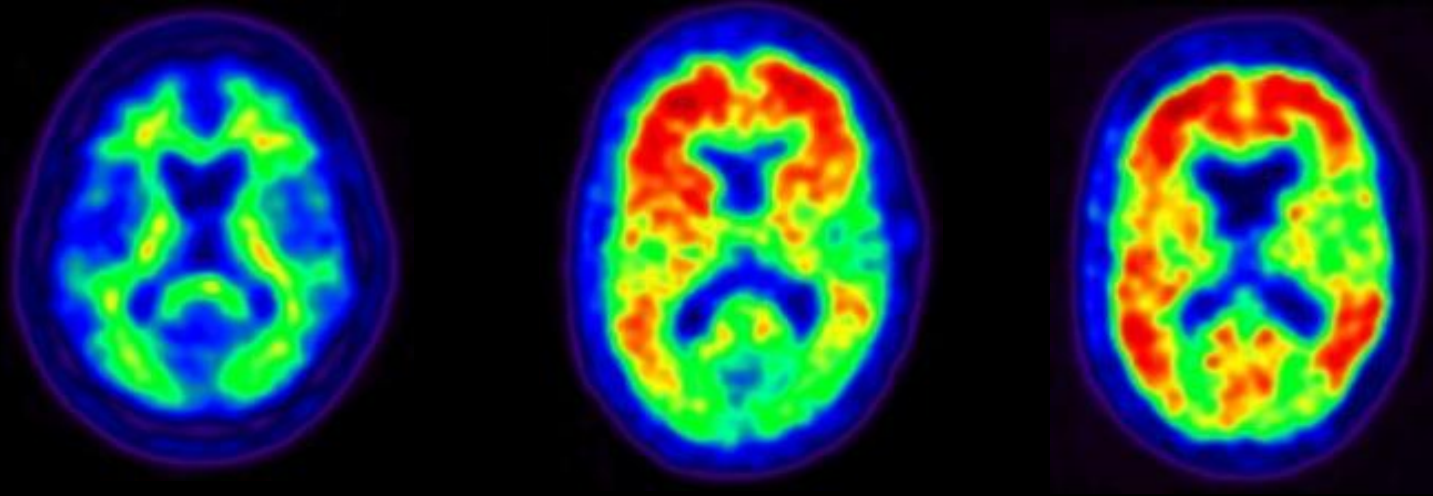


Understanding biomarker relationships in Alzheimer's disease: The ADNI experience

Susan Landau



The Alzheimer's disease neuroimaging initiative



Helen Wills Neuroscience Institute
University of California, Berkeley

Lawrence Berkeley National Lab



Disclosures

Synarc

Biogen

Genentech

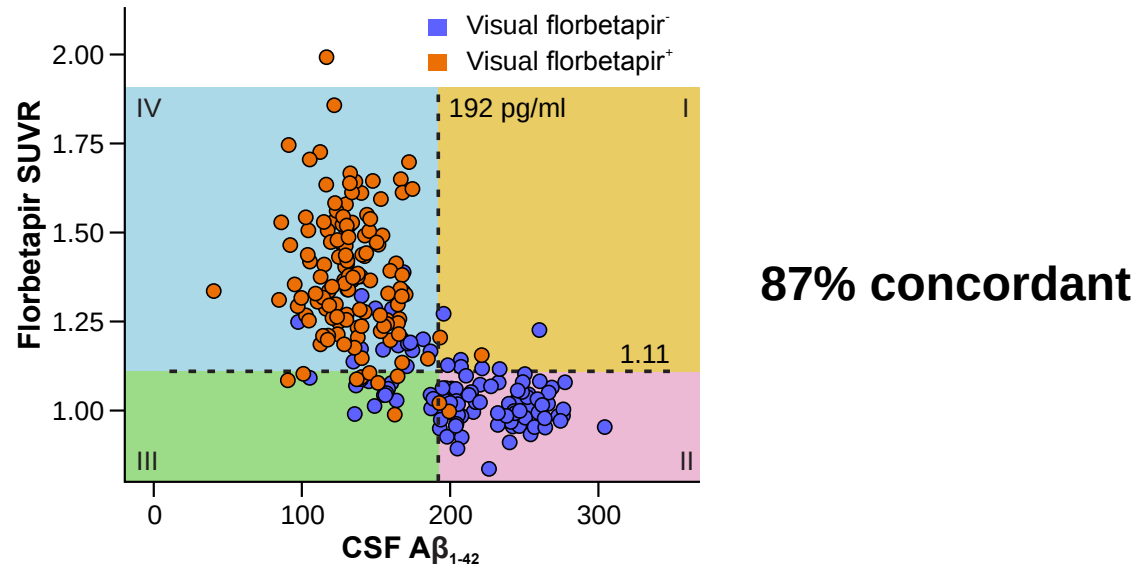
Goals

Define relationships between quantitative and qualitative florbetapir-PET, and CSF A β

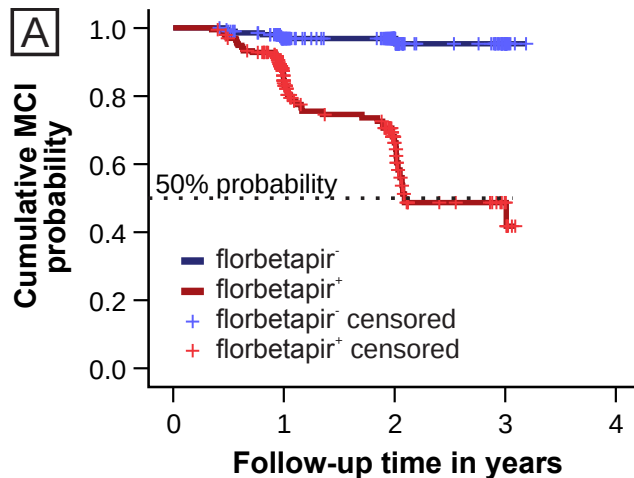
Examine longitudinal A β and cognitive relationships

Amyloid negative status in clinically-diagnosed AD and MCI

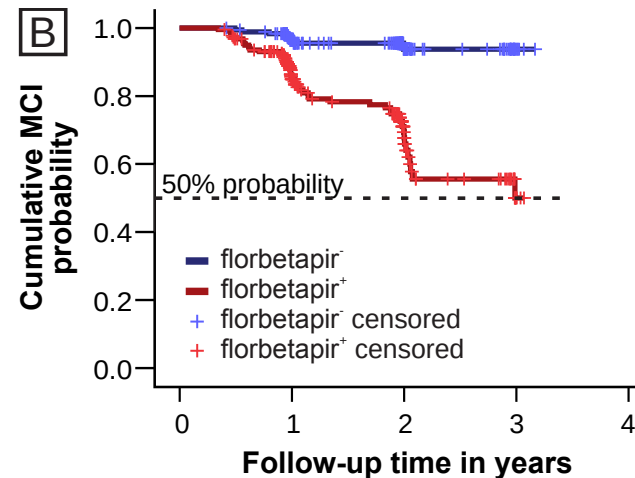
Visual and quantitative florbetapir agreement



