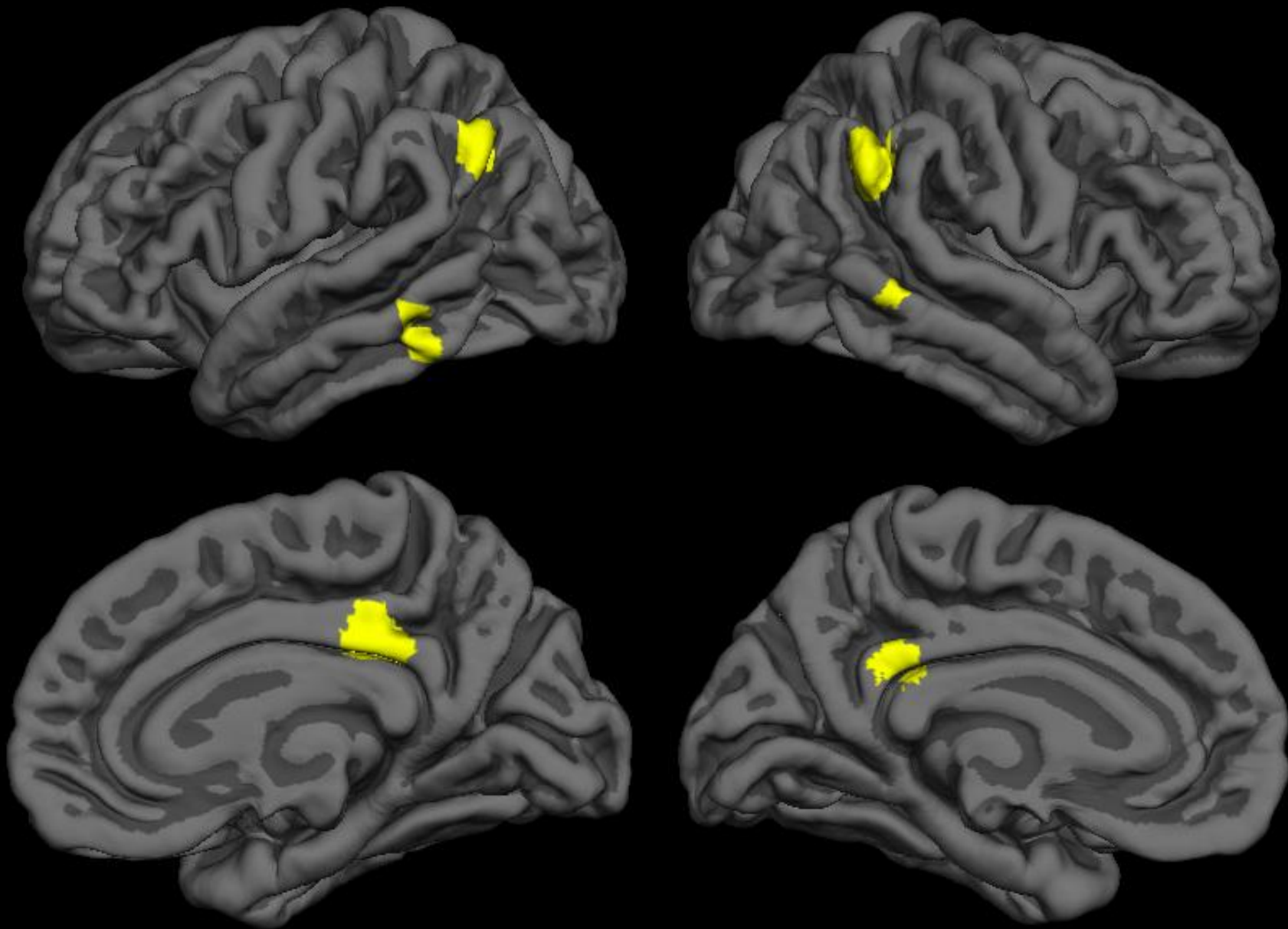


ADNI PET Core Update

An aerial photograph of the University of California, San Diego campus. The image shows a mix of architectural styles, from classical buildings with red-tiled roofs to modern high-rise structures. A prominent feature is the tall, white Campanile tower on the right side. The campus is surrounded by lush green trees and a clear blue sky.

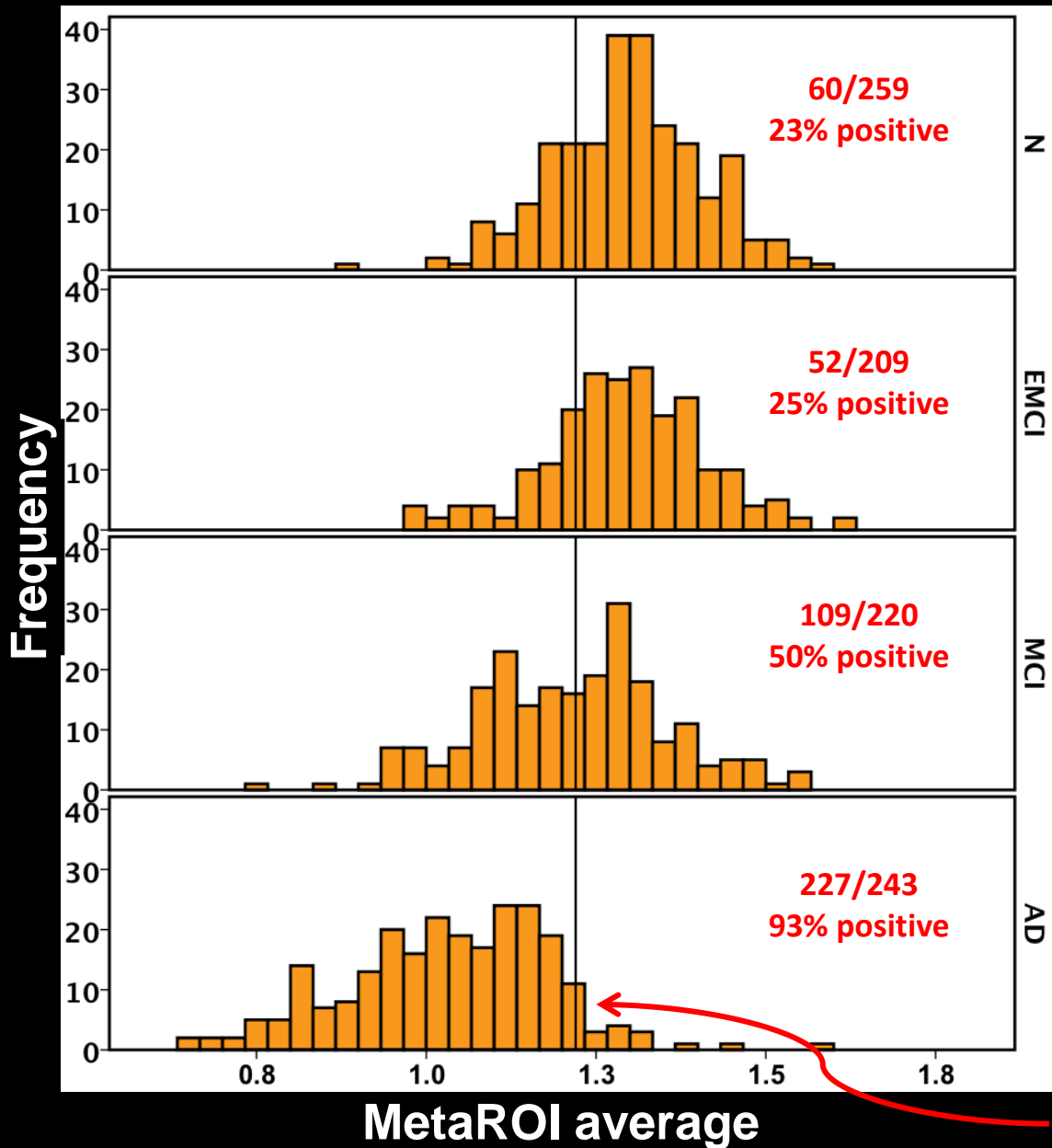
**WW-ADNI
Vancouver
July 2012**

FDG "Meta ROIs"



Baseline FDG-PET in ADNI2/GO

(N=931)



1.21 threshold: 82% sensitivity, 70% specificity for AD vs Controls (Landau et al, Neurology 2010)

ADNI (Freesurfer) Processing

ADNI and Avid Processing

Avid Processing

ADNI PIB
(N=32)

ADNI
Florbetapir
(N=32)

ADNI
Florbetapir
(N=324)

