ADNI PET CORE

Washington DC

4/20

2015

Susan Landau, Allie Fero, Suzanne Baker, Bob Koeppe, Eric Reiman, Kewei Chen, Norman Foster, Chet Mathis, Julie Price

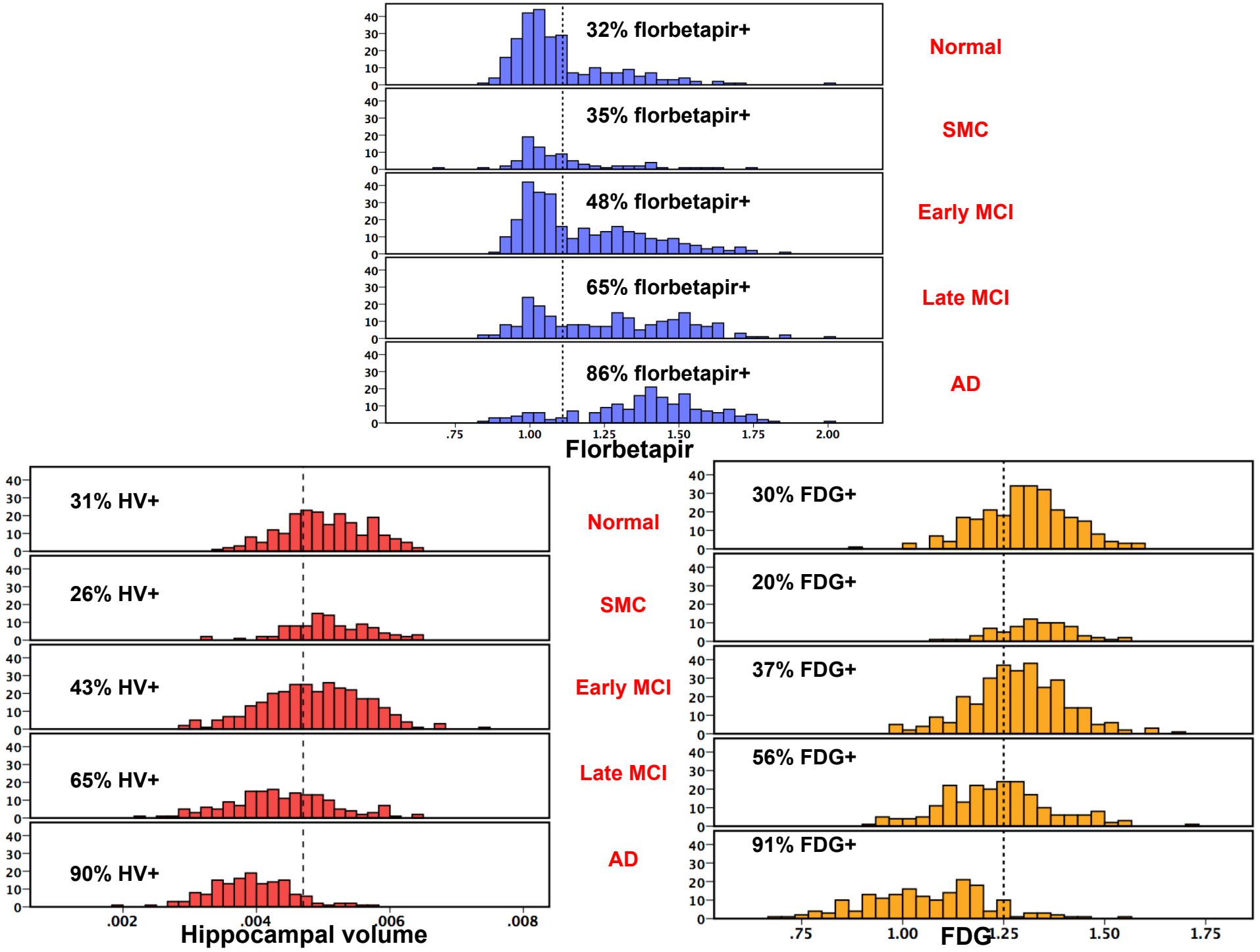
2015 Recipient: Society of Nuclear Medicine and Molecular Imaging Hal Anger Lectureship and Award

FDG scan counts (as of 04/14/15)

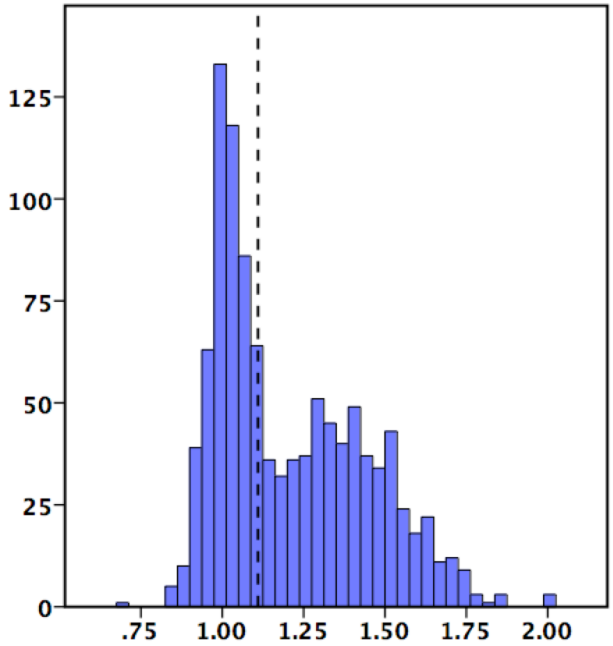
Number of FDG scans	N	SMC	EMCI	LMCI	AD	Total
1	343	106	307	410	241	1407
2	258	0	167	279	112	816
3	91	0	1	180	75	347
4	85	0	0	162	58	305
5	72	0	0	146	0	218
6	39	0	0	105	0	144
7	25	0	0	56	0	81
8	5	0	0	28	0	33
9	0	0	0	5	0	5
Total	**918**	**106**	**475**	**1371**	**486**	**3356**

Florbetapir scan counts (as of 04/14/15)

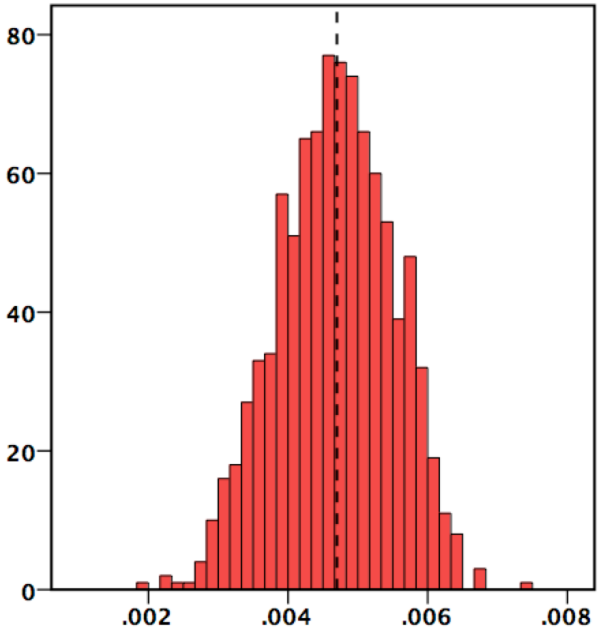
Number of Florbetapir scans	N	SMC	EMCI	LMCI	AD	Total
1	273	104	305	259	148	**1089**
2	201	7	211	165	27	**611**
3	19	0	33	16	0	**68**
Total	**493**	**111**	**549**	**440**	**175**	**1768**


32% florbetapir+
35% florbetapir+
48% florbetapir+
65% florbetapir+
86% florbetapir+
Normal
SMC
Early MCI
Late MCI
AD
.75
1.00
1.25
1.50
1.75
2.00
Florbetapir
31% HV+
26% HV+
43% HV+
65% HV+
90% HV+
.002
.004
.006
.008
Hippocampal volume
30% FDG+
20% FDG+
37% FDG+
56% FDG+
91% FDG+
FDG