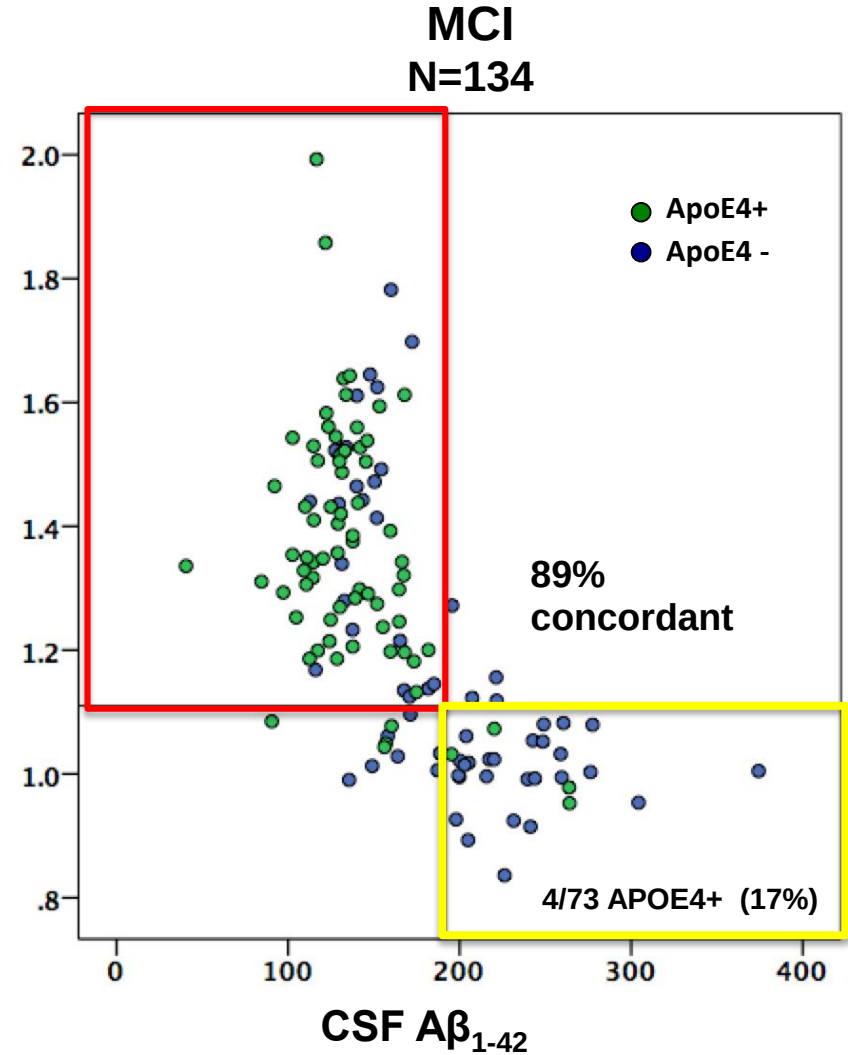
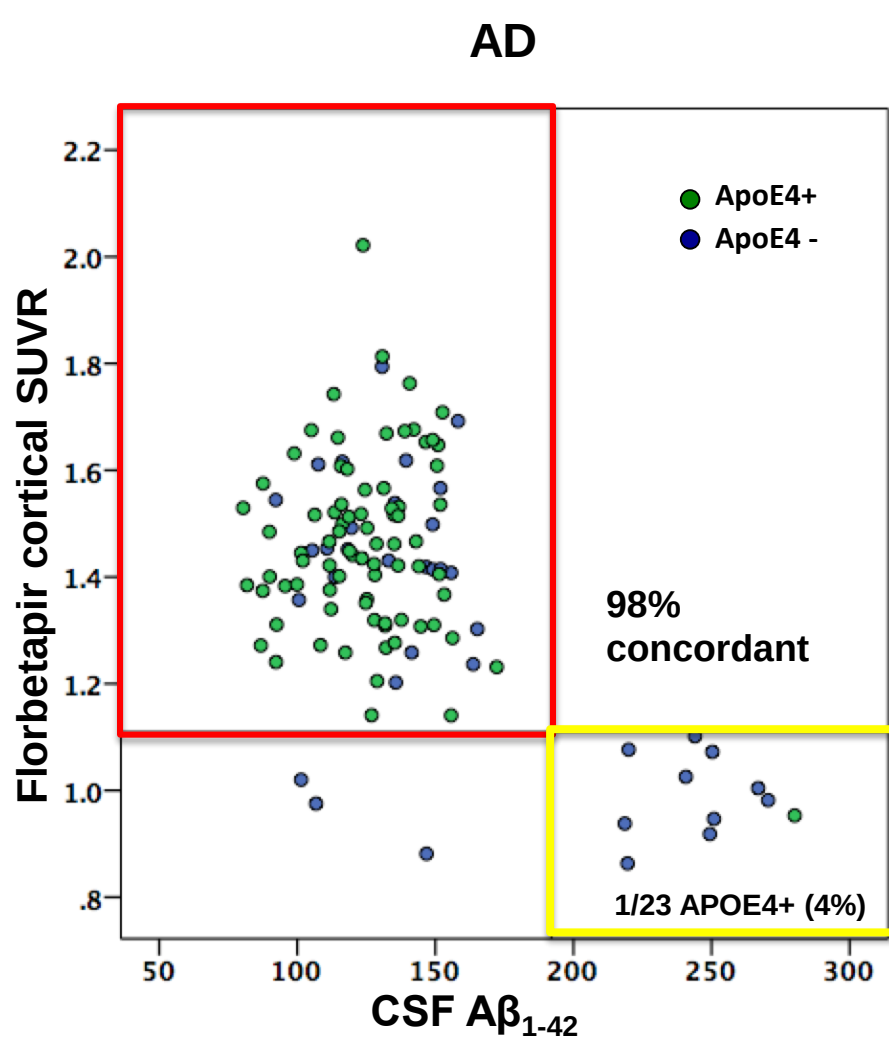
Visual