AVID Autopsy
Data

Comparing Tracers

1 same subjects studied with
both tracers

or

2 Compare 2 tracers to the
same third tracer

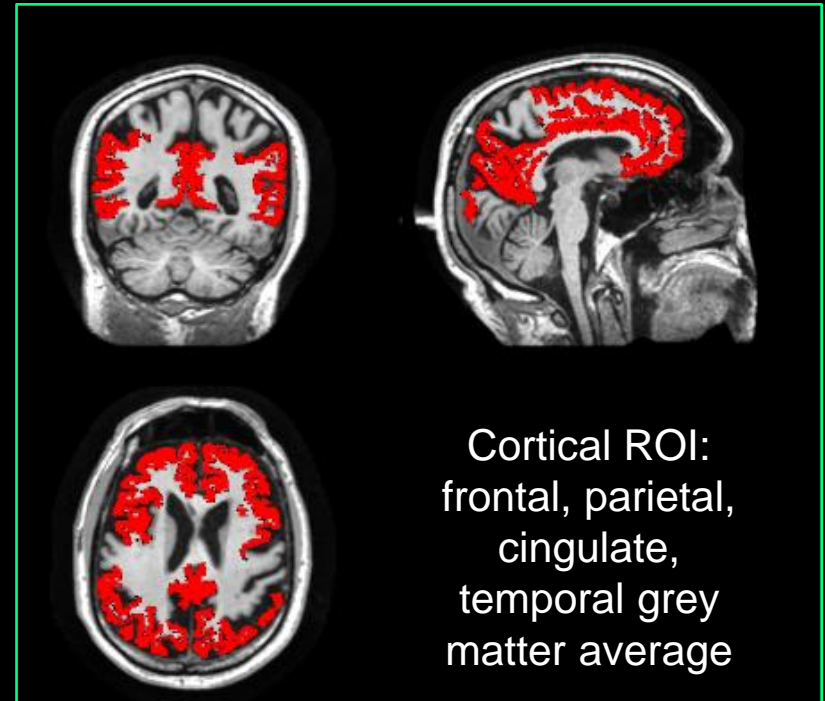
Comparing Methods

Analyze data 2 ways

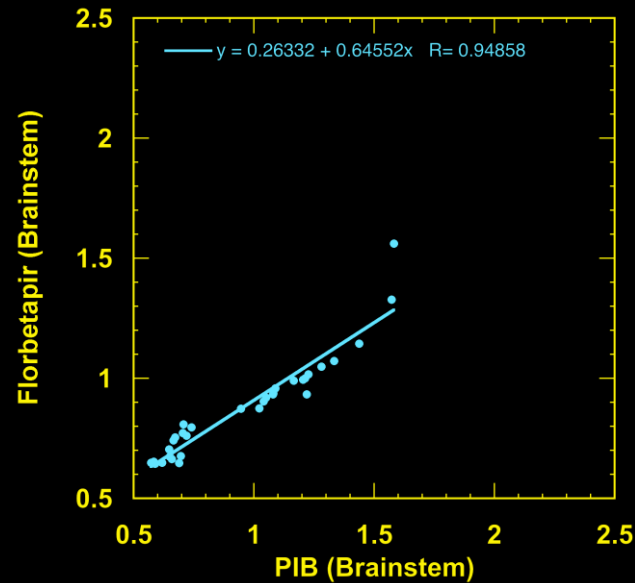
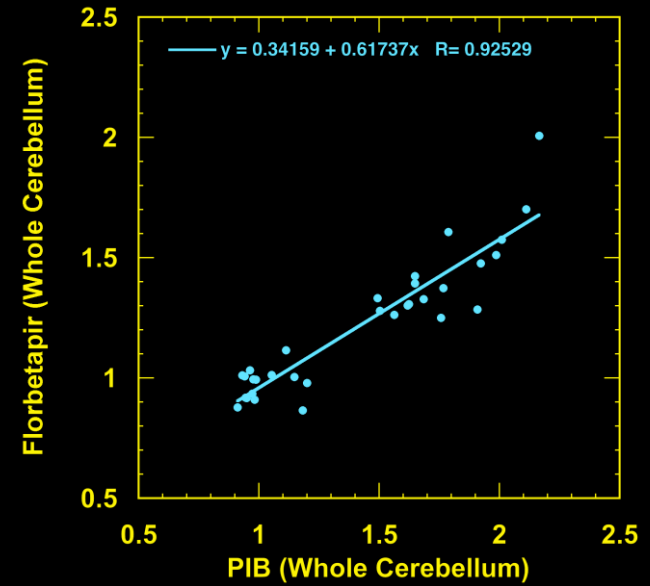
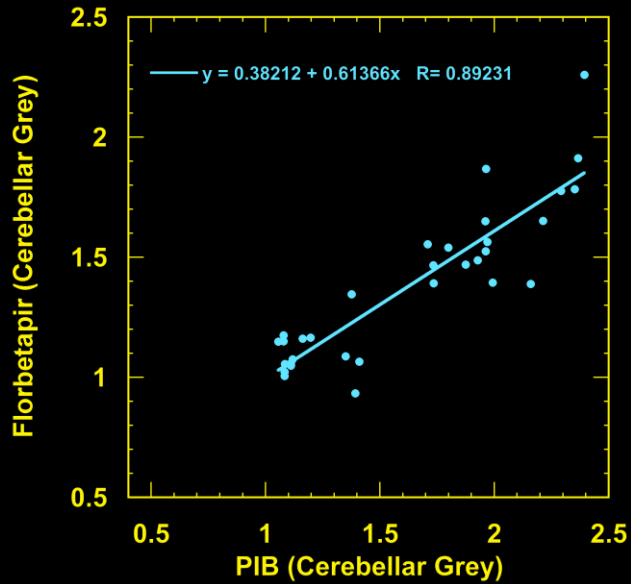
Florbetapir and PIB in ADNI

- Freesurfer Processing
- Cerebellar Gray matter Reference ROI
- Mean 1.5 years apart
- N=32
- 6 normals
- 22 MCI (5 converted)
- 4 AD

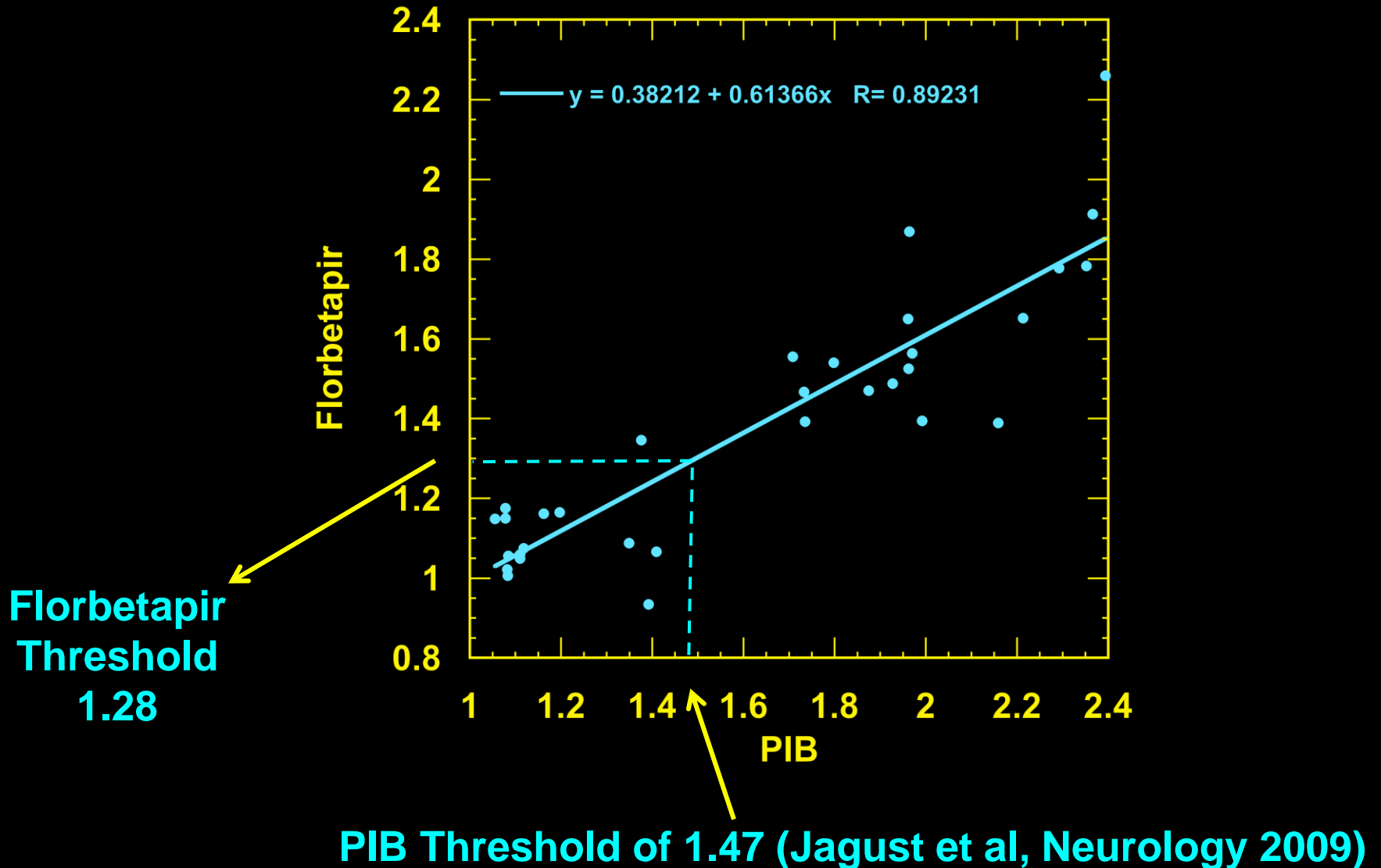
Currently In press: Landau et al,
J Nucl Med



