ADNI PET CORE

Vancouver BC
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ADNI FDG scan counts

Number of FDG scans	N	SMC	EMCI	LMCI	AD	Total
1	343	106	306	409	241	1408
2	258		167	279	112	816
3	92		1	181	75	349
4	85			162	58	305
5	72			146		218
6	39			105		144
7	25			56		81
8	5			28		33
9				5		5
Total	919	106	474	1371	486	3359

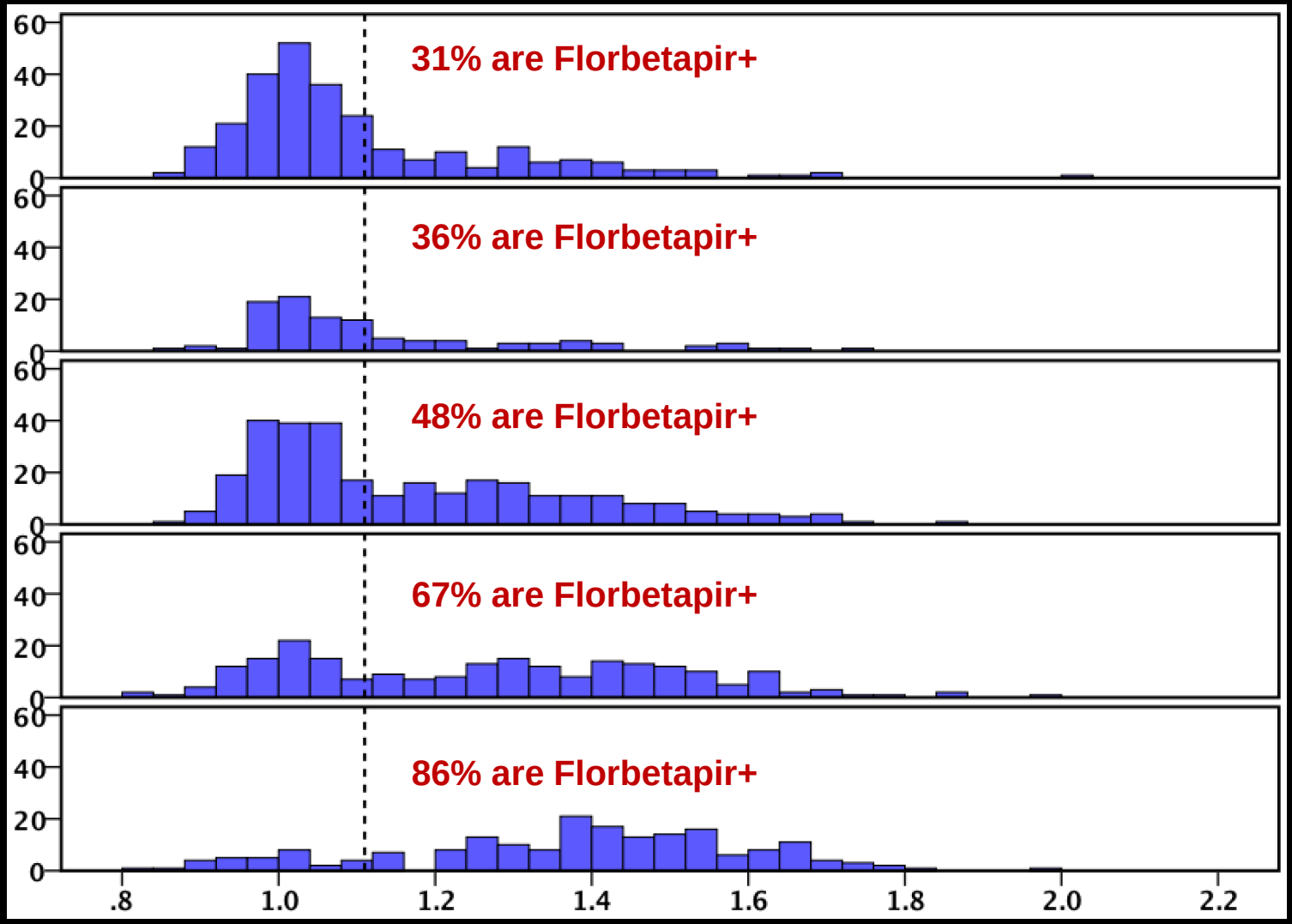
ADNI Florbetapir scan counts

Number of Florbetapir scans	N	SMC	EMCI	LMCI	AD	Total
1	264	104	303	224	193	1089
2	210	74	218	150	49	701
3	93	0	94	49	5	241
Total	567	178	615	423	247	2031