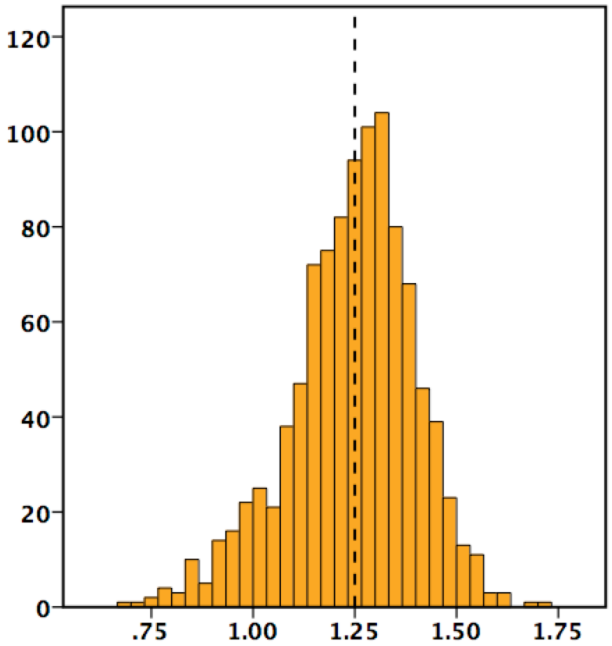
Distributions of 3 biomarkers across ~1000 ADNI participants



Cortical florbetapir SUVR

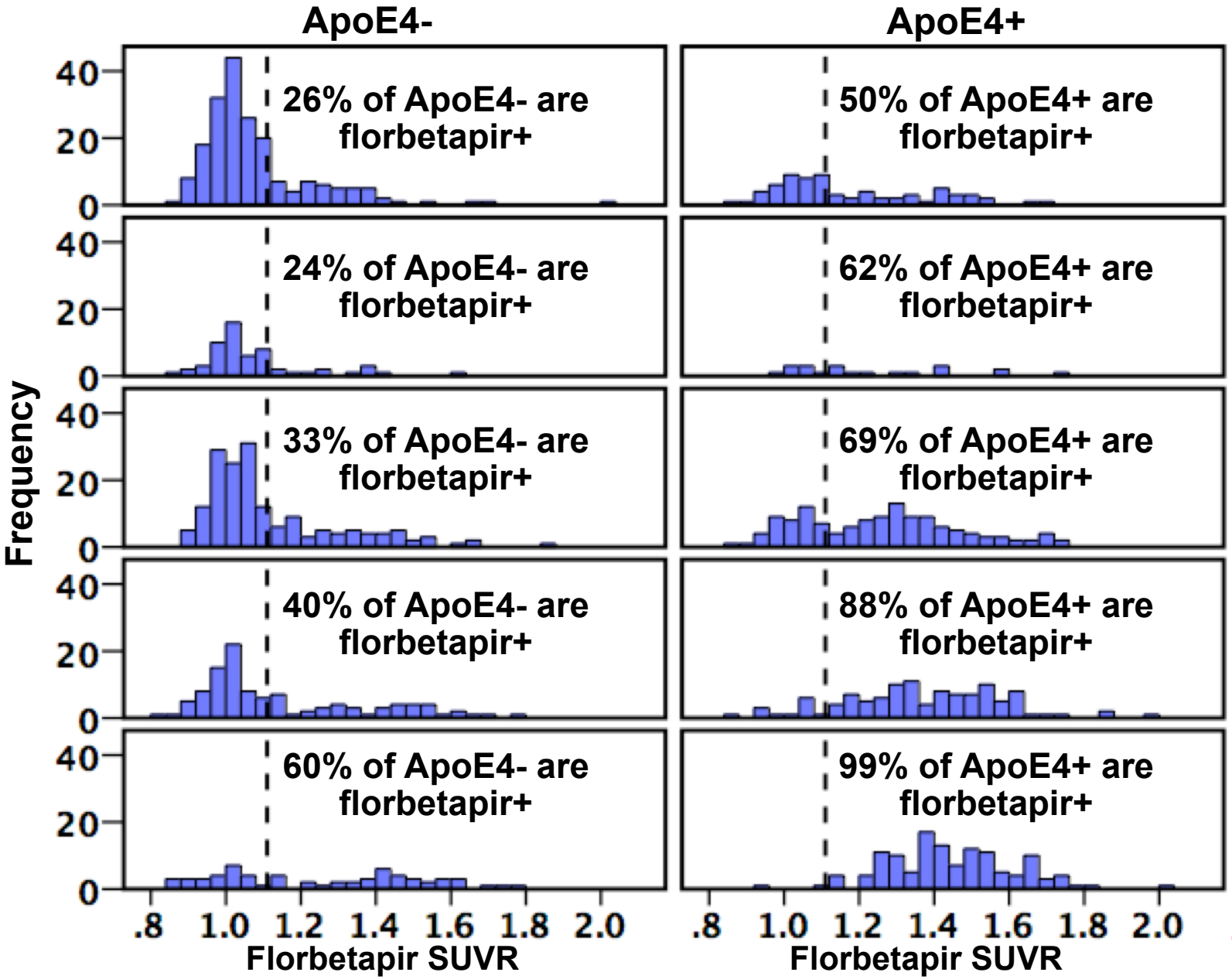


Hippocampal Volume (normalized by ICV)



FDG metaROI

ADNI florbetapir stratified by ApoE4 status



Normal
N=265

SMC
N=79

Early MCI
N=299

Late MCI
N=219

AD
N=188

Total N=1050

ELSEVIER

CrossMark

Alzheimer's & Dementia 11 (2015) 1-15

Alzheimer's & Dementia

Featured Articles

The Centiloid Project: Standardizing quantitative amyloid plaque estimation by PET

William E. Klunk[a,b,*], Robert A. Koeppe[c], Julie C. Price[d], Tammie L. Benzinger[e,f], Michael D. Devous, Sr.,[g,h], William J. Jagust[i], Keith A. Johnson[e,j], Chester A. Mathis[k], Davneet Minhas[d], Michael J. Pontecorvo[l], Christopher C. Rowe[m], Daniel M. Skovronsky[l], Mark A. Mintun[l]

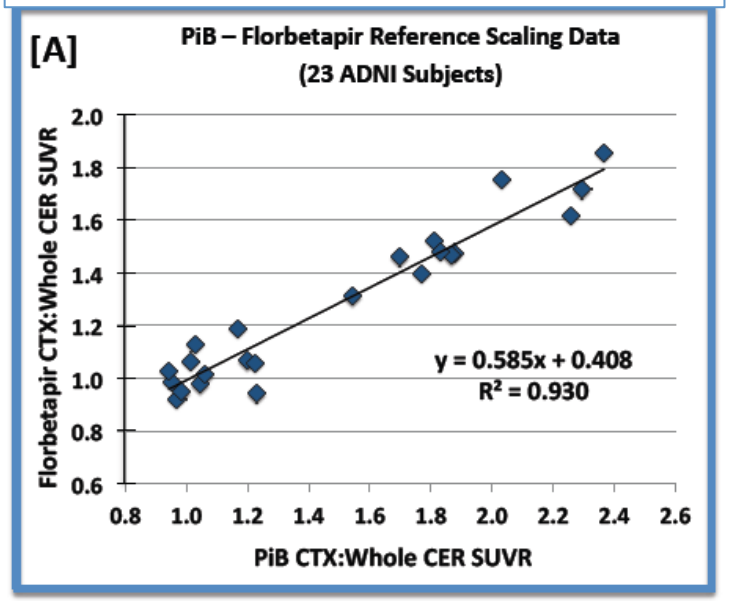
[a]*Department of Psychiatry, Massachusetts General Hospital, Boston, MA, USA*
[b]*Department of Neurology, University of Pittsburgh, Pittsburgh. PA, USA*
[c]*Department of Radiology, University of Michigan, Ann Arbor, MI, USA*
[d]*Department of Radiology, University of Pittsburgh, Pittsburgh, PA, USA*
[e]*Department of Radiology, Massachusetts General Hospital, Boston, MA, USA*
[f]*Department of Neurosurgery, Washington University, Saint Louis, MO, USA*
[g]*Department of Neurology, UT Southwestern Medical Center, Dallas, TX, USA*
[h]*Department of Radiology, UT Southwestern Medical Center, Dallas, TX, USA*
[i]*Helen Wills Neuroscience Institute, University of California Berkeley, Berkeley, CA, USA*
[j]*Department of Neurology, Massachusetts General Hospital, Boston, MA, USA*
[k]*Departments of Radiology, Pharmacology and Biological Chemistry, and Pharmaceutical Sciences, University of Pittsburgh, Pittsburgh, PA, USA*
[l]*Avid Radiopharmaceuticals, Philadelphia, PA, USA*
[m]*Department of Nuclear Medicine and Centre for PET, Austin Health, Melbourne, VIC, Australia*