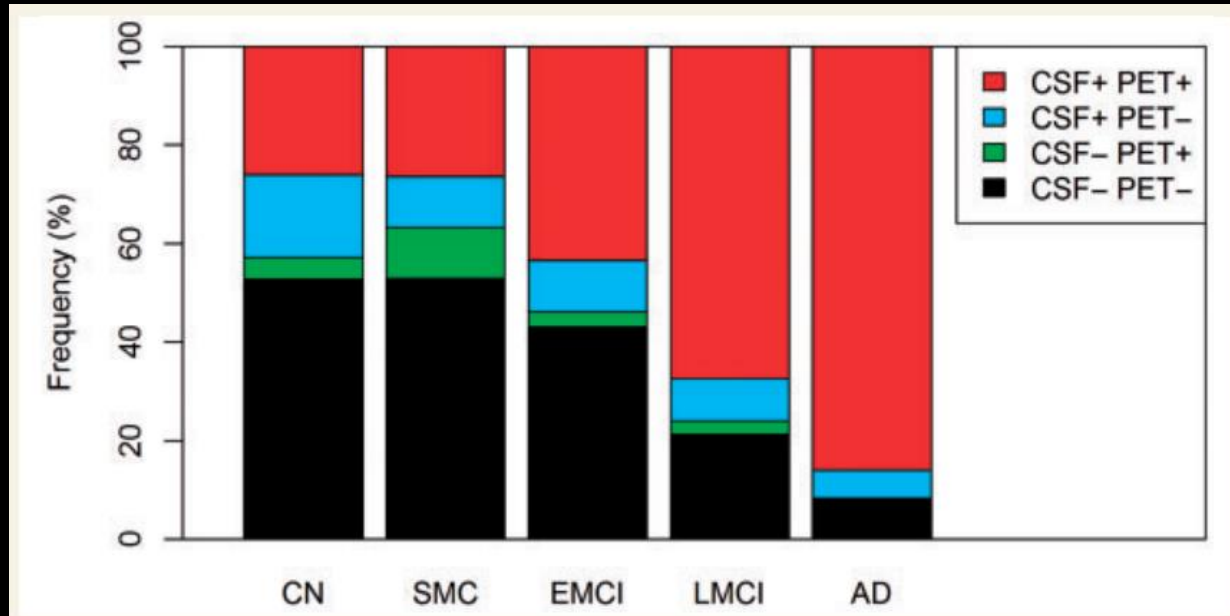
Quantitative



Florbetapir and CSF A β agreement

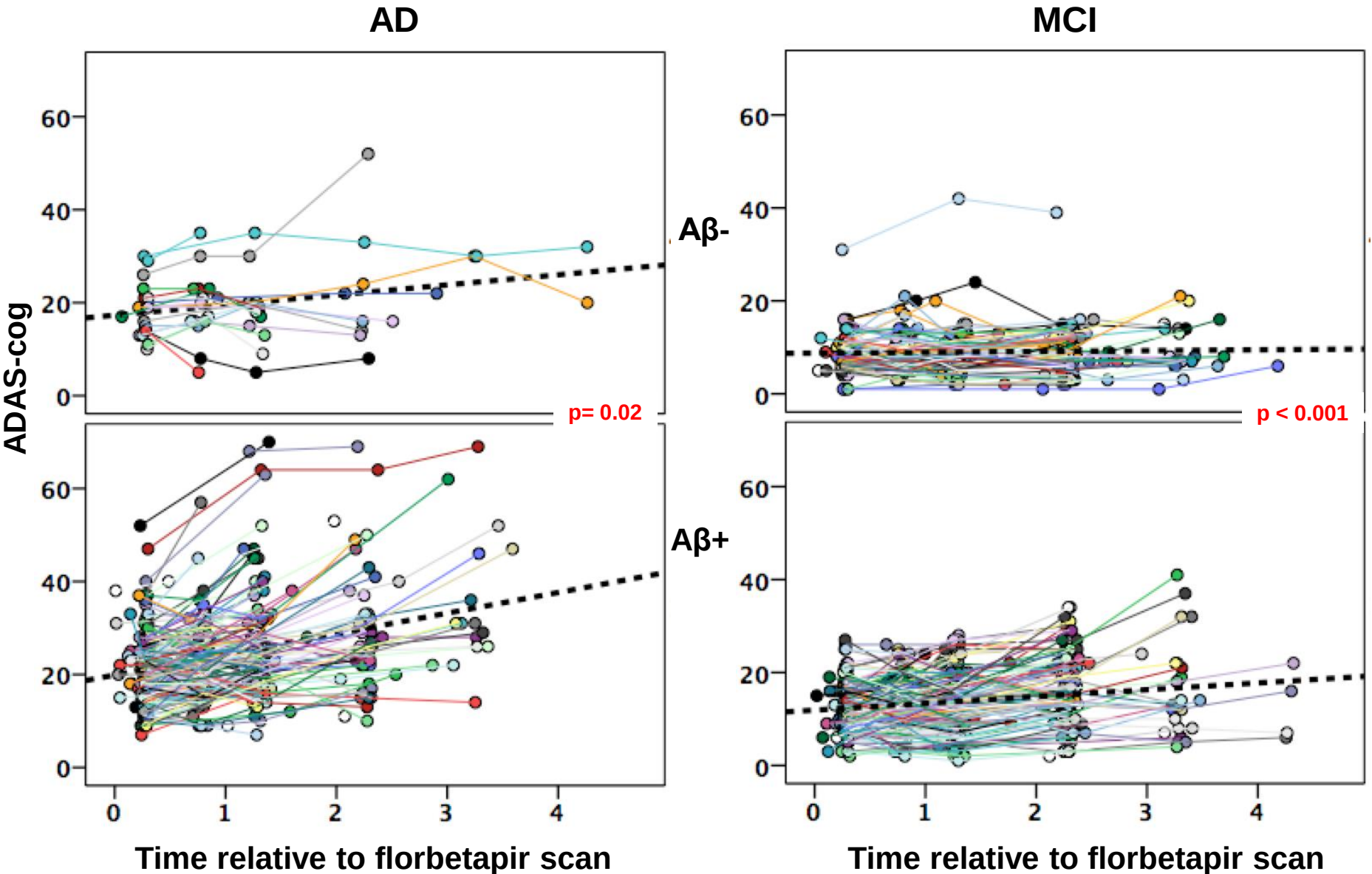


CSF A β and florbetapir agreement

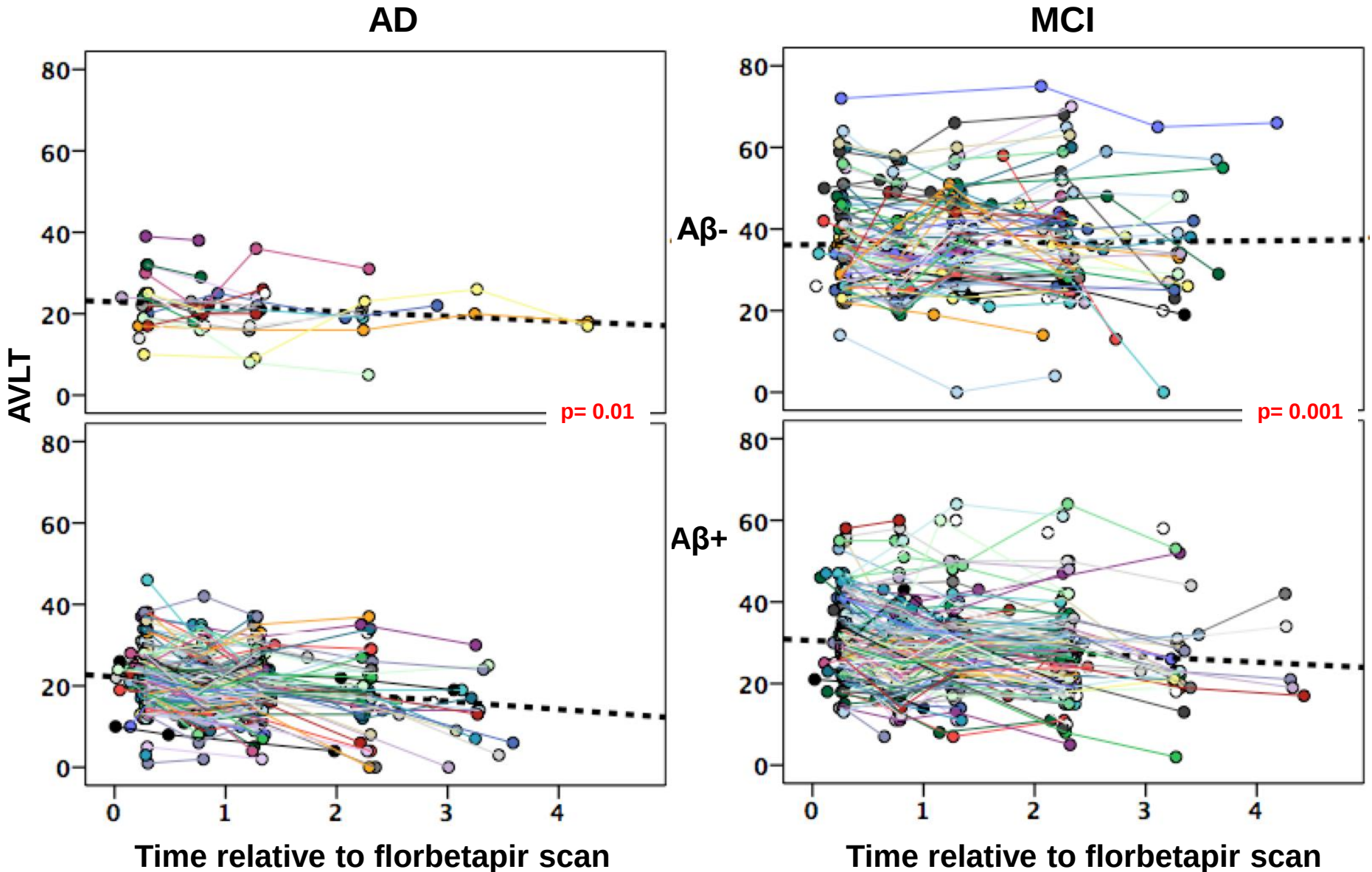


Mattsson et al. Brain 2014

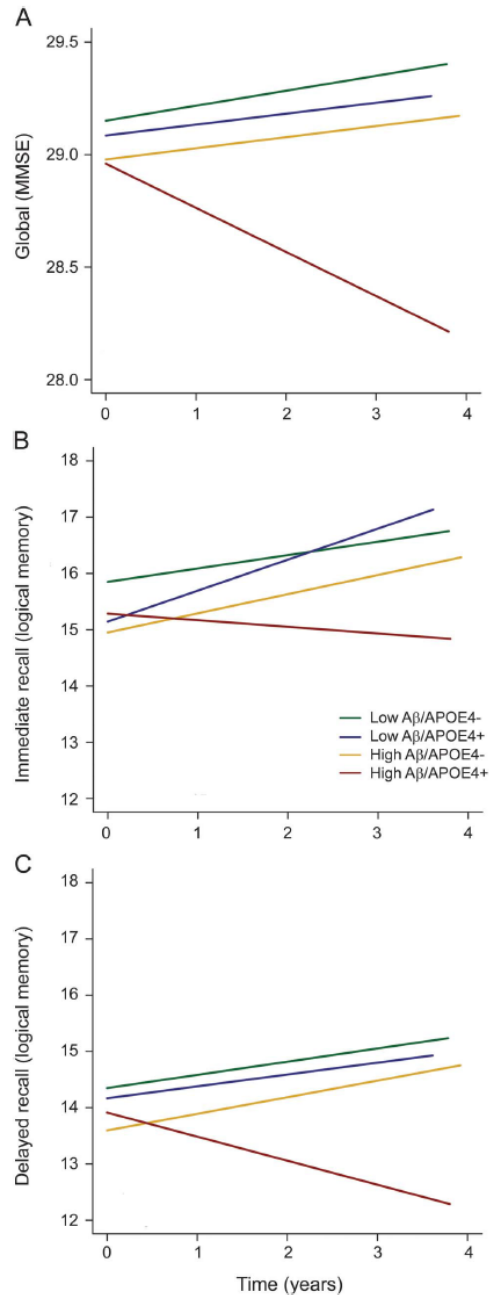
$A\beta$ negatives decline on ADAS-cog at a slower rate than $A\beta$ positives