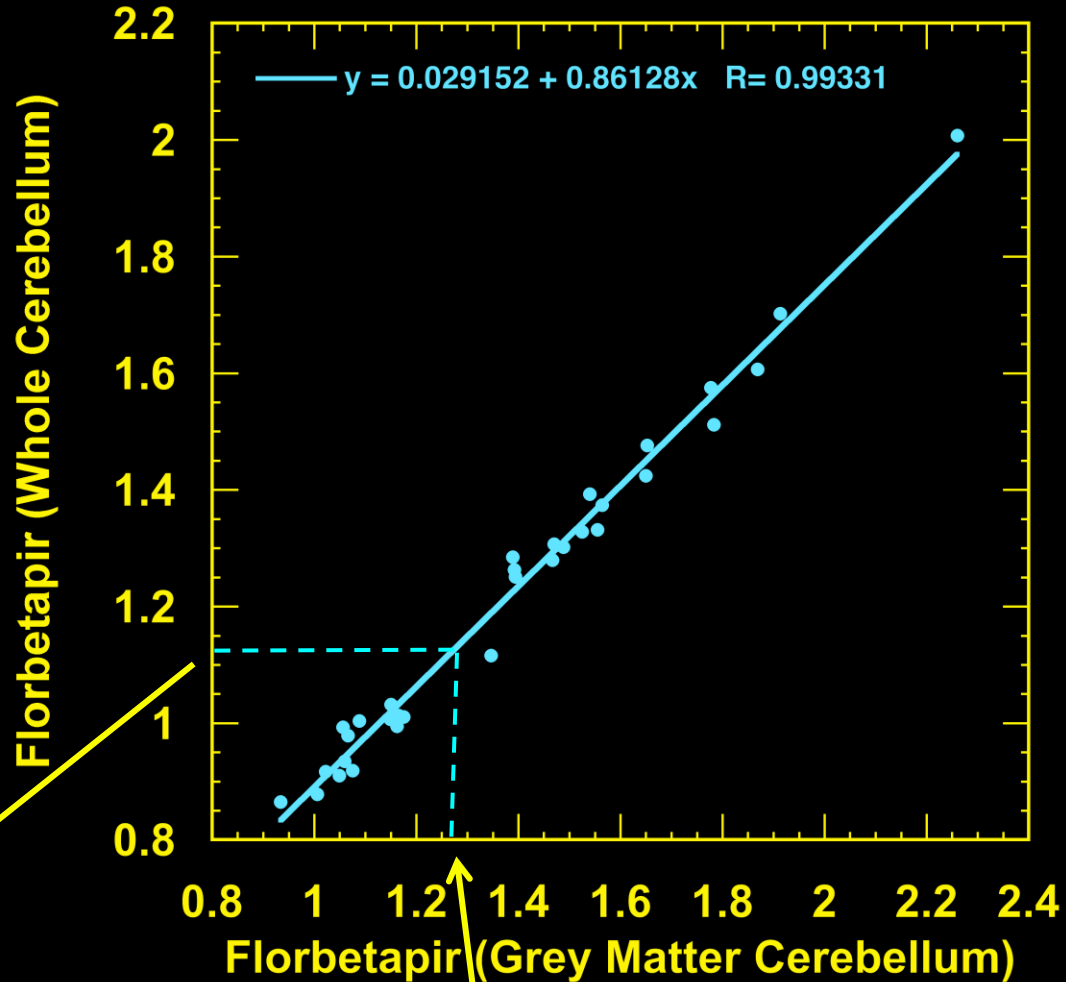
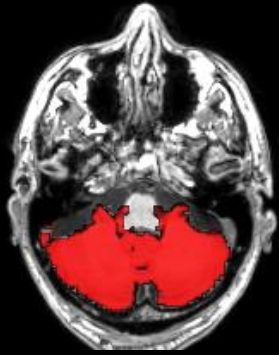
Effect of Reference Region PIB-Florbetapir



PIB vs Florbetapir Cerebellar Gray Matter Reference Freesurfer Processing

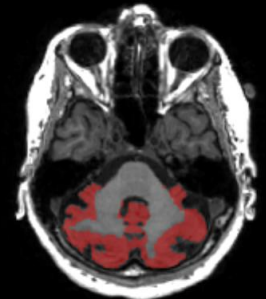


Freesurfer: Grey matter vs whole cerebellum



1.13

1.28



**1.47 (PIB) = 1.28 (Florbetapir) = 1.13
(Florbetapir, Whole Cerebellum Reference)**

We can convert from PIB to Florbetapir Values

**We can convert from a cerebellar grey
reference to a whole cerebellar reference**

How about different processing streams?

**Avid also works up Florbetapir data - how
does their processing compare?**

**And....Avid has imaging-Neuropathology
correlations!**

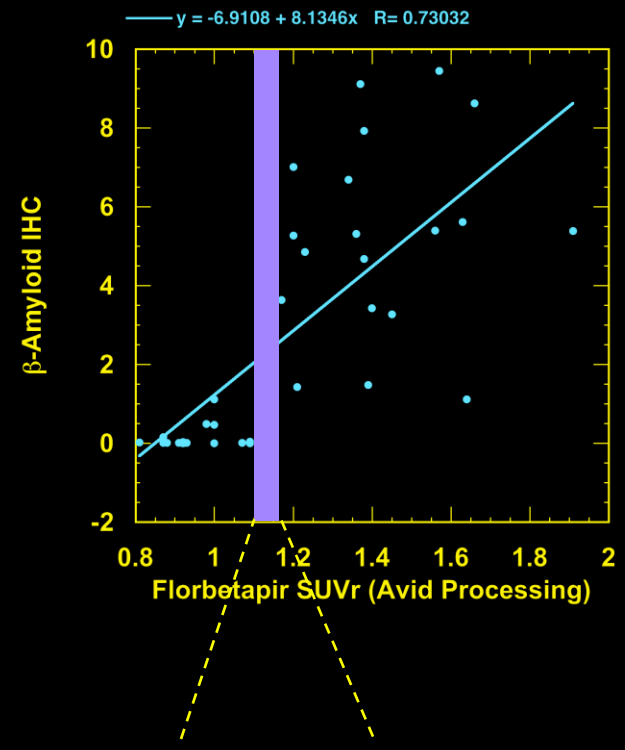
Table 1. Clinical and Outcome Values for 35 Participants With a Postmortem Evaluation^a