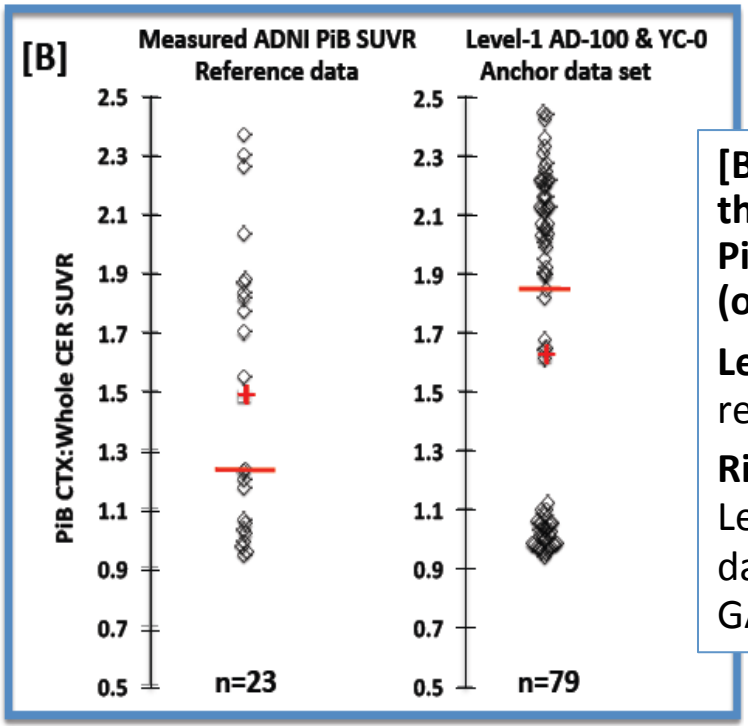
Standardize reporting of amyloid PET results by performing studies with F18 ligands and PIB in the same subjects and translating SUVr measures to a scale from 0-100

Approximate Centiloid Scaling

- *CTX ROI (Reference ROI: Whole cerebellum)*
- *median and mean depicted by red bar and cross, respectively*

[A] ADNI reference data: Linear correlation between PiB and Florbetapir SUVR (scans acquired within 24 months)





[B] Comparison of the distribution of PiB SUVR values (or SUVRs):

Left: ADNI reference data

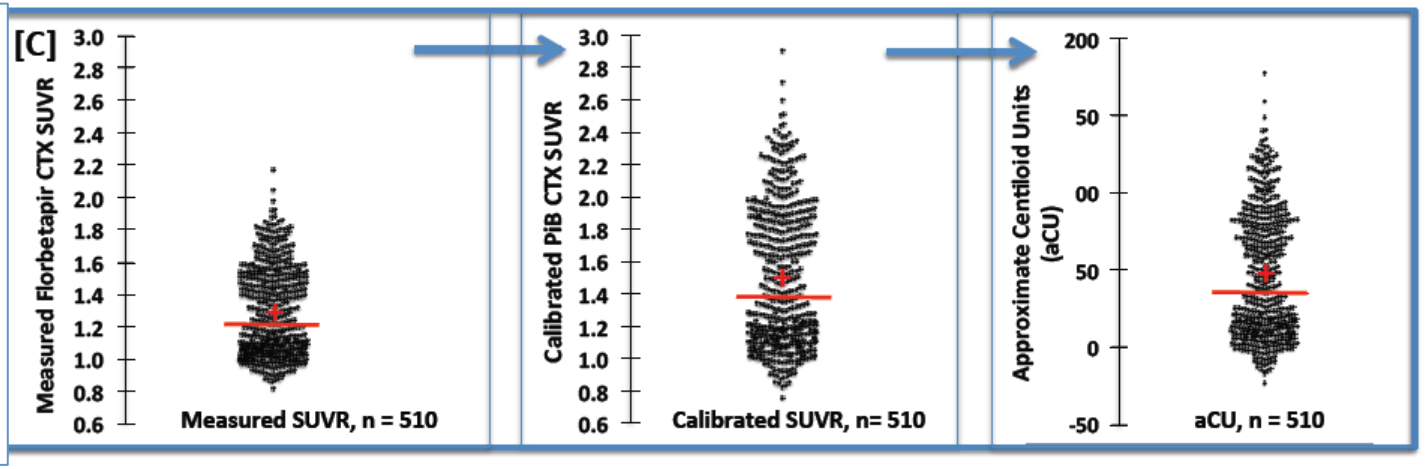
Right : Centiloid Level-1 anchor data (available via GAAIN website)

[C] Scaling Steps:

Left: 510 measured ADNI Florbetapir SUVRs

Middle: Calculated "PiB-calibrated" Florbetapir SUVRs

Right: The converted approximate Centiloid units, or aCU



Julie Price/Chet Mathis

NeuroImage 108 (2015) 450–459

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Improved longitudinal [^{18}F]-AV45 amyloid PET by white matter reference and VOI-based partial volume effect correction

Matthias Brendel [a], Marcus Högenauer [a], Andreas Delker [a], Julia Sauerbeck [a], Peter Bartenstein [a], John Seibyl [b], Axel Rominger [a,*], for the Alzheimer's Disease Neuroimaging Initiative [1]

[a] Dept. of Nuclear Medicine, University of Munich, Germany
[b] MNI, New Haven, USA

Improved Power for Characterizing Longitudinal Amyloid-β PET Changes and Evaluating Amyloid-Modifying Treatments with a Cerebral White Matter Reference Region

Kewei Chen[1–4], Auttawut Roontiva[1,4], Pradeep Thiyyagura[1,4], Wendy Lee[1,4], Xiaofen Liu[1,4], Napatkamon Ayutyanont[1,4], Hillary Protas[1,4], Ji.Luo Luo[1,4], Robert Bauer[1,4], Cole Reschke[1,4], Daniel Bandy[1,4], Robert A. Koeppe[5], Adam S. Fleisher[4,6,7], Richard J. Caselli[4,8], Susan Landau[9], William J. Jagust[9], Michael W. Weiner[10–12], and Eric M. Reiman[1,4,13,14], for the Alzheimer's Disease Neuroimaging Initiative

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increases, to characterize their relationship to longitudinal clinical declines, and to evaluate Aβ-modifying treatments in randomized clinical trials.

Key Words: Alzheimer disease; florbetapir PET; biomarkers; image analysis; statistical power; clinical trial sample size

J Nucl Med 2015; 56:560–566
DOI: 10.2967/jnumed.114.149732

Measurement of Longitudinal β-Amyloid Change with ^{18}F-Florbetapir PET and Standardized Uptake Value Ratios

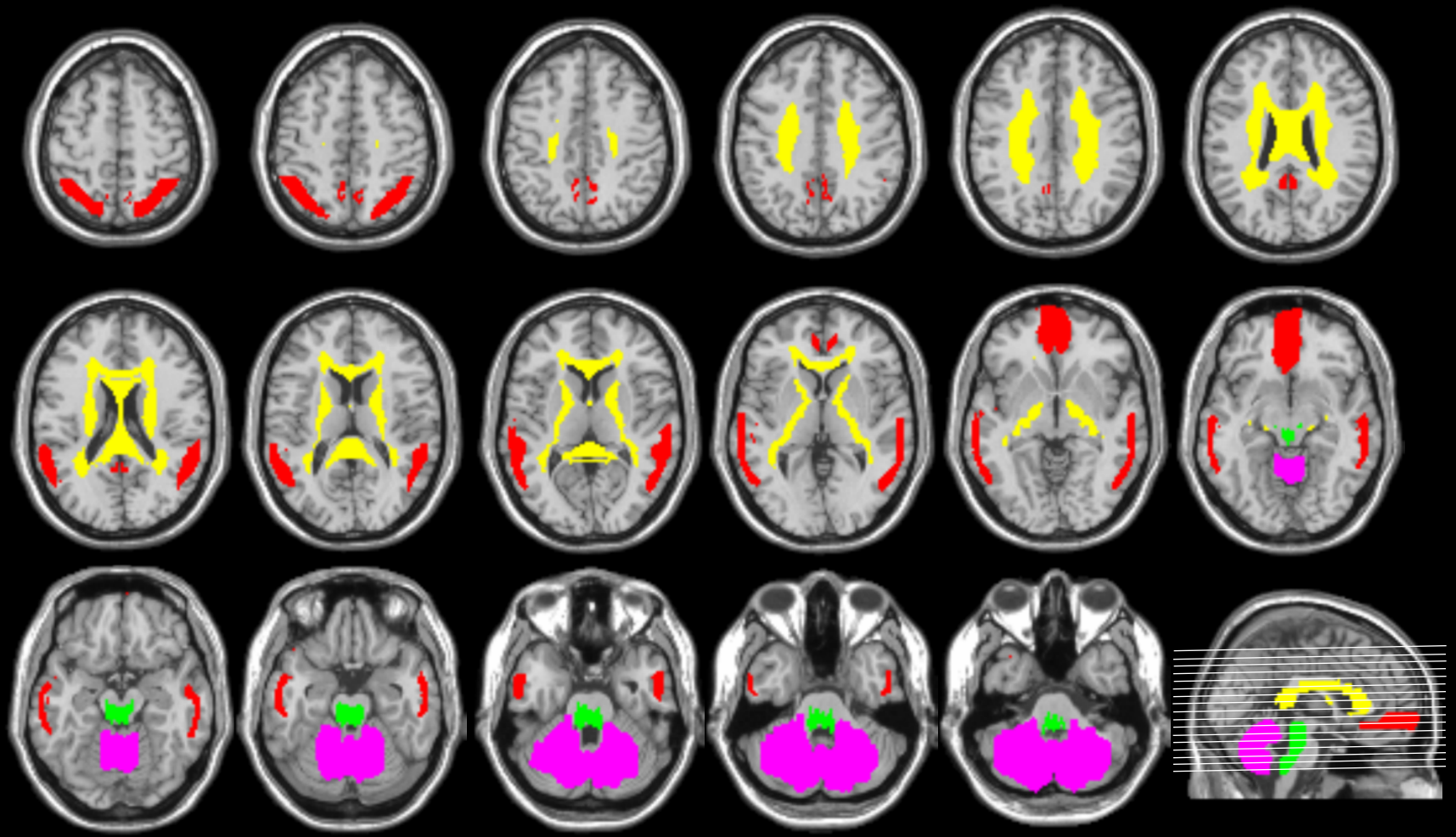
Susan M. Landau[1,2], Allison Fero[2], Suzanne L. Baker[2], Robert Koeppe[3], Mark Mintun[4], Kewei Chen[5], Eric M. Reiman[5], and William J. Jagust[1,2]