$A\beta$ negatives decline on AVLT at a slower rate than $A\beta$ positives

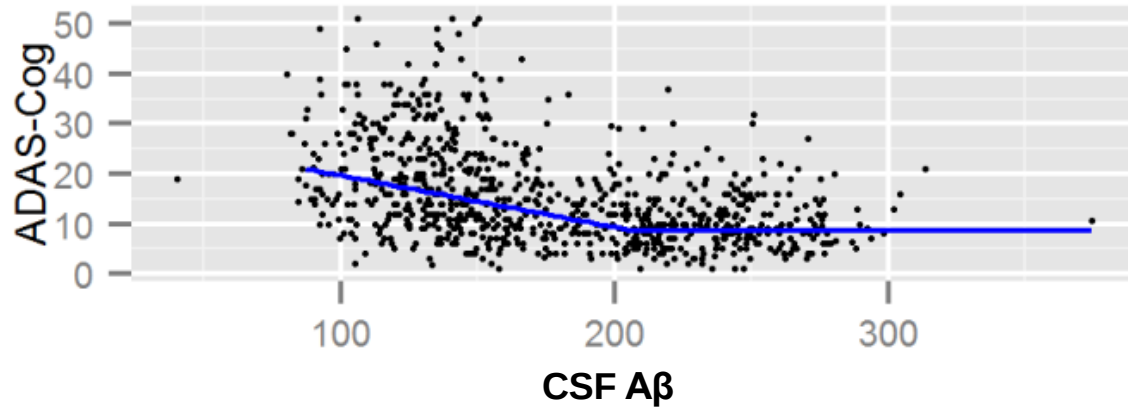
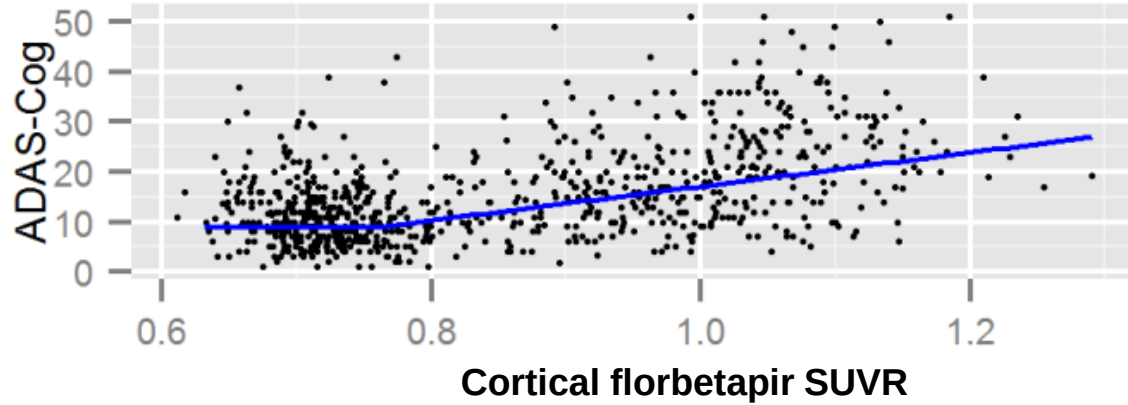


A β status and longitudinal cognitive change in normals



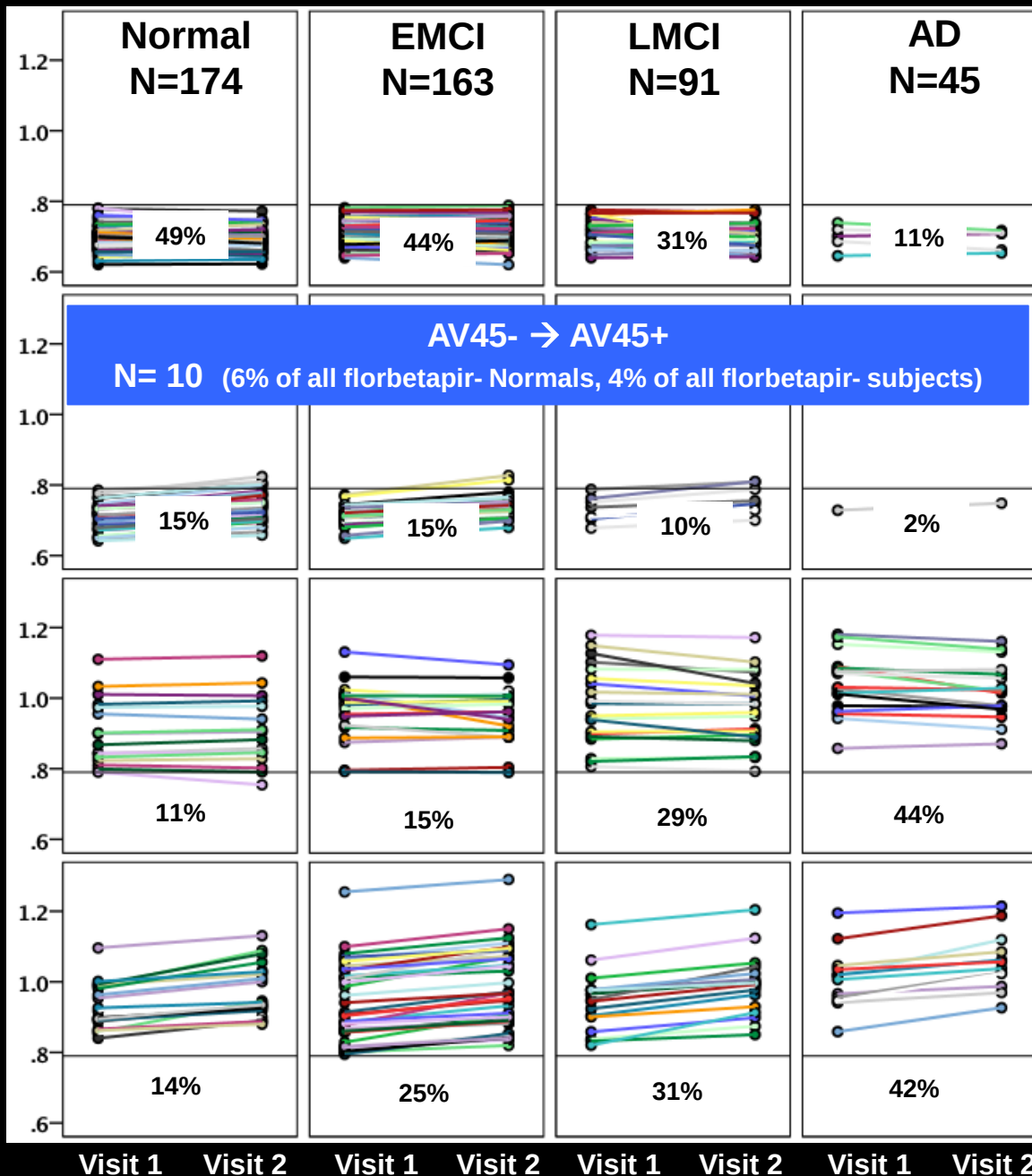
**ApoE4 + amyloid-PET
positivity associated
with subsequent
decline in normals**