| Clinical Diagnosis Category | Age at Death, y | Cause of Death | Autopsy Reference Standard | | | | | | |
|-----------------------------|-----------------|--------------------------------|----------------------------|-----------------------|----------------------|-----|--------------------------|----------|-------------------------|
| | | | Florbetapir-PET Imaging | | AD Diagnosis | | | | |
| | | | SUVr | Median Visual Reading | β -Amyloid IHC | NPS | Braak Stage ^b | CERAD | NIA/Reagan Institute |
| ODD | 87.4 | Esophageal cancer | 0.81 | 1 | 0.02 | 0 | 2 | No | Low likelihood |
| AD ^b | 82.8 | Congestive heart failure | 0.87 | 0 | 0.15 | 0 | 3 | No | Low likelihood |
| MCI | 92.2 | Congestive heart failure | 0.87 | 0 | 0.01 | 0 | 4 | No | Low likelihood |
| HC | 62.5 | Respiratory arrest | 0.88 | 0 | 0.01 | 0 | 1 | No | Low likelihood |
| HC | 85.9 | Respiratory failure | 0.88 | 0 | 0.01 | 0 | 1 | No | Low likelihood |
| HC | 84.6 | Lung cancer | 0.91 | 1 | 0.01 | 0 | 1 | No | Low likelihood |
| MCI | 86.2 | Cardiac arrest | 0.92 | 1 | 0.03 | 0 | 3 | No | Low likelihood |
| HC | 99.9 | Heart failure | 0.92 | 1 | 0 | 0 | 3 | No | Low likelihood |
| HC | 62.1 | Infection | 0.93 | 0 | 0.01 | 0 | 1 | No | Low likelihood |
| ODD | 104.3 | End-stage dementia | 0.98 | 0 | 0.49 | 1 | 1 | Possible | Low likelihood |
| HC | 70.1 | Prostate cancer | 1.00 | 0 | 0.47 | 1 | 1 | Possible | Low likelihood |
| HC | 93.2 | Acute MI | 1.00 | 1 | 1.11 | 0 | 0 | No | No AD |
| HC | 85.7 | Hepatic cancer | 1.00 | 1 | 0 | 0 | 3 | No | Low likelihood |
| ODD | 73.9 | Advanced PD | 1.07 | 0 | 0.01 | 0 | 3 | No | Low likelihood |
| MCI ^b | 48.0 | Respiratory and renal failure | 1.09 | 1 | 0 | 0 | 1 | No | Low likelihood |
| HC | 55.9 | Prostate cancer | 1.09 | 0 | 0.04 | 0 | 1 | No | Low likelihood |
| ODD ^b | 78.5 | Acute respiratory failure | 1.17 | 2 | 3.63 | 2 | 5 | Definite | High likelihood |
| AD | 81.5 | Respiratory failure | 1.20 | 3 | 7.01 | 3 | 5 | Definite | High likelihood |
| AD | 76.3 | AD | 1.20 | 3 | 5.27 | 2 | 5 | Definite | High likelihood |
| ODD | 88.7 | Cardiac and respiratory arrest | 1.21 | 3 | 1.42 | 3 | 5 | Definite | High likelihood |
| AD | 88.1 | AD | 1.23 | 1 | 4.85 | 2 | 5 | Probable | Intermediate likelihood |
| ODD | 67.9 | Pick disease and stroke | 1.34 | 4 | 6.69 | 2 | 5 | Definite | High likelihood |
| AD | 72.1 | AD | 1.36 | 3 | 5.31 | 3 | 6 | Definite | High likelihood |
| AD | 91.8 | Acute MI | 1.37 | 3 | 9.11 | 2 | 5 | Definite | High likelihood |
| AD | 55.5 | Cardiac and respiratory arrest | 1.38 | 3 | 4.67 | 3 | 6 | Definite | High likelihood |
| AD ^b | 79.8 | AD | 1.38 | 4 | 7.92 | 2 | 6 | Definite | High likelihood |
| AD | 89.2 | Pneumonia | 1.39 | 3 | 1.48 | 2 | 3 | Definite | Intermediate likelihood |
| AD | 88.2 | Respiratory failure | 1.40 | 3 | 3.42 | 2 | 5 | Definite | High likelihood |
| AD | 86.8 | AD | 1.45 | 4 | 3.27 | 1 | 4 | Probable | Intermediate likelihood |
| AD ^b | 86.5 | AD | 1.56 | 3 | 5.39 | 3 | 5 | Definite | High likelihood |
| AD | 60.0 | Unknown | 1.57 | 4 | 9.44 | 3 | 6 | Definite | High likelihood |
| AD | 69.3 | Respiratory failure | 1.63 | 4 | 5.61 | 2 | 5 | Definite | High likelihood |
| AD | 92.3 | AD | 1.64 | 3 | 1.11 | 1 | 4 | Probable | Intermediate likelihood |
| AD ^b | 84.6 | AD | 1.66 | 4 | 8.62 | 3 | 6 | Definite | High likelihood |
| AD | 91.7 | AD | 1.91 | 4 | 5.38 | 2 | 4 | Probable | Intermediate likelihood |

Abbreviations: AD, Alzheimer disease; CERAD, Consortium to Establish a Registry for Alzheimer's Disease; HC, cognitively healthy control; IHC, immunohistochemistry; MCI, mild cognitive impairment; MI, myocardial infarction; NIA/Reagan Institute, National Institute on Aging and Reagan Institute Working Group on Diagnostic Criteria for the Neuropathological Assessment of Alzheimer's Disease; NPS, neuritic plaque score; ODD, other dementing disorder; PD, Parkinson disease; PET, positron emission tomographic; SUVr, semiautomated quantitative analysis of the ratio of cortical to cerebellar signal.

^aParticipants are ordered by increasing florbetapir-PET SUVr score.

^bIndicates participant was in the interim analysis (n=6).