[1]Helen Wills Neuroscience Institute, University of California, Berkeley, California; [2]Life Sciences Division, Lawrence Berkeley National Laboratory, Berkeley, California; [3]Radiology Department, University of Michigan, Ann Arbor, Michigan; [4]Avid Radiopharmaceuticals, Inc., Philadelphia, Pennsylvania; and [5]Banner Alzheimer's Institute, Phoenix, Arizona

Key Words: amyloid; Alzheimer's disease; PET imaging

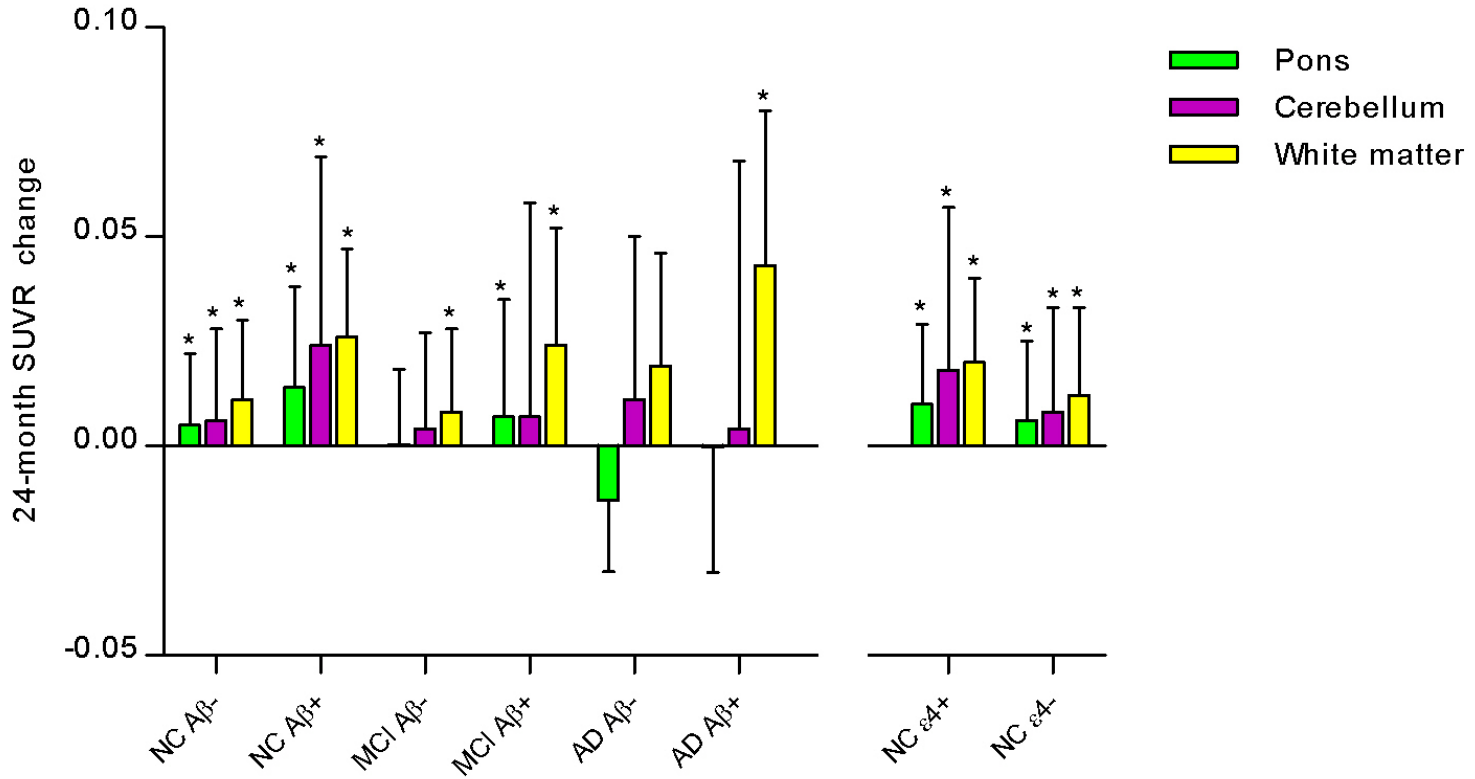
J Nucl Med 2015; 56:567–574
DOI: 10.2967/jnumed.114.148981