CSF A β status and longitudinal cognitive change



Florbetapir change

Florbetapir cortical SUVR



Total N=473

Florbetapir -
not increasing
N=190 (18% APOE4+)

Florbetapir -
Increasing
N=79 (24% APOE4+)

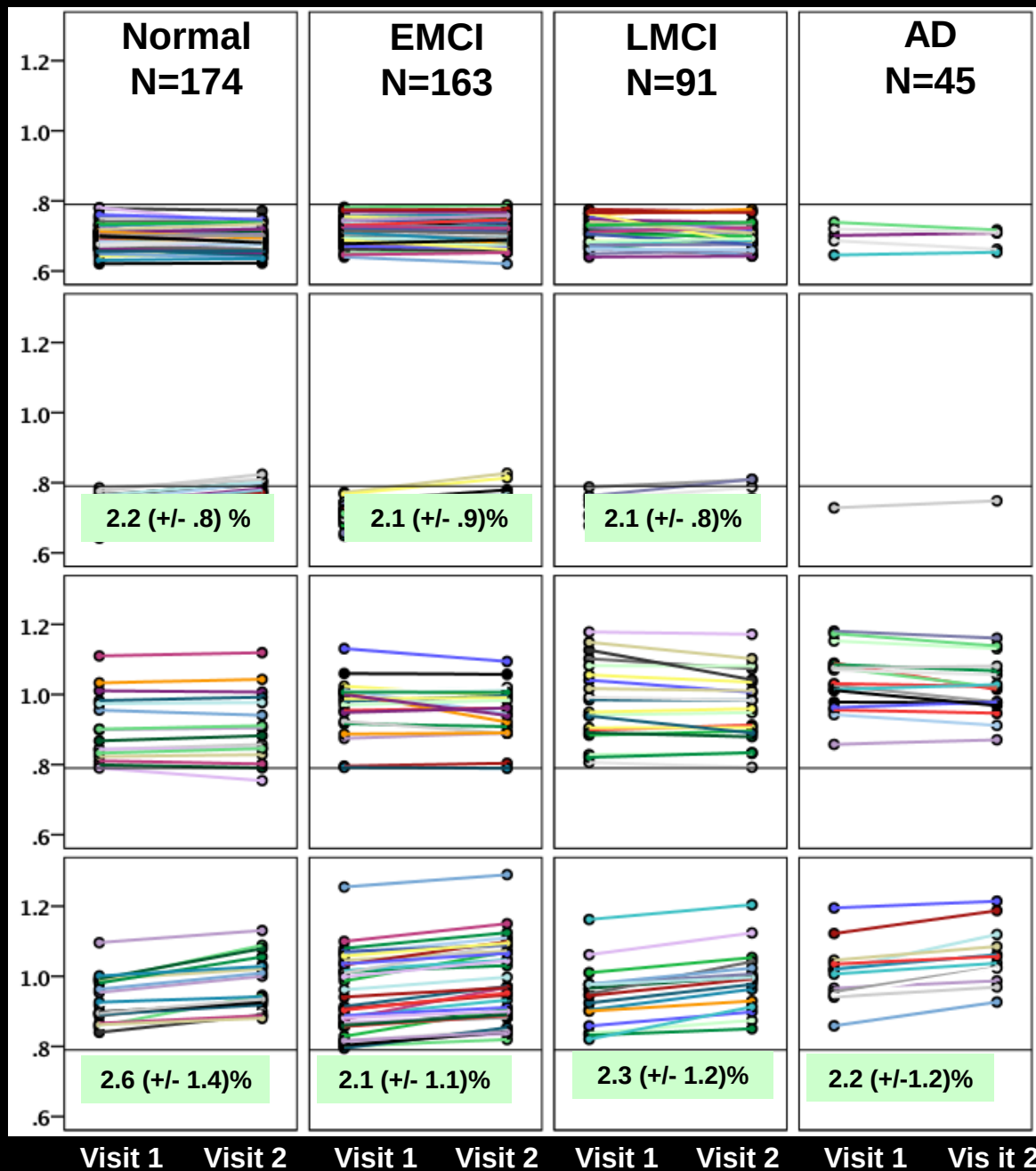
Florbetapir +
not increasing
N=91 (60% APOE4+)

Florbetapir +
Increasing
N=113 (70% APOE4+)

Florbetapir change

Annual
florbetapir
change

Florbetapir cortical SUVR



Total N=473

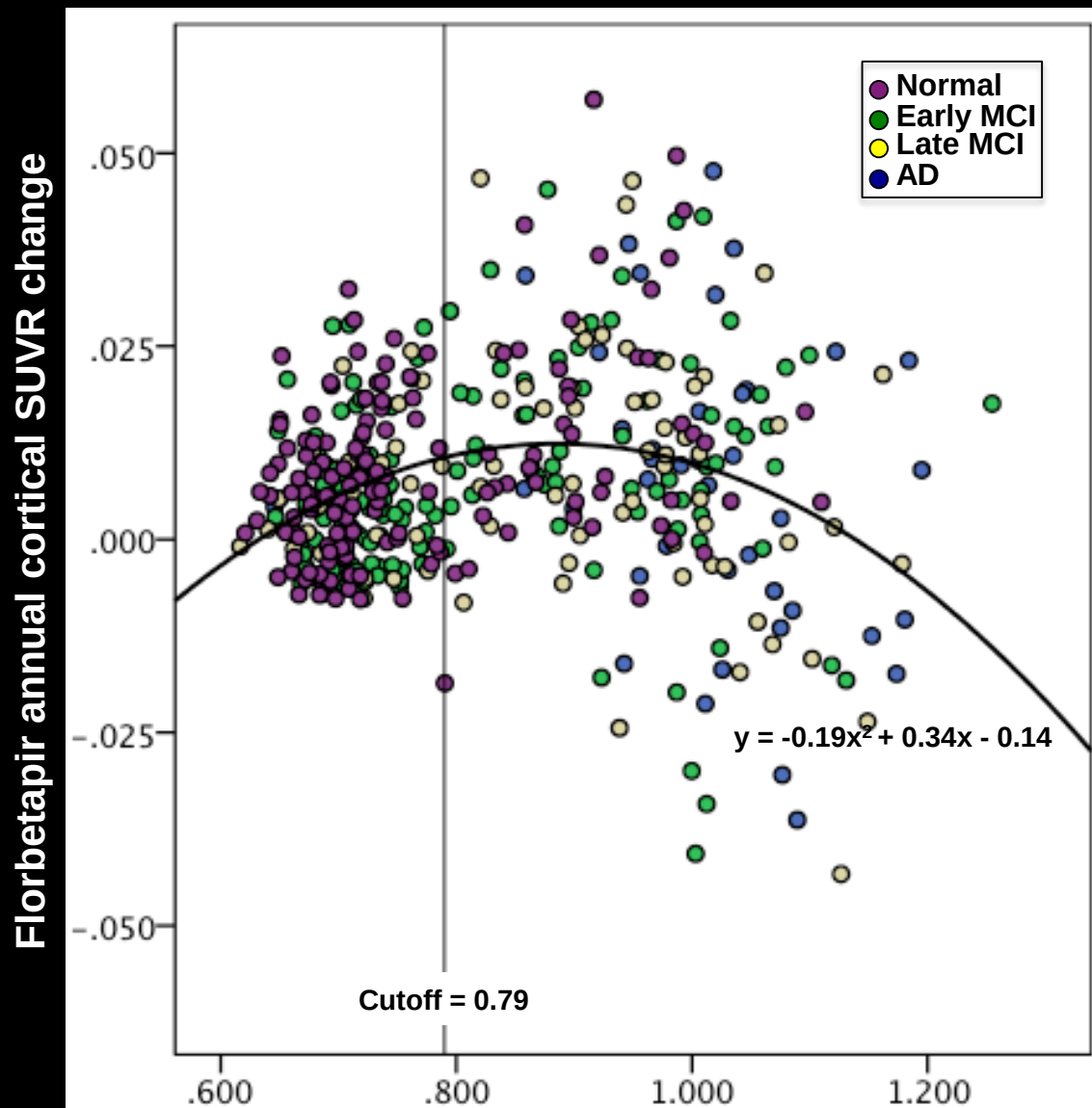
Florbetapir -
not increasing
N=190 (18% APOE4+)