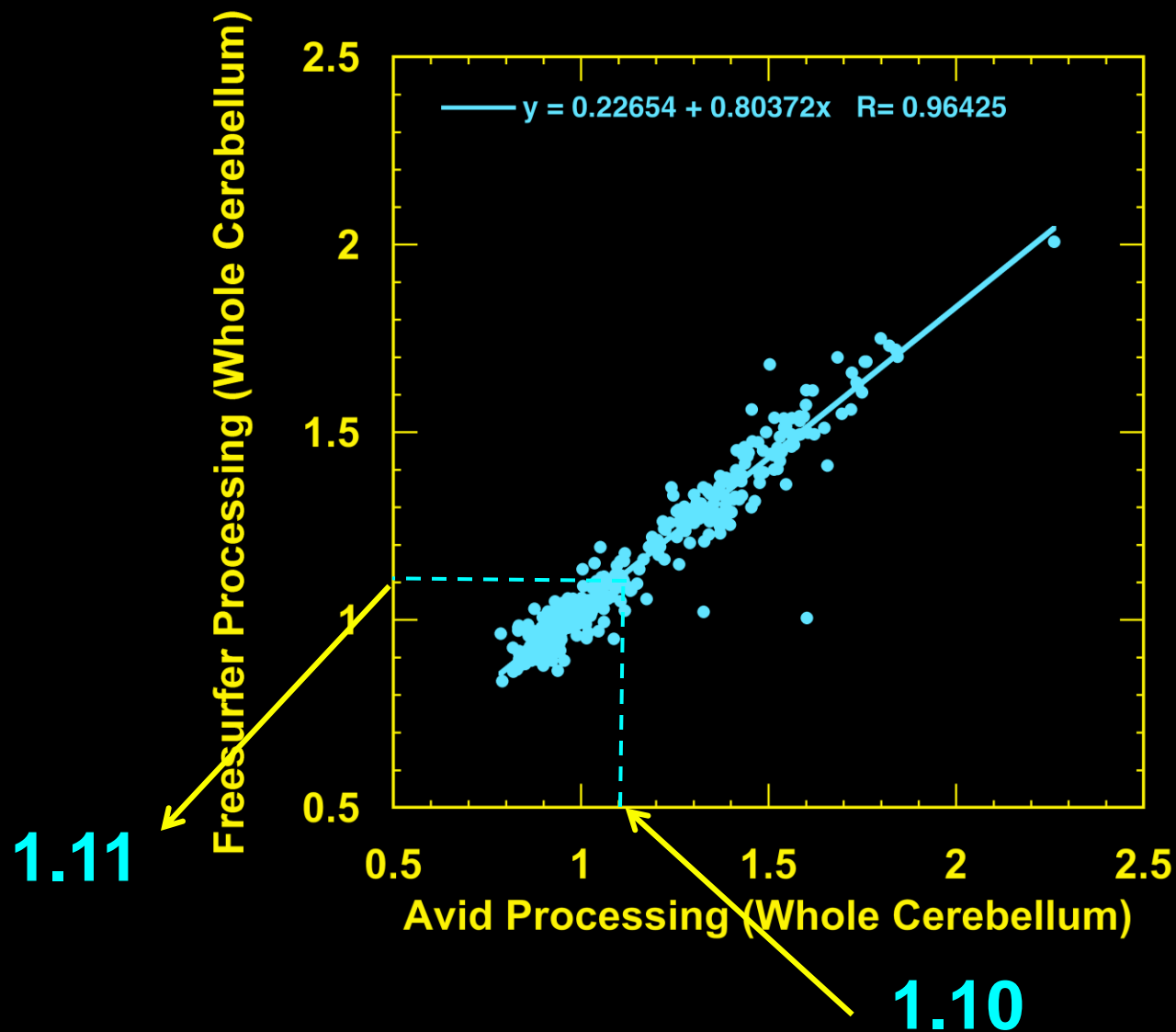
1.09 ↔ 1.17

**Joshi et al
J Nucl Med 2012:
1.10 = 95% CI upper interval for
subjects < 55**

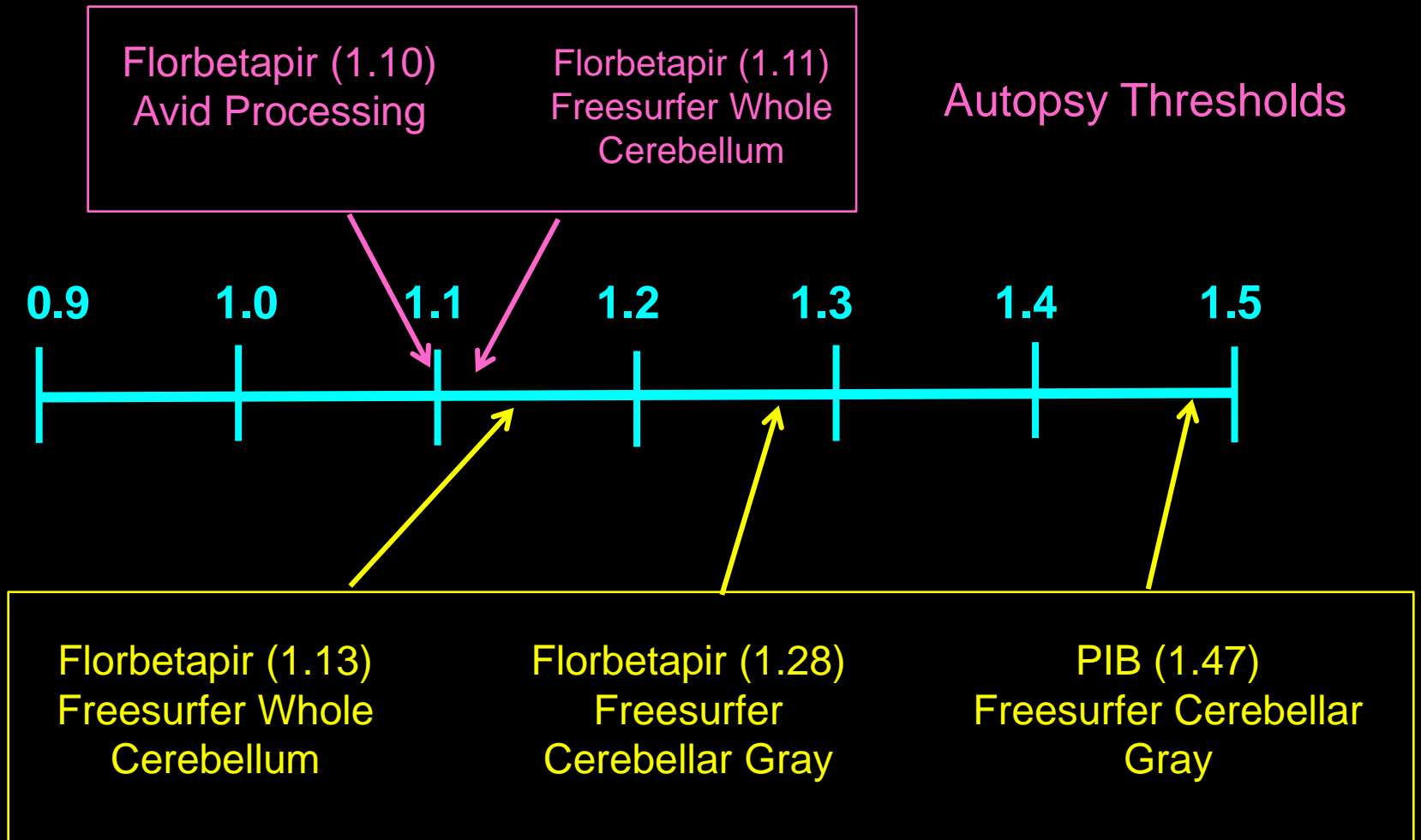
324 ADNI subjects

Freesurfer processing (whole cerebellar reference)

Avid processing (whole cerebellar reference)



Comparisons



Caveats

Although numerical values can be compared, that does not mean they are “correct” in detecting $A\beta$

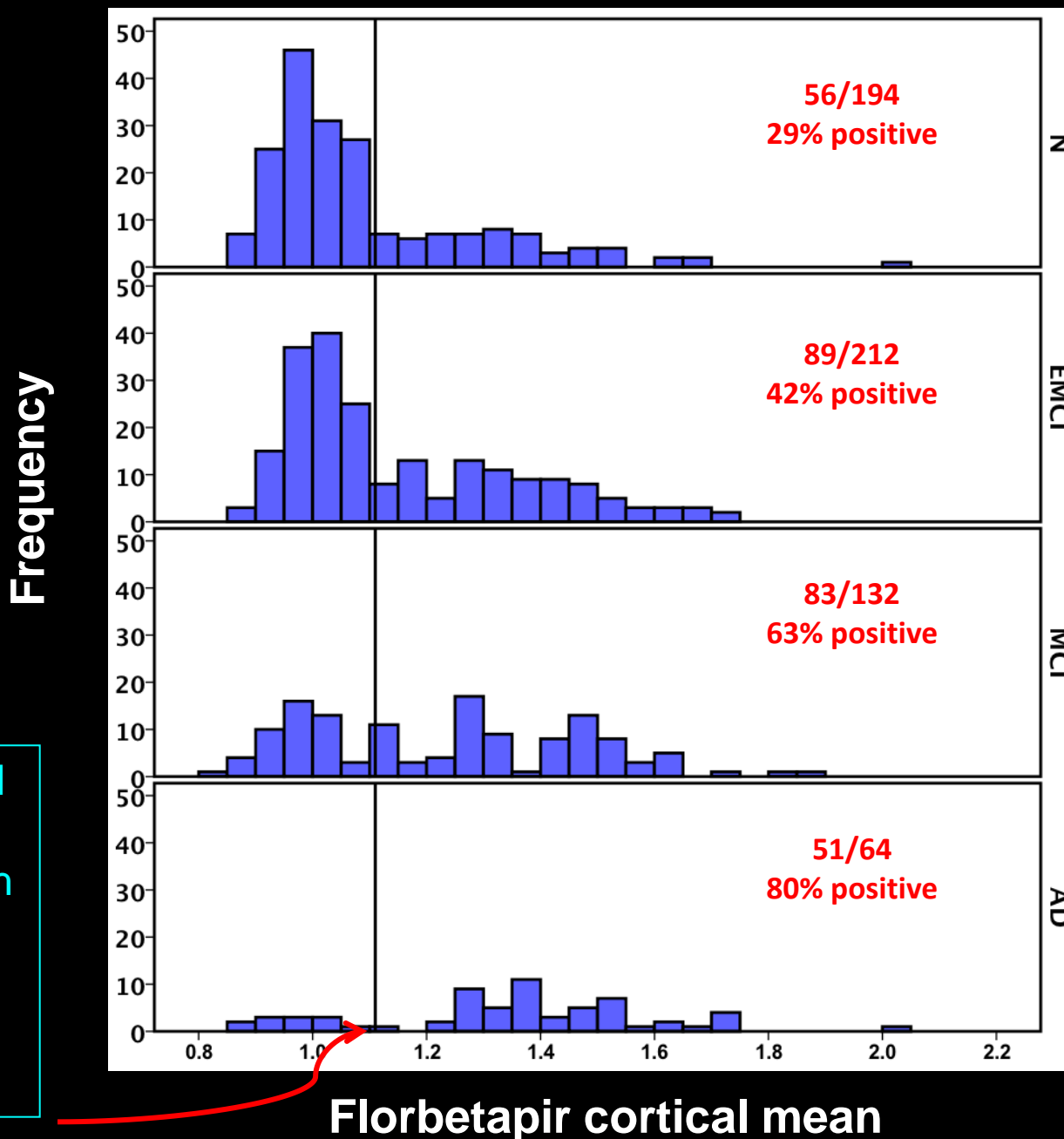
Thresholds are associated with errors – false negatives and positives

Tracer performance characteristics differ in ways we still do not fully understand: false negative and positive rates will differ

Factors such as instrument resolution, sensitivity, reconstruction algorithms will affect results