Mean Cortical and Cerebellar, Pontine and White Matter ROIs

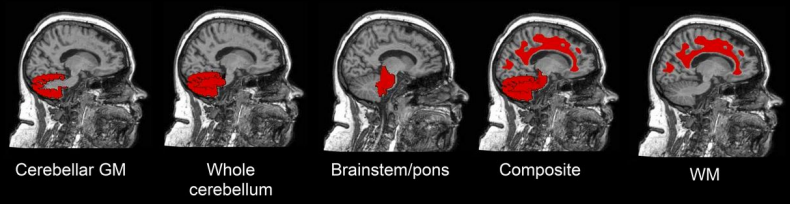


Chen, et al., JNM, 2015

Greater Power to Track 24-mo SUVR Increases Using a Cerebral White Matter ROI

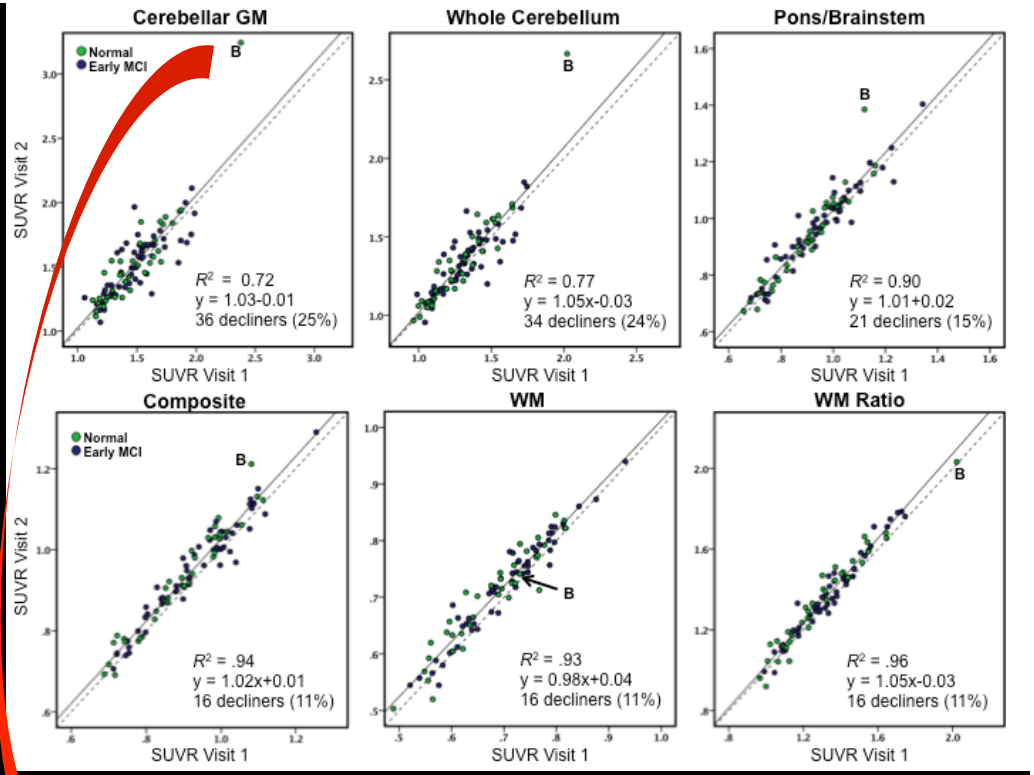


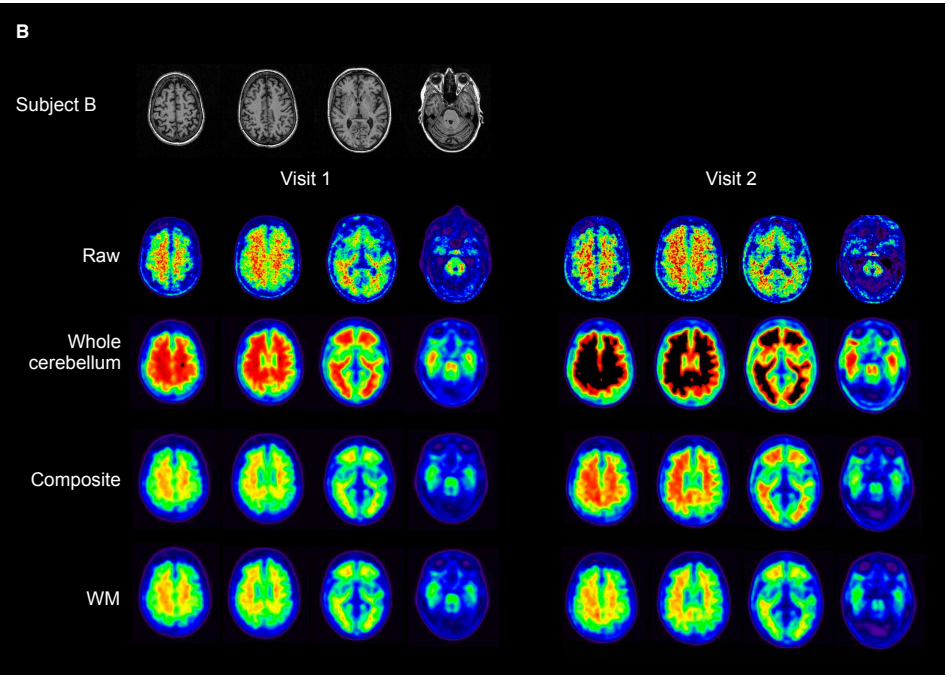
Chen, et al., JNM, 2015



Subjects with positive CSF Aβ at baseline, normal or EMCI, should be increasing florbetapir SUVR from visit 1 to visit 2

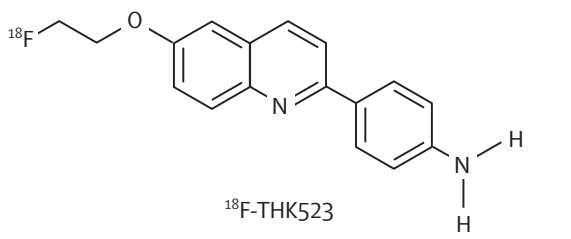
Fewer decliners with white matter in reference region



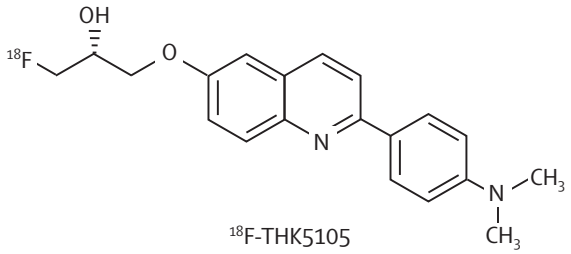


Landau et al, J Nucl Med 2015

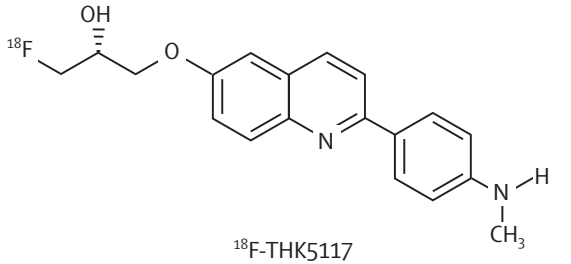
Tau Ligands: Molecular Families



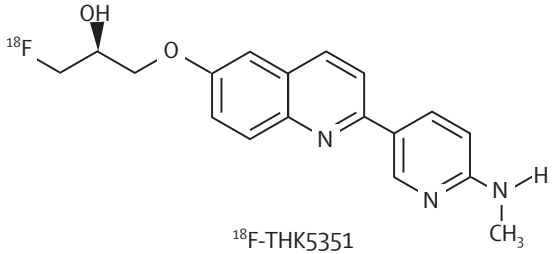
^{18}F-THK523



^{18}F-THK5105

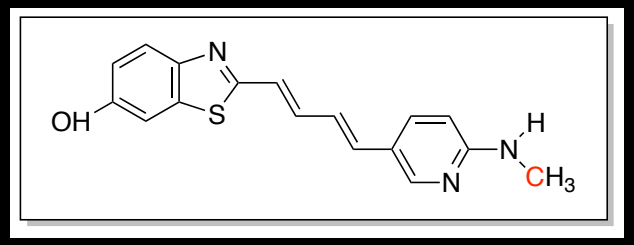


^{18}F-THK5117

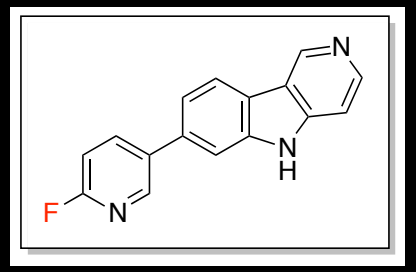


^{18}F-THK5351

THK Series - Tohuku Compounds

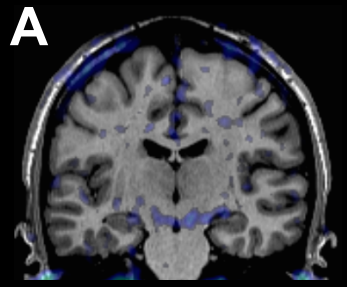


[^{11}C]PBB-3

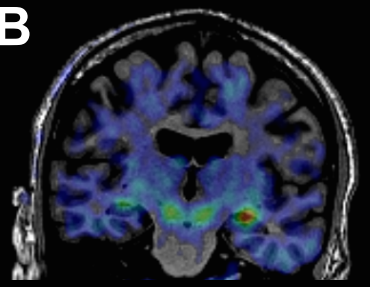


[^{18}F]T807 ➔ [^{18}F]AV-1451

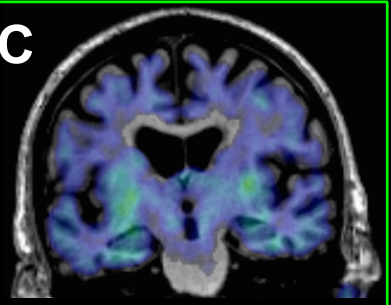
Tau Imaging with [^{18}F]AV-1451



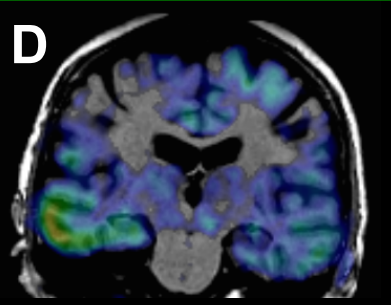
Control: Male 22
Hippocampus: 0.8
Entorhinal Ctx: 0.9
Temporal Ctx: 0.9