Florbetapir -
Increasing
N=79 (24% APOE4+)

Florbetapir +
not increasing
N=91 (60% APOE4+)

Florbetapir +
Increasing
N=113 (70% APOE4+)

Florbetapir change



Whole cereb ref units

.8

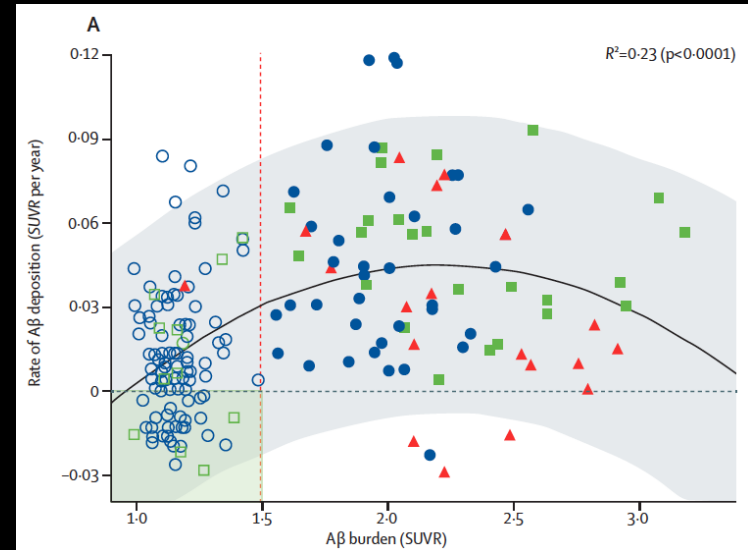
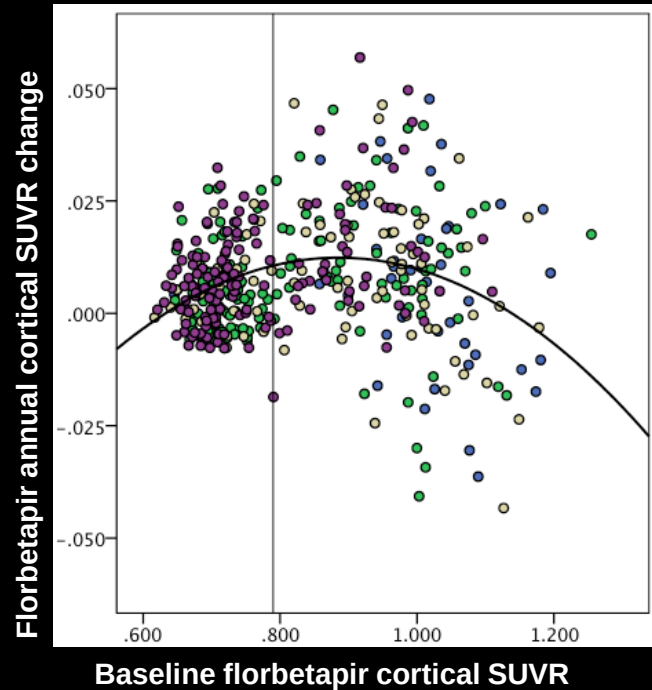
1.1

1.4

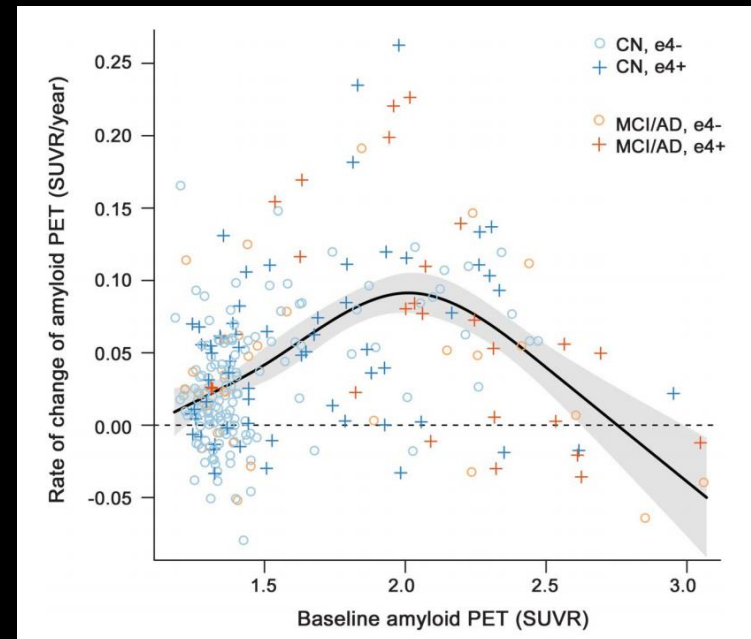
1.8

Baseline florbetapir cortical SUVR

Previous longitudinal amyloid PET studies

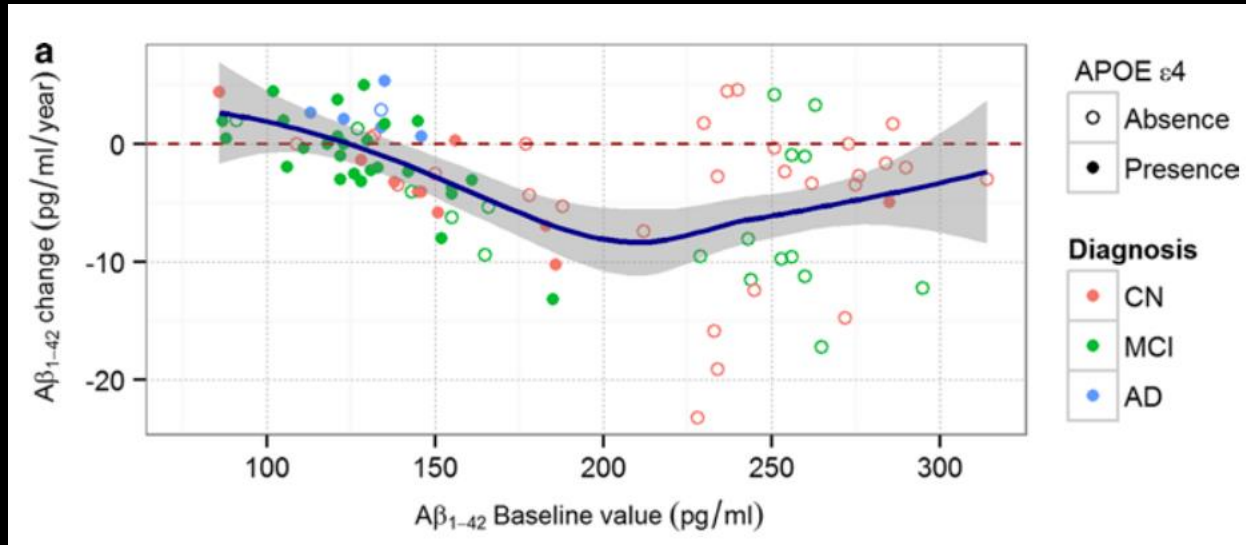


Villemagne et al. Lancet Neurol (2013)