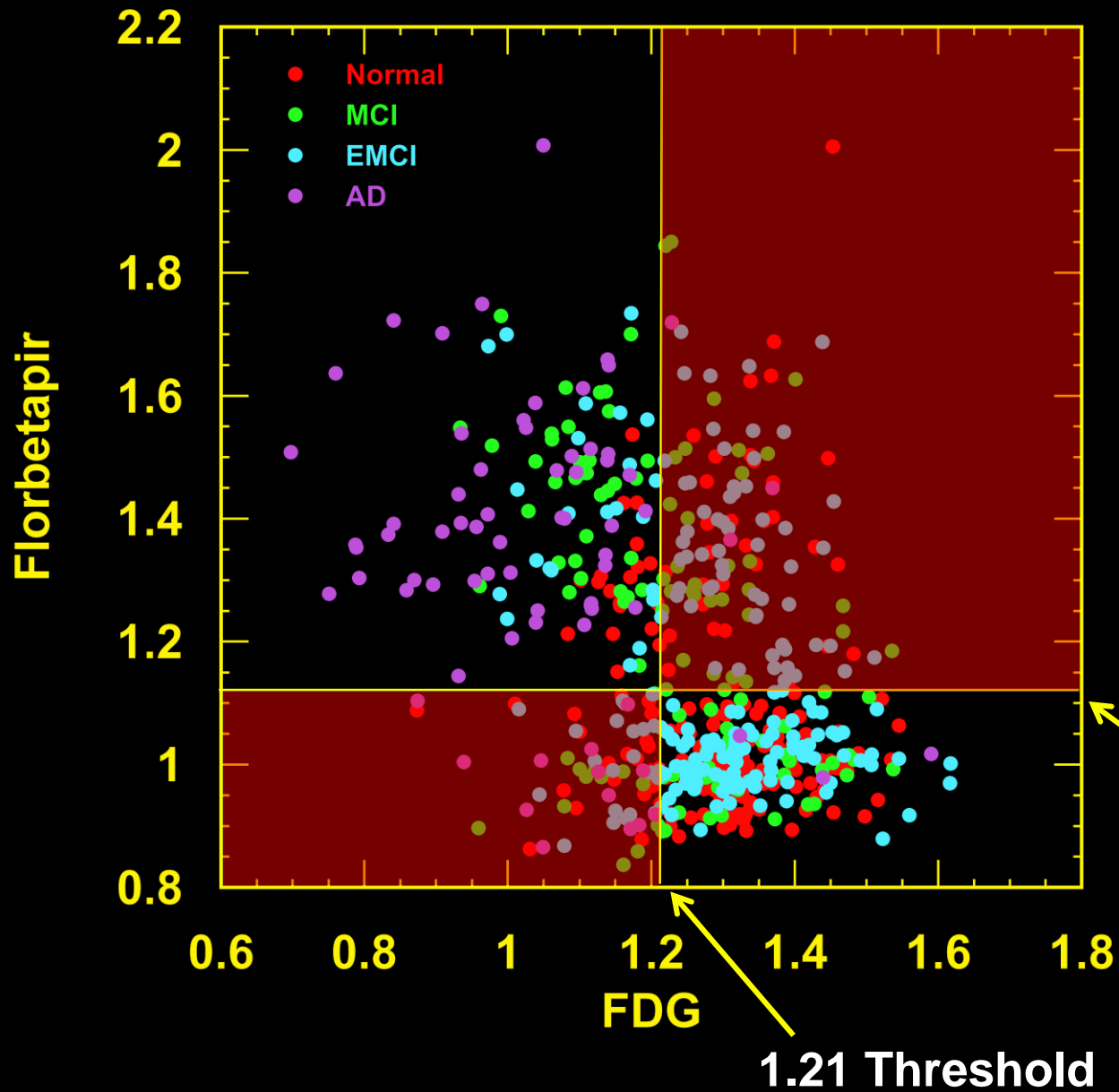
These are research-focused analyses and are not ready for clinical prime time

ADNI GO/2 Florbetapir (N=602)