Control: Male 74
Hippocampus: 1.3
Entorhinal Ctx: 1.2
Temporal Ctx: 1.1

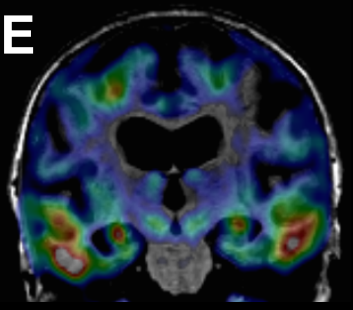


Control: Male 90
Hippocampus: 1.4
Entorhinal Ctx: 1.2
Temporal Ctx: 1.2



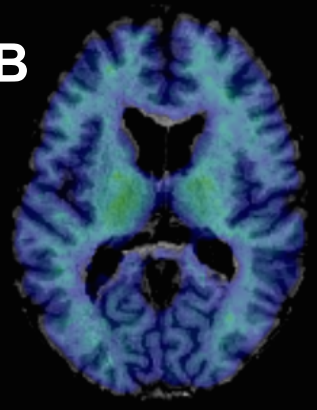
Control: Female 75
Hippocampus: 1.3
Entorhinal Ctx: 1.4
Temporal Ctx: 1.6

AV-1451

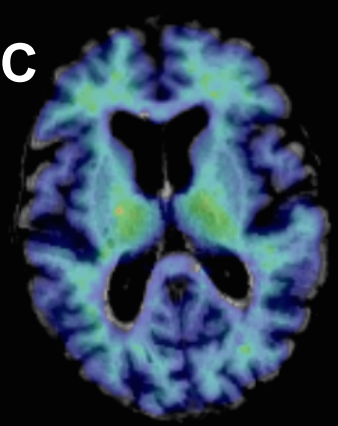


AD: Female 75
MMSE 17
Hippocampus: 1.7
Entorhinal Ctx: 1.7
Temporal Ctx: 2.3

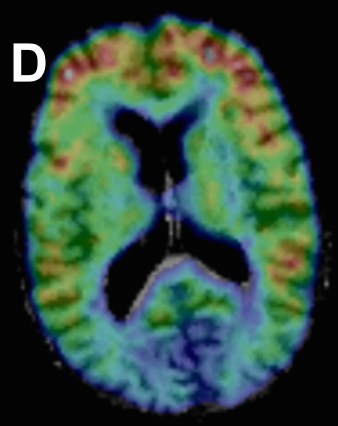
PIB



DVR=1.05

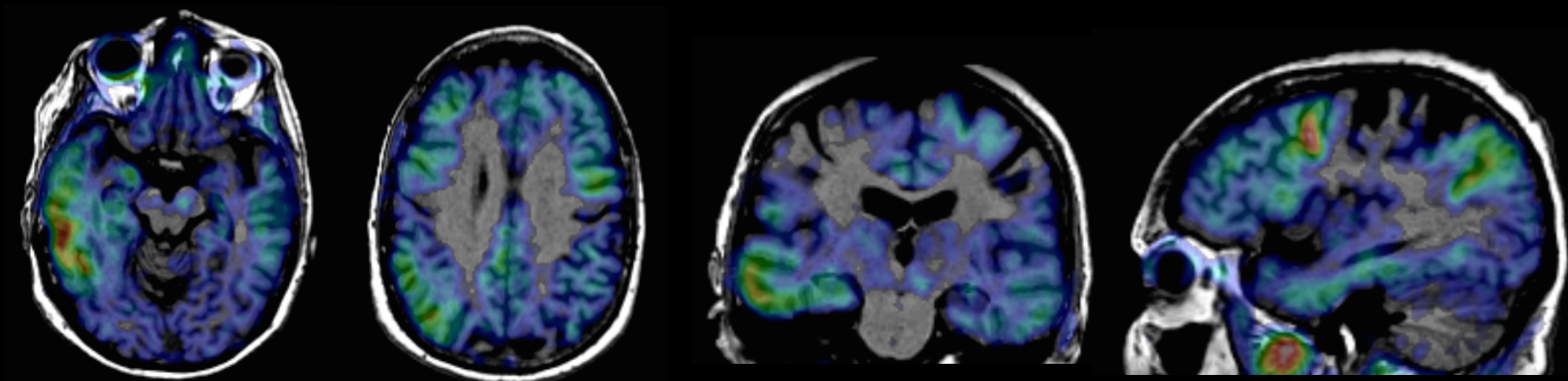


DVR=1.03

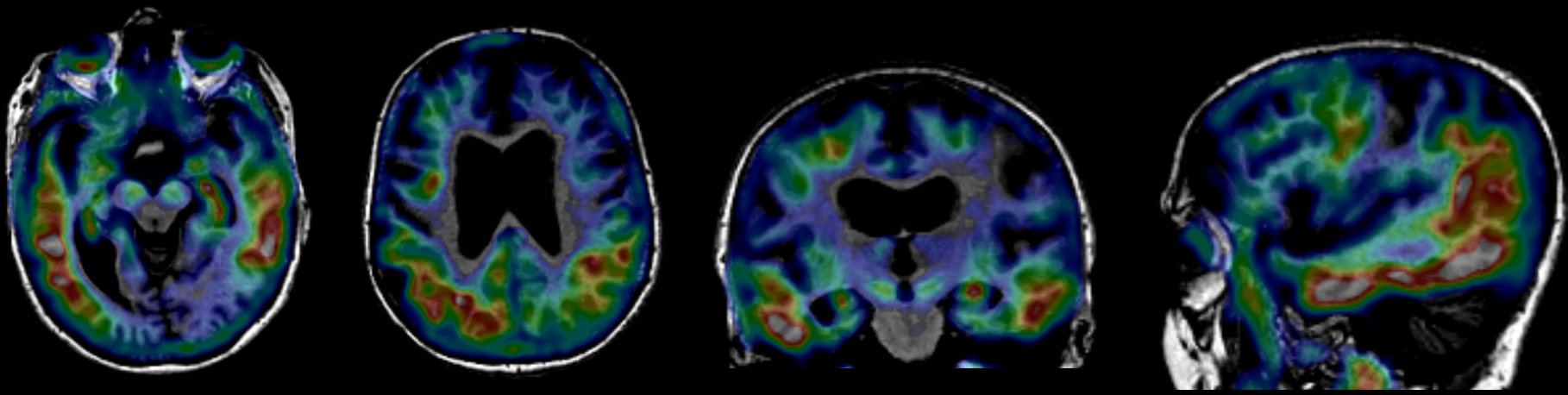


DVR=1.76

Case D (75 year old control, DVR = 1.76)



Case E (AD, 75 year old, MMSE=17)