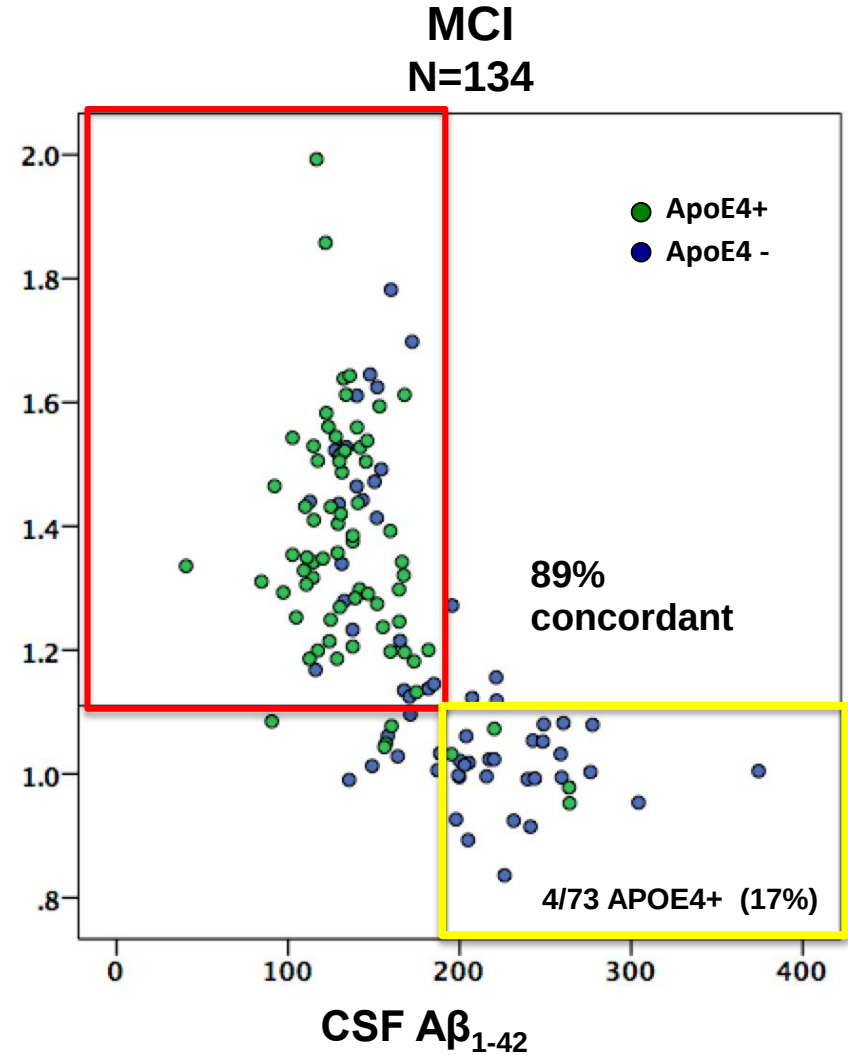
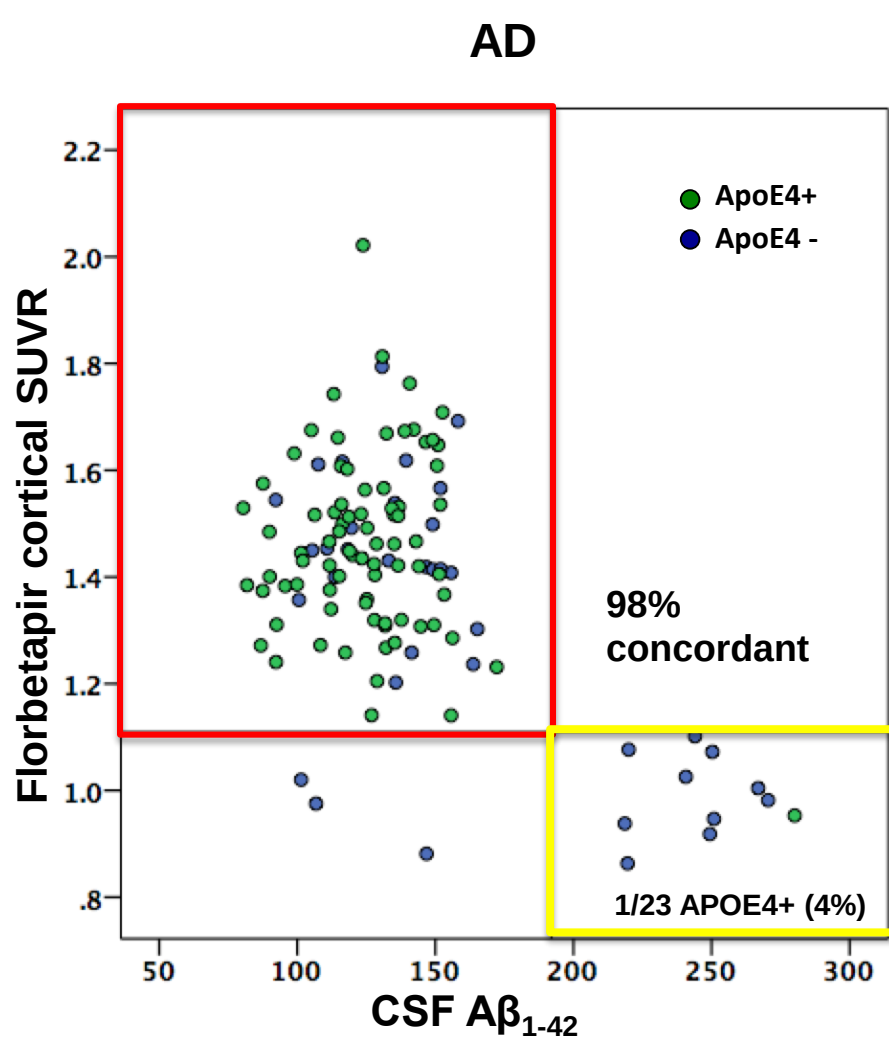
Jack et al. Neurology (2013)

Longitudinal CSF Abeta change



Toledo et al. Acta Neuropathol 2013

Florbetapir and CSF A β agreement



Voxelwise FDG

AD
(N=169)

MCI
(N=208)

$A\beta^+ < A\beta^-$

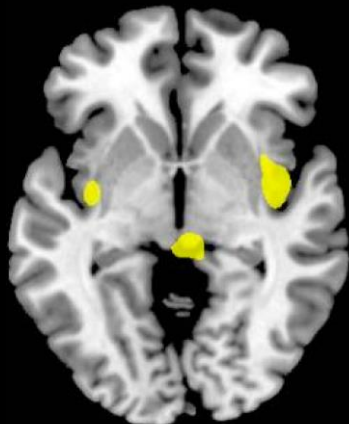
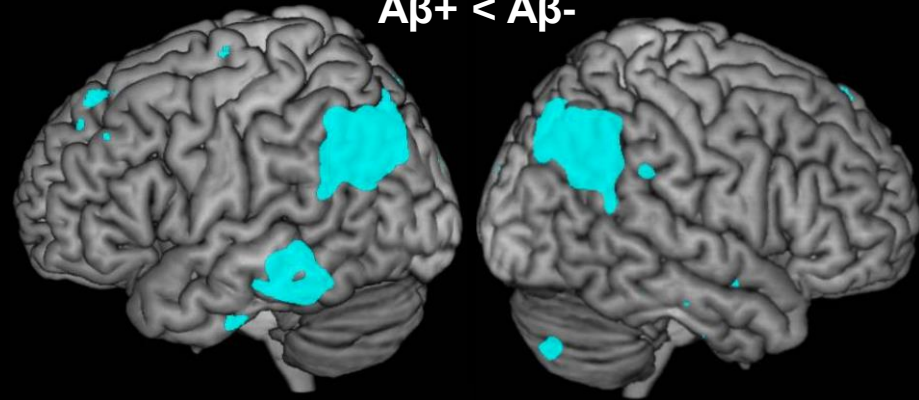
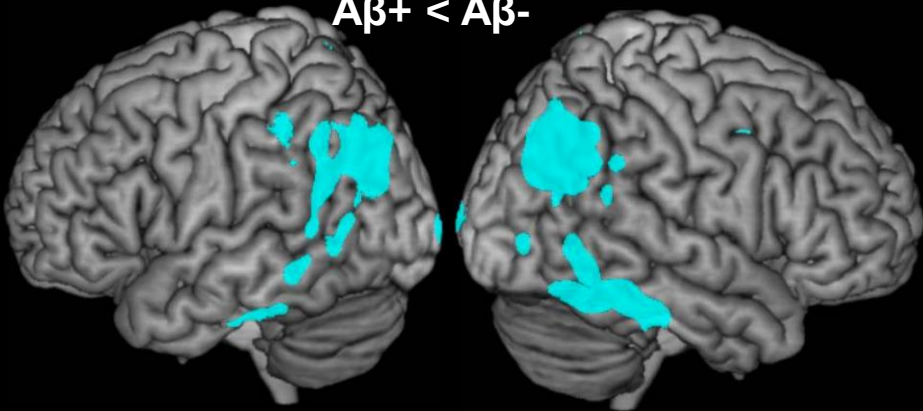
$A\beta^+ < A\beta^-$