1.11 threshold
ADNI Data
processed with
freesurfer &
whole
cerebellum
reference

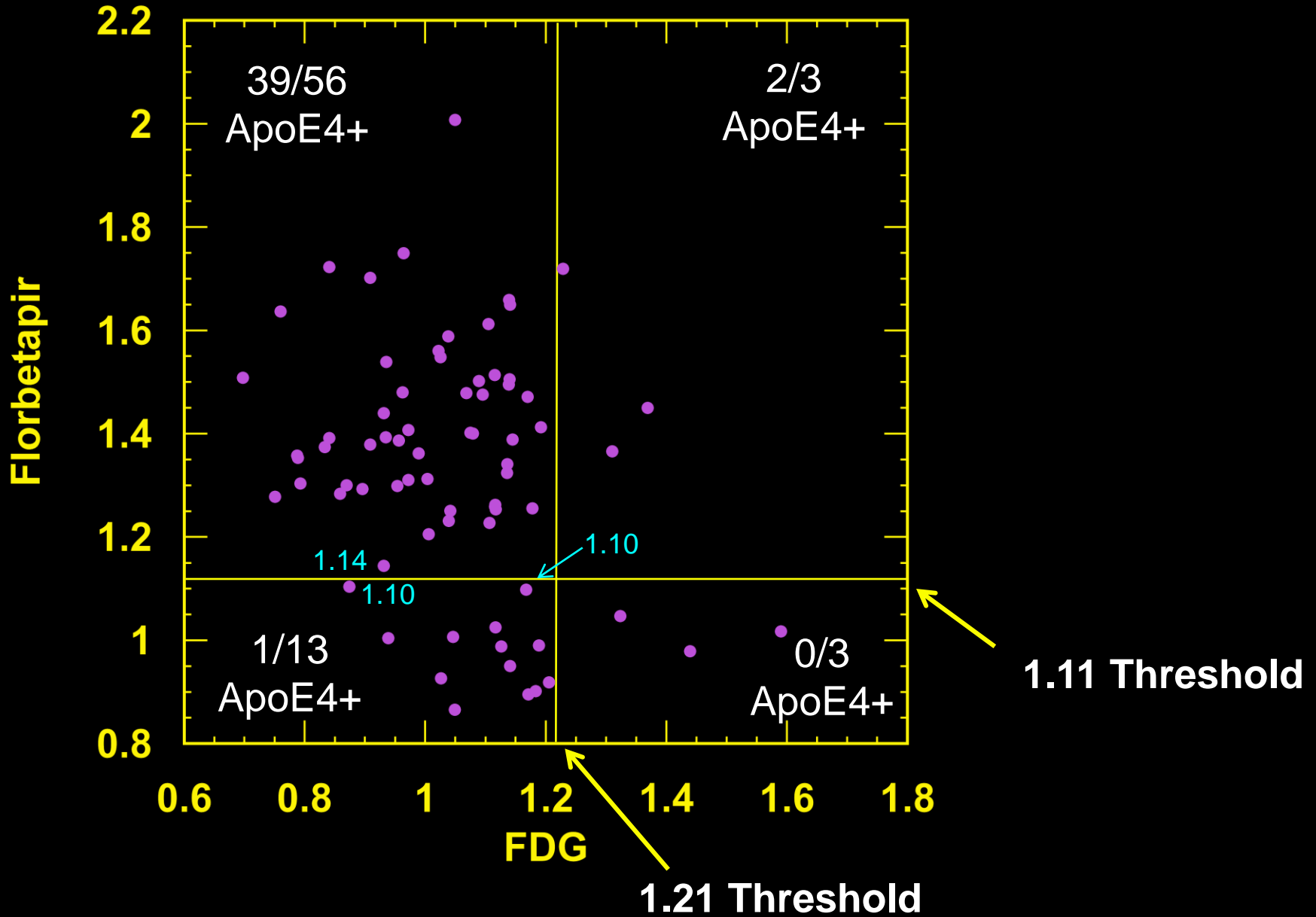
Florbetapir cortical mean



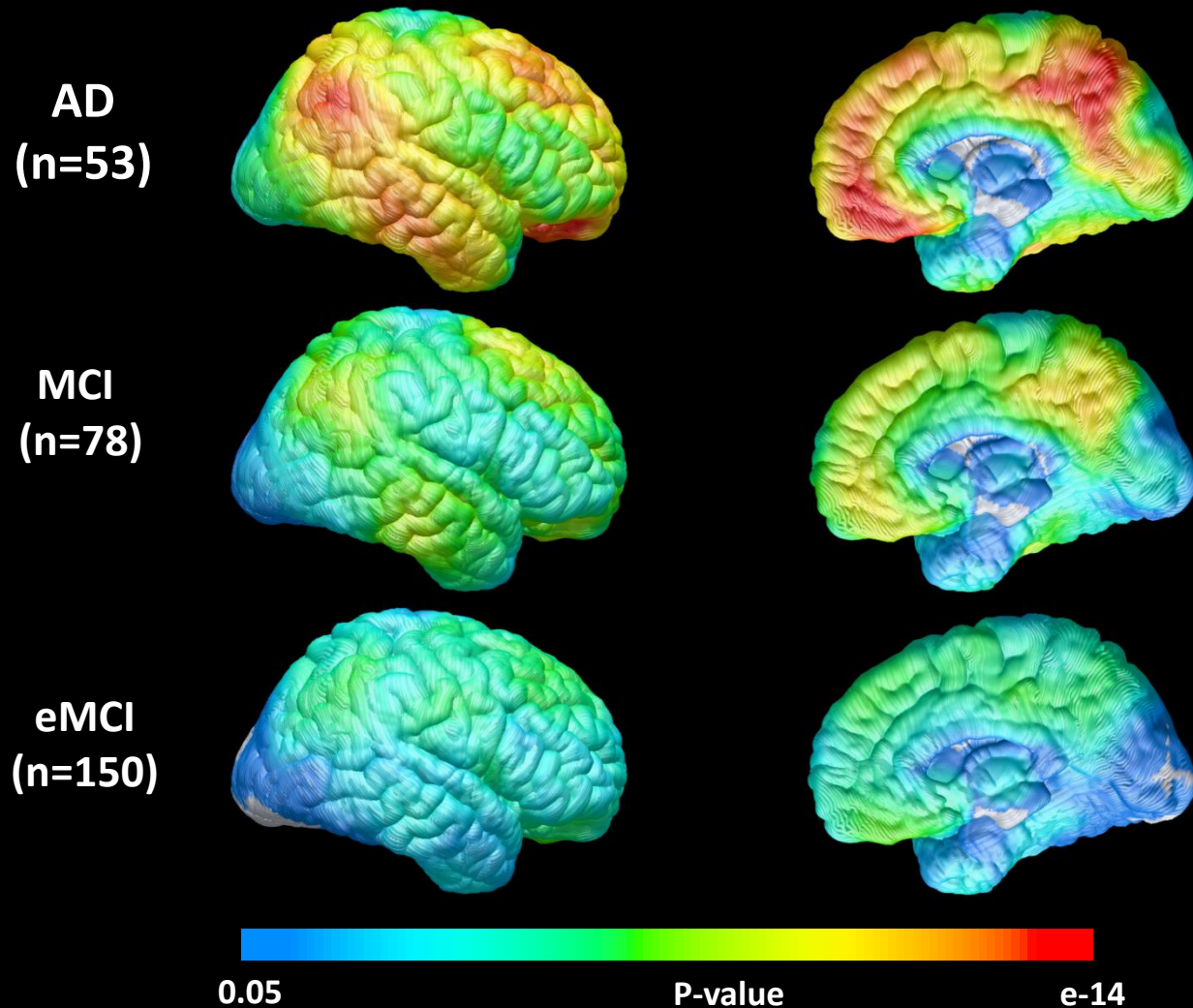
1.11 Threshold

1.21 Threshold

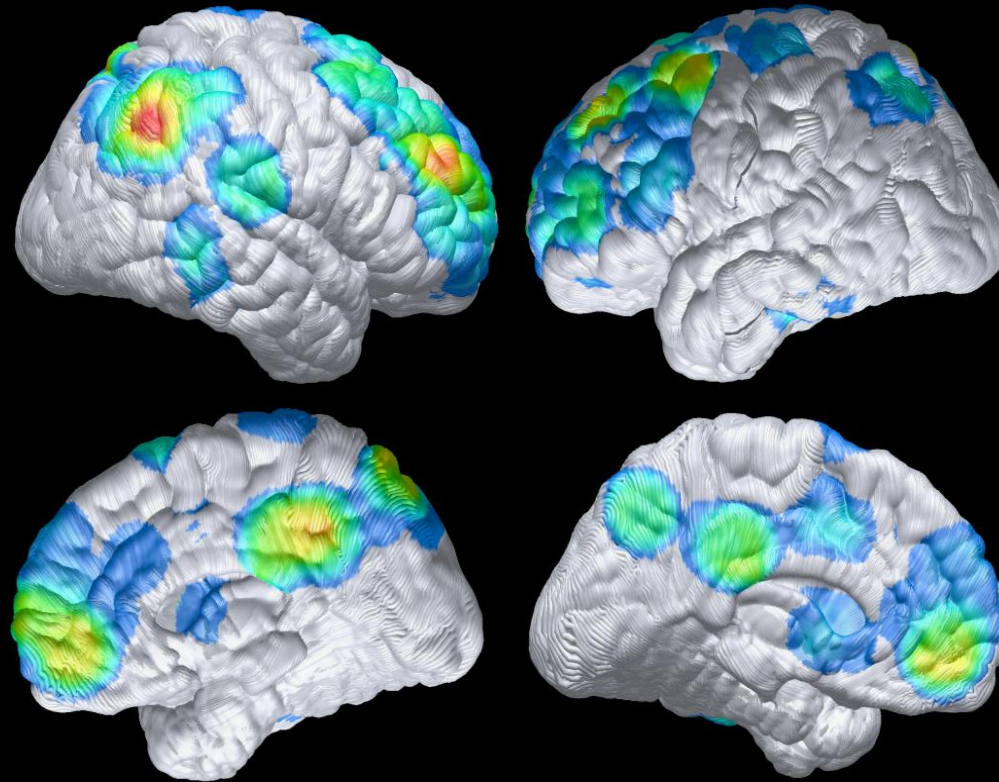
Alzheimer Cases



fibrillar A β deposition in ADNI subject groups
in comparison with 78 cognitively normal *APOE* $\epsilon 4$ non-carriers



cerebral glucose hypometabolism in 51 $A\beta$ -positive eMCI patients in comparison with 99 $A\beta$ -negative eMCI patients



0.05

P-value

e-4

ADNI Participants: Longitudinal analyses

| | Normal | MCI | |
|-----------------------------|--------|------|---|
| N | 72 | 81 | ← 37 (46%) converted from MCI to AD during followup |
| Age | 81 | 78 | |
| Sex, female (%) | 50% | 37% | |
| Education | 16 | 16 | |
| MMSE | 28.8 | 24.5 | |
| ADAS-cog | 6.1 | 15.3 | |
| FDG (meta-ROI mean) | 1.27 | 1.14 | |
| FDG % AD-like | 35% | 64% | |
| florbetapir (cortical mean) | 1.10 | 1.25 | |
| florbetapir % AD-like | 32% | 65% | |

Longitudinal associations: Diagnosis at time of ADNI enrollment
Mean followup = 4.5 yrs