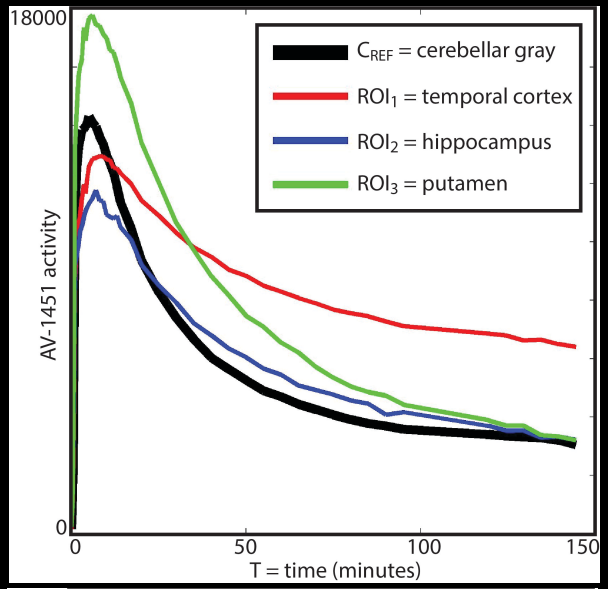


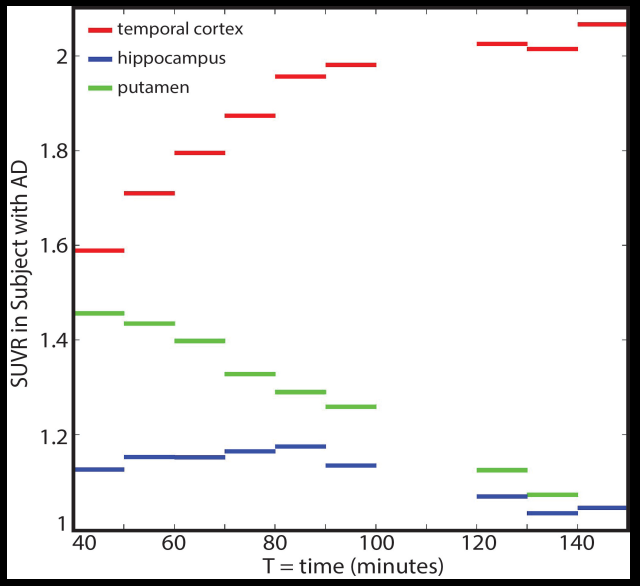
[^{18}F]AV-1451 Pharmacokinetics

Time Activity Curves

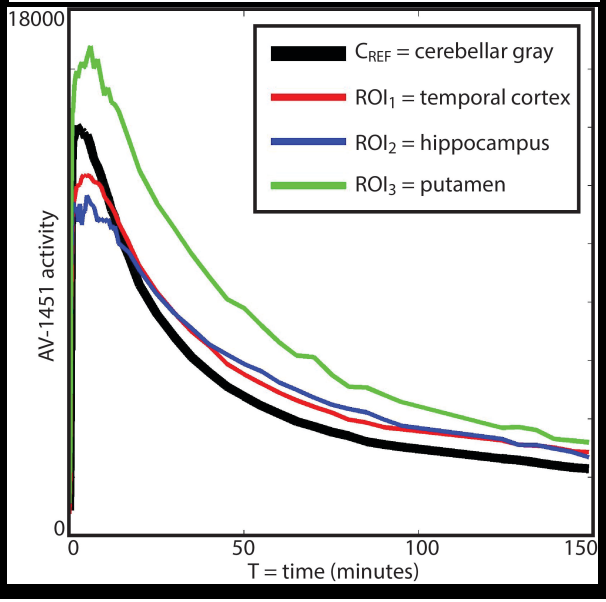
SUVRs over time

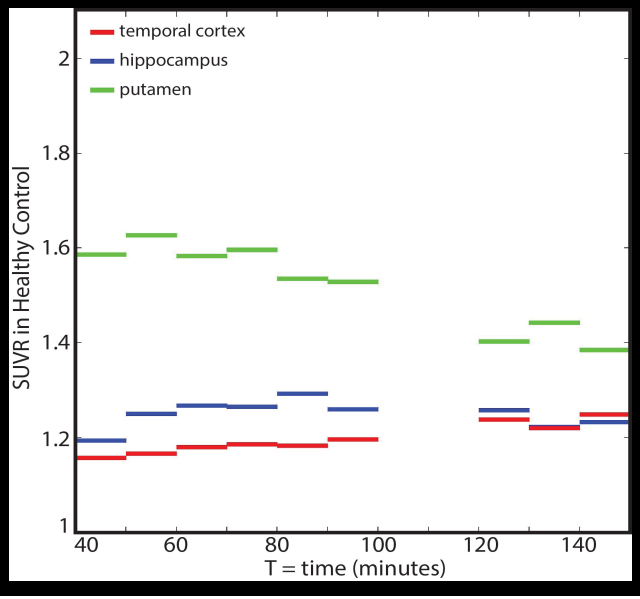
AD





Control

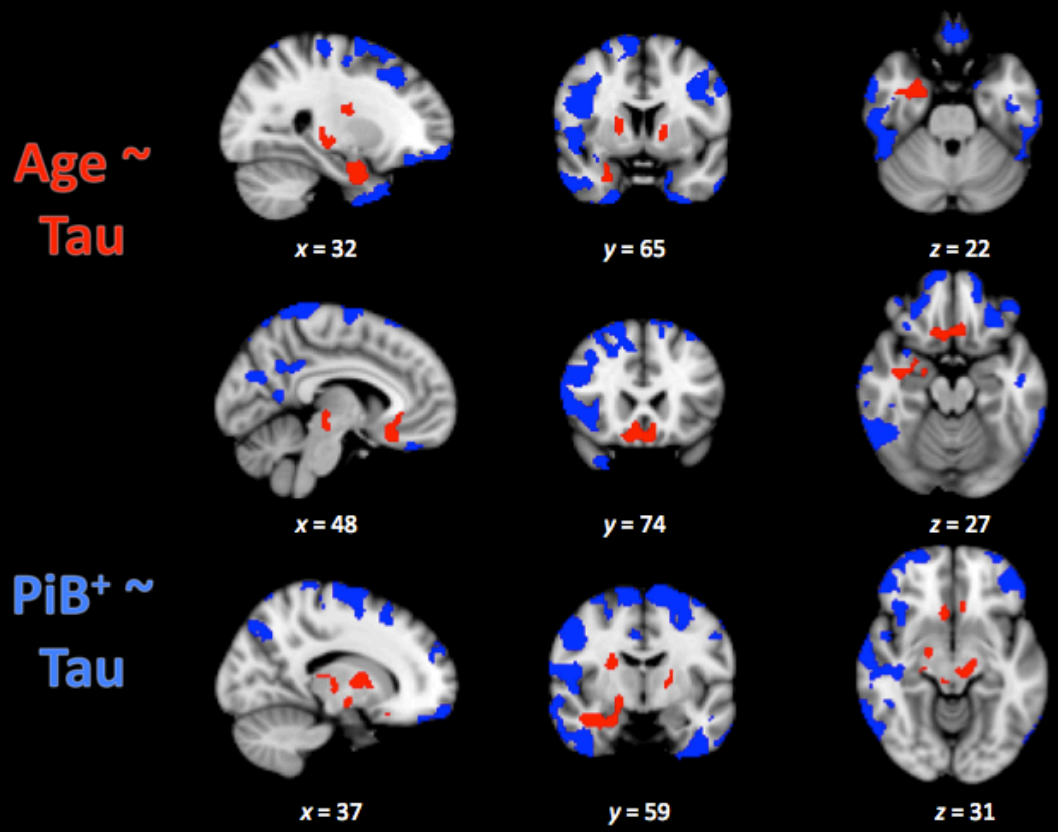


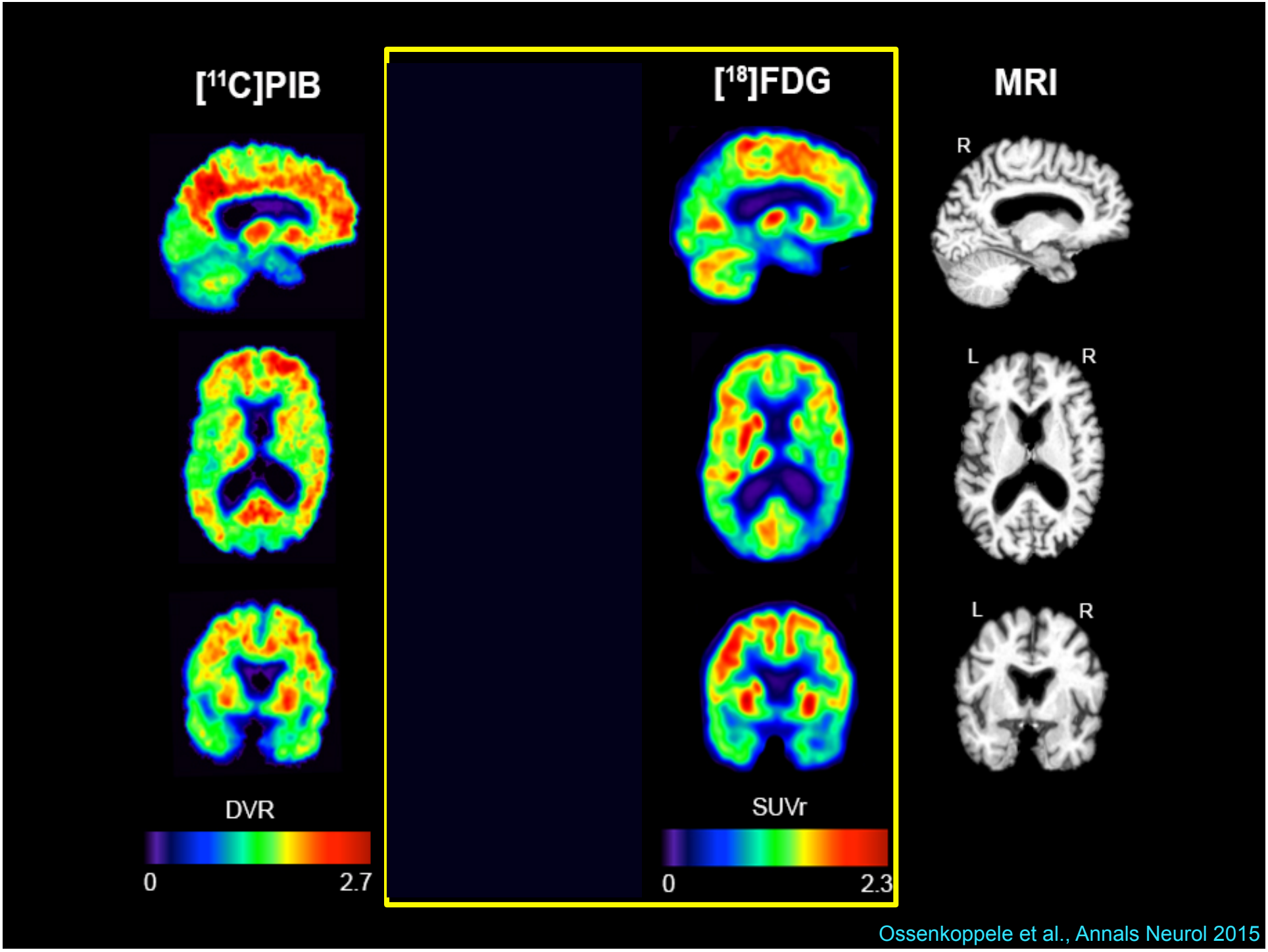


Tau Deposition by Age and Aβ

18 Cognitively Normal People Mean Age 79

Significant associations with
age and PIB

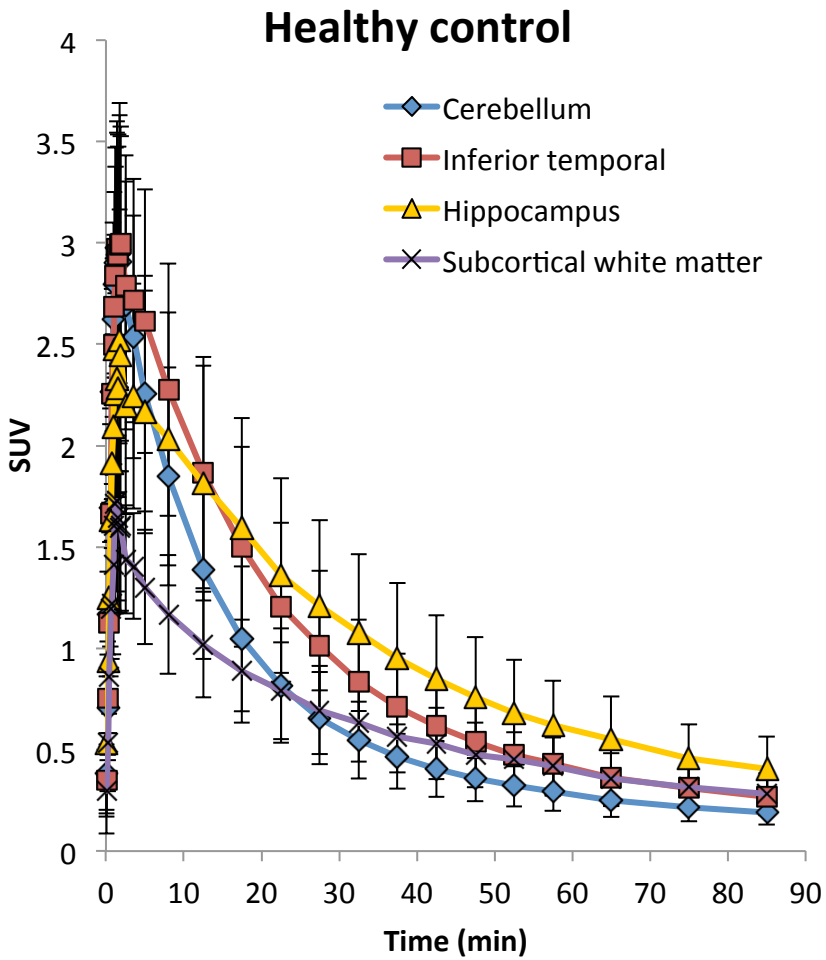


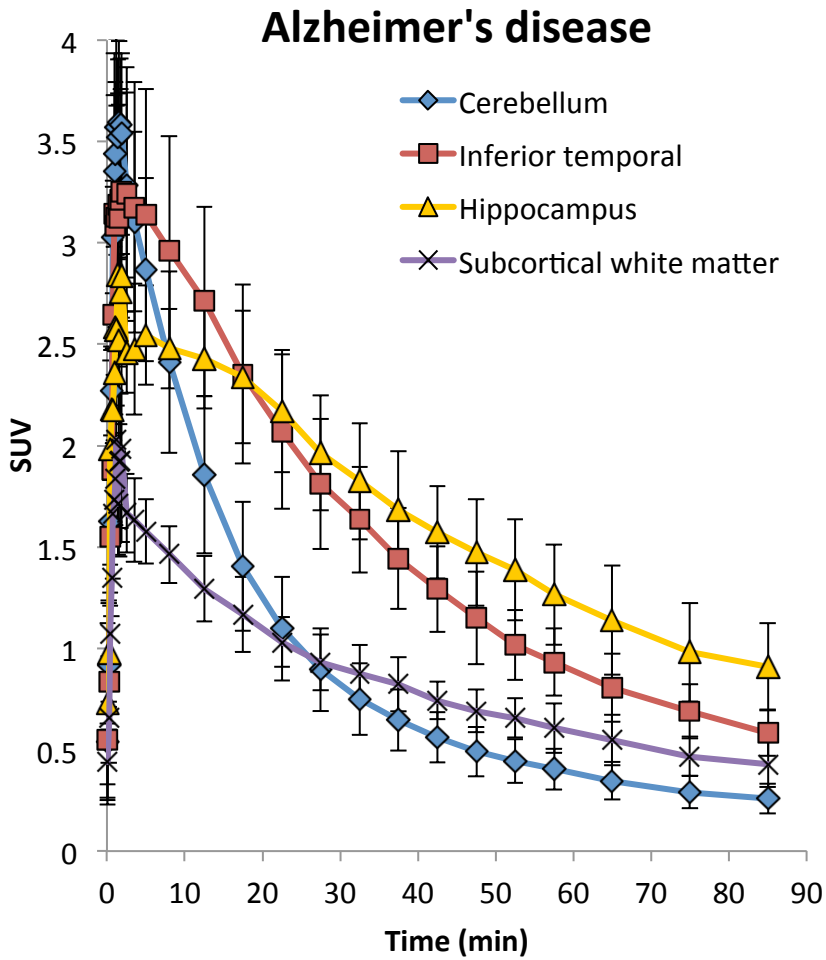


Ossenkoppele et al., Annals Neurol 2015

Time activity curves of [^{18}F]THK-5351

Healthy controls vs AD patients





ADNI3 Specific Aims

Continue Amyloid Imaging every 2 years

- All continuing subjects and new

Multiple amyloid imaging agents

Tau Imaging every year

- All continuing subjects and new

Eliminate FDG?

Major Hypotheses

Tau accumulation will conform to Braak staging

Tau accumulation will occur in MTL in Aβ negative controls

The presence of Aβ in controls and MCI patients will be associated with neocortical tau

Longitudinal accumulation of tau in neocortex will be more rapid in those with Aβ

Tau Imaging will be related to cognition cross-sectionally and longitudinally

Amyloid Imaging in ADNI3

Multiple amyloid imaging agents are planned

- Florbetapir (amyavid)
- Florbetaben (neuraceq)
- Flutemetamol (vizamyl)????

Companies to perform centiloid standardization

- Compound vs PIB
- Publicly available data

Delivery to a reasonable number of sites

Tau Imaging: Tracer Characteristics

Multisite Study

- Tracer delivery to multiple sites
- Management of regulatory issues is clear
- PET data acquisition protocol is simple, well tolerated, reliable

Tracer "validation"

- Preclinical data showing specificity, affinity, brain uptake
- Pharmacokinetics are favorable
- Clinical data in a reasonable number of subjects with diverse diagnoses
- Data analysis methods yield results with face validity, parallel the biology

Full kinetic models in comparison to SUVr

Plans for tau Imaging in ADNI3

To the extent possible, application will review the state of the field as of mid-2015

Application will propose [^{18}F]AV-1451 for multisite tau imaging in ADNI3

Application will outline the features of acceptable tracers and note that we will use the best tracer at the time ADNI3 starts

FDG?

Pros

Parallels phenotype/correlates with behavior

Relationship to tau?

May be predictive of outcomes

Cons

Another scan – subject burden

Is FDG being included in clinical trials?

ADNI already has considerable longitudinal FDG data