$p < 0001$ uncorr

$A\beta^+ > A\beta^-$

L hipp

R hipp



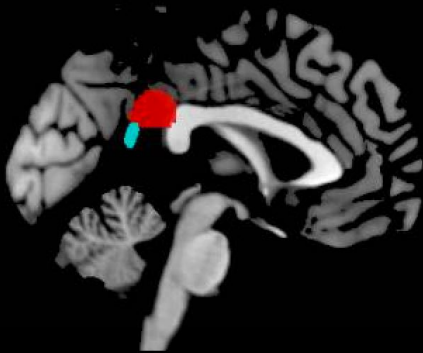
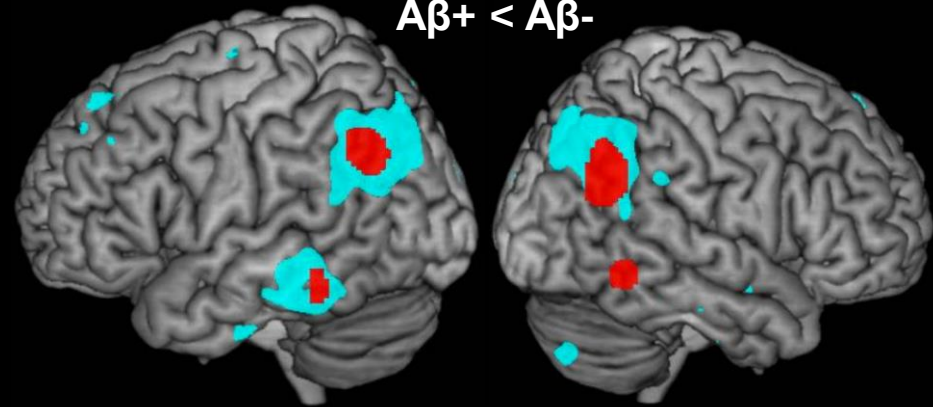
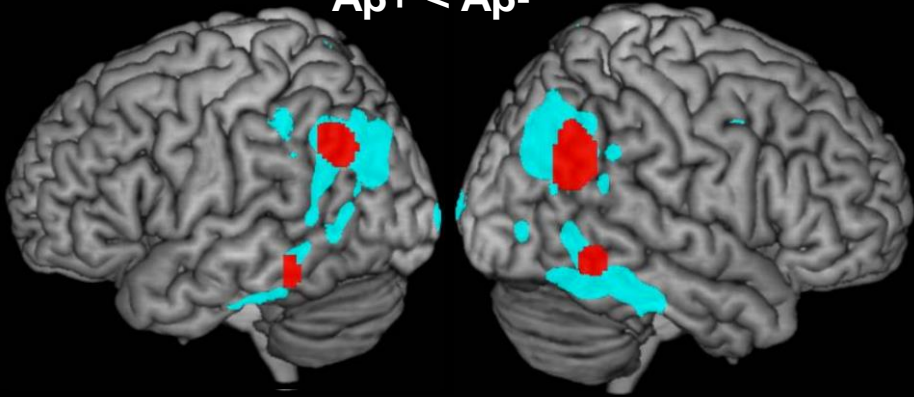
Voxelwise FDG

AD

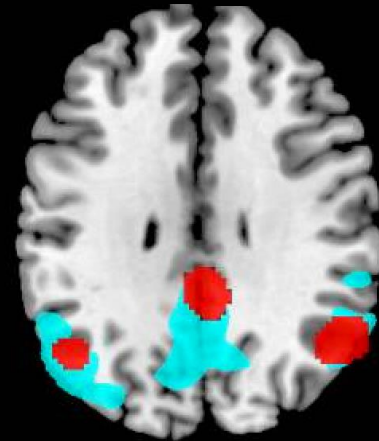
MCI

$A\beta^+ < A\beta^-$

$A\beta^+ < A\beta^-$



AD-specific Meta ROIs



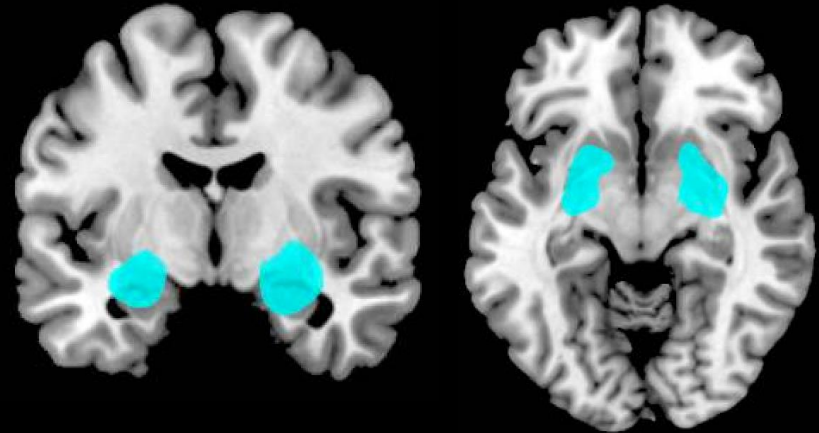
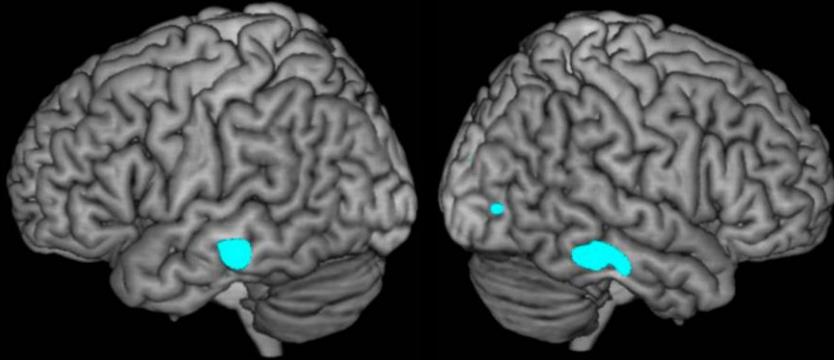
Structural comparison (VBM)

AD

MCI

$A\beta^+ < A\beta^-$

$A\beta^+ < A\beta^-$



$p < 0.0001$ uncorrected

$A\beta^+ > A\beta^-$



Summary

Visual and quantitative reads are concordant in most cases

Amyloid PET and CSF A β agreement is high cross-sectionally and longitudinally

A β positivity is associated with cognitive decline across the disease spectrum

Florbetapir negative AD and MCI patients have a distinct biomarker profile compared with their positive counterparts

Thank you

ADNI participants & staff

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

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Andrew Saykin
Ron Petersen
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Anthony Gamst
Art Toga
Karen Crawford
Paul Aisen

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Bill Jagust
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Allison Fero
Gil Rabinovici
Stefanie Schreiber

Mark Mintun
Abhinav Joshi

Beth Mormino
Sylvia Villeneuve