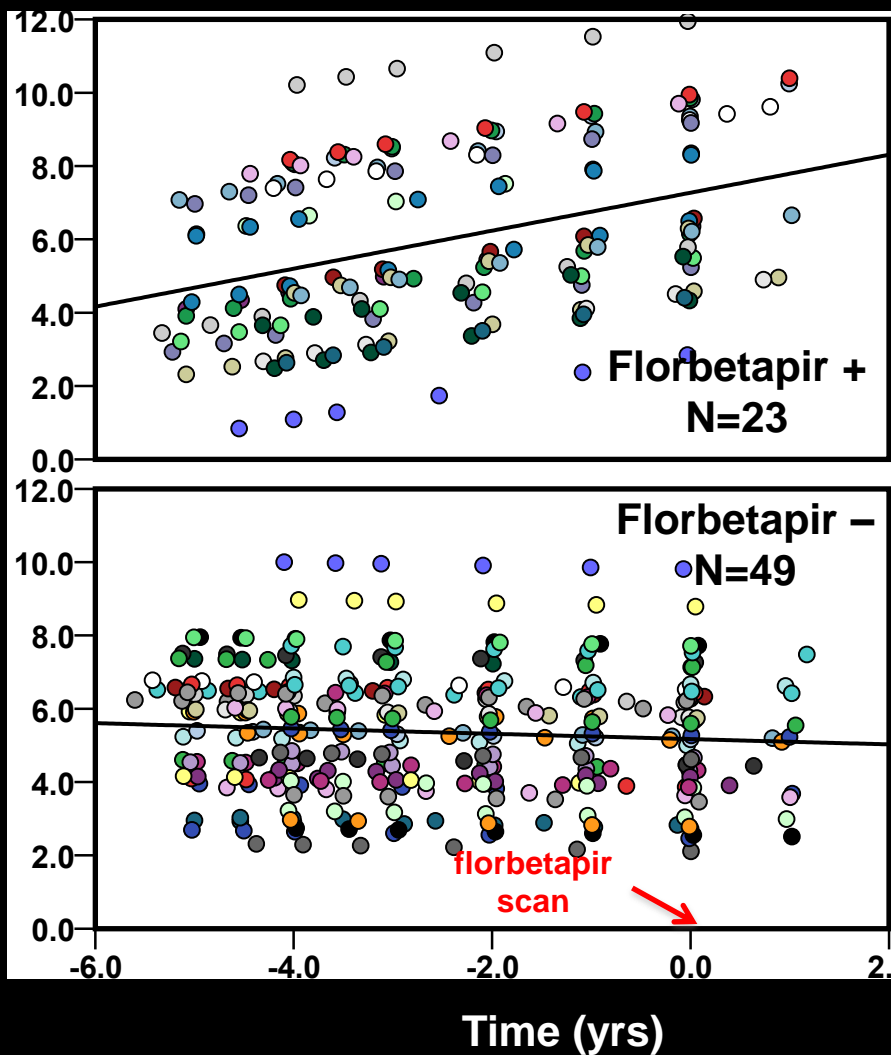
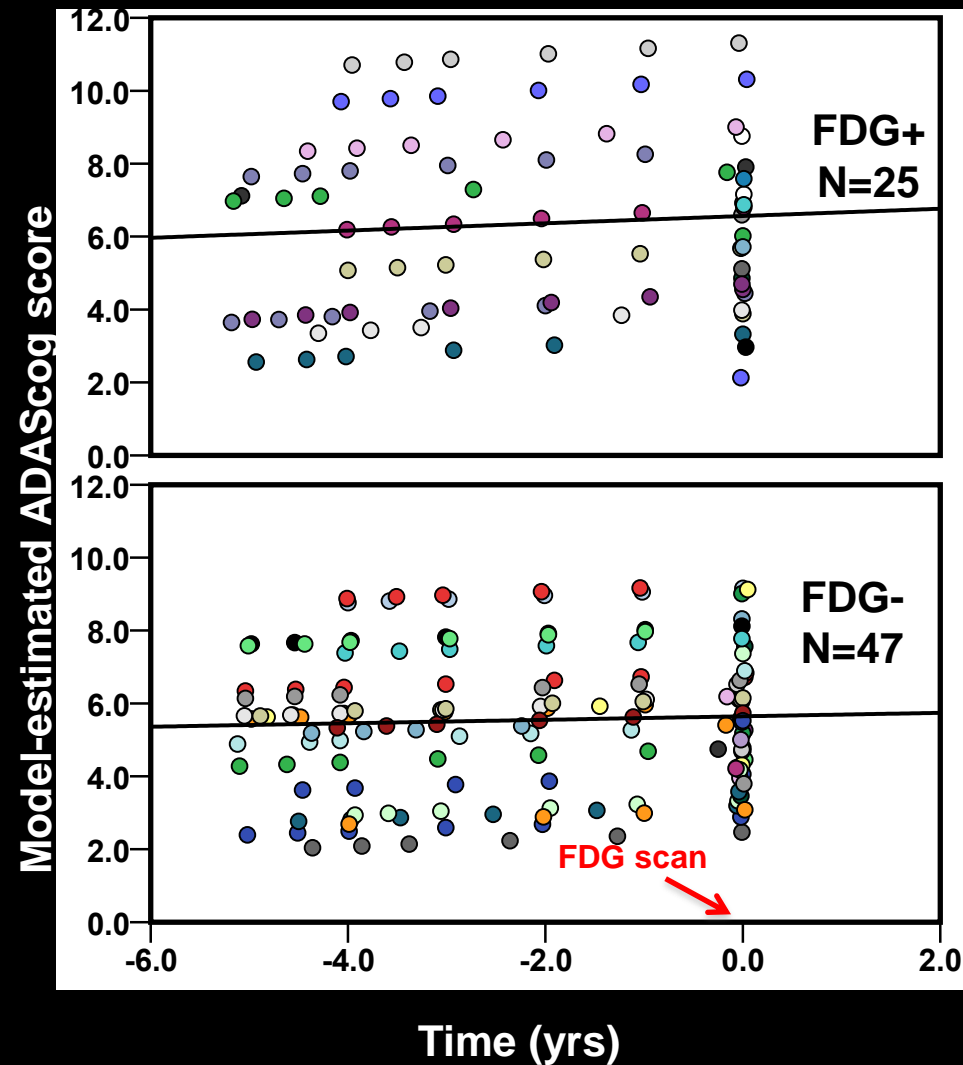
Mixed effects regression models examined concurrent florbetapir (+/-) and FDG (+/-) associations with longitudinal ADAS-cog measurements

Longitudinal Cognitive Decline

72 ADNI Normal Subjects

No difference in rate of decline

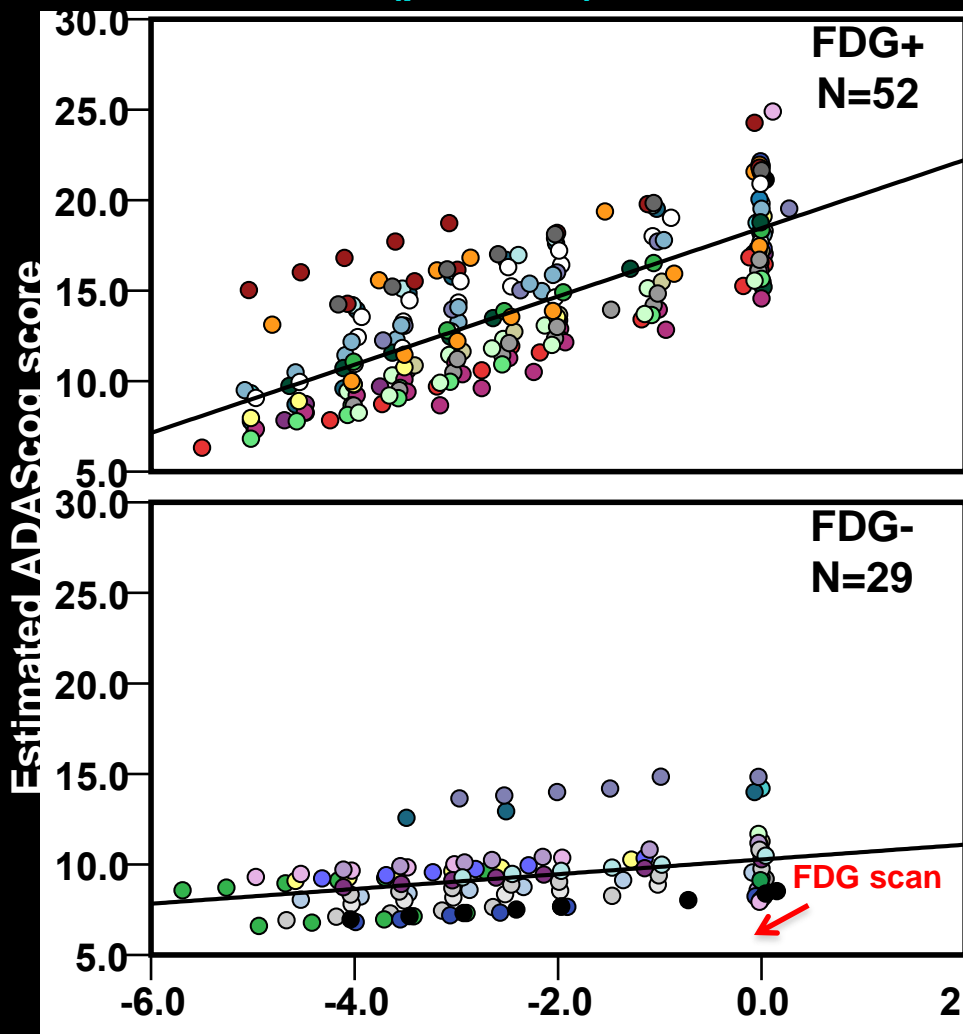
Florbetapir+ 0.5 pt/year
greater decline ($p < 0.001$)



Longitudinal cognitive decline in ADNI

81 ADNI MCI Patients

FDG+ 1.5 pt/yr greater decline
($p < 0.001$)



Acknowledgements

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Site PIs

Participants

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Mike Pontecorvo

Abhinay Joshi

Chris Breault