ADNI AV1451 scan counts

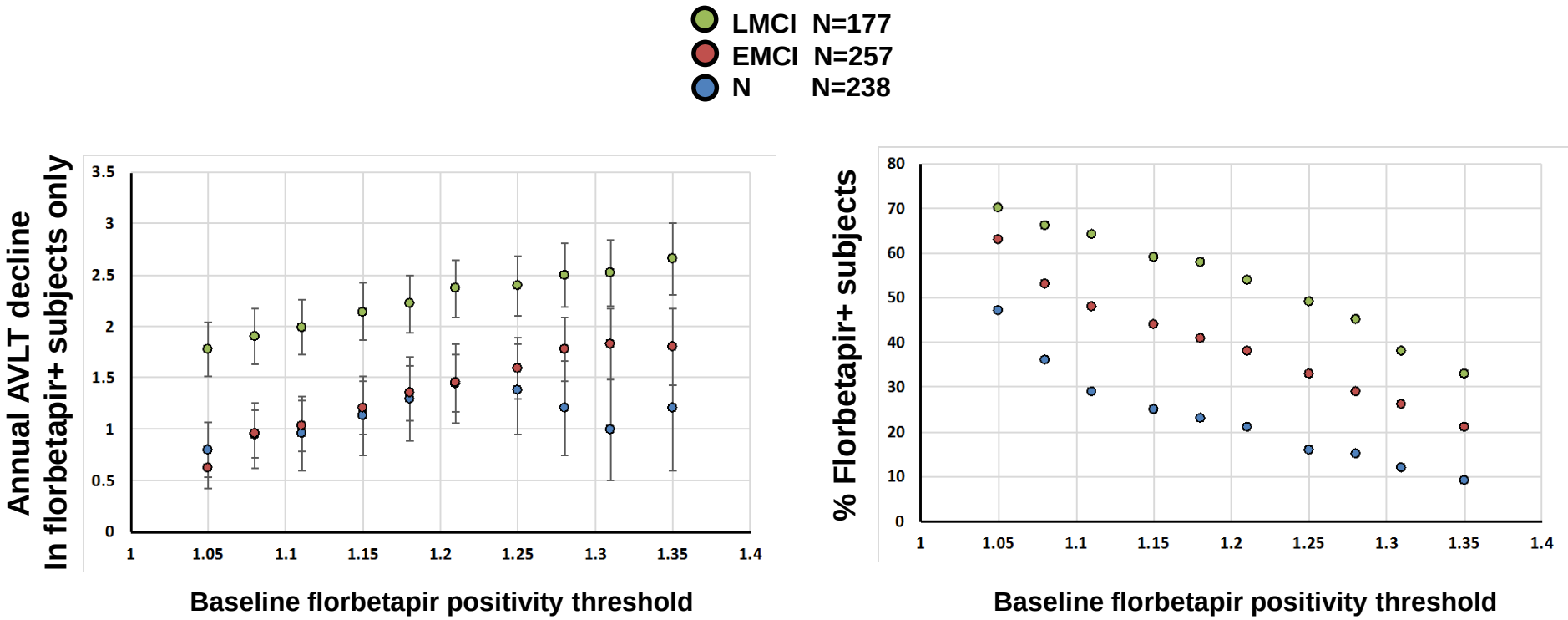
Number of AV1451 scans	N	SMC	EMCI	LMCI	AD	Total
1	7	8	8	11	1	35

Baseline Florbetapir Distribution



Total N=1089

Does Baseline Florbetapir Threshold Affect Rate of Cognitive Decline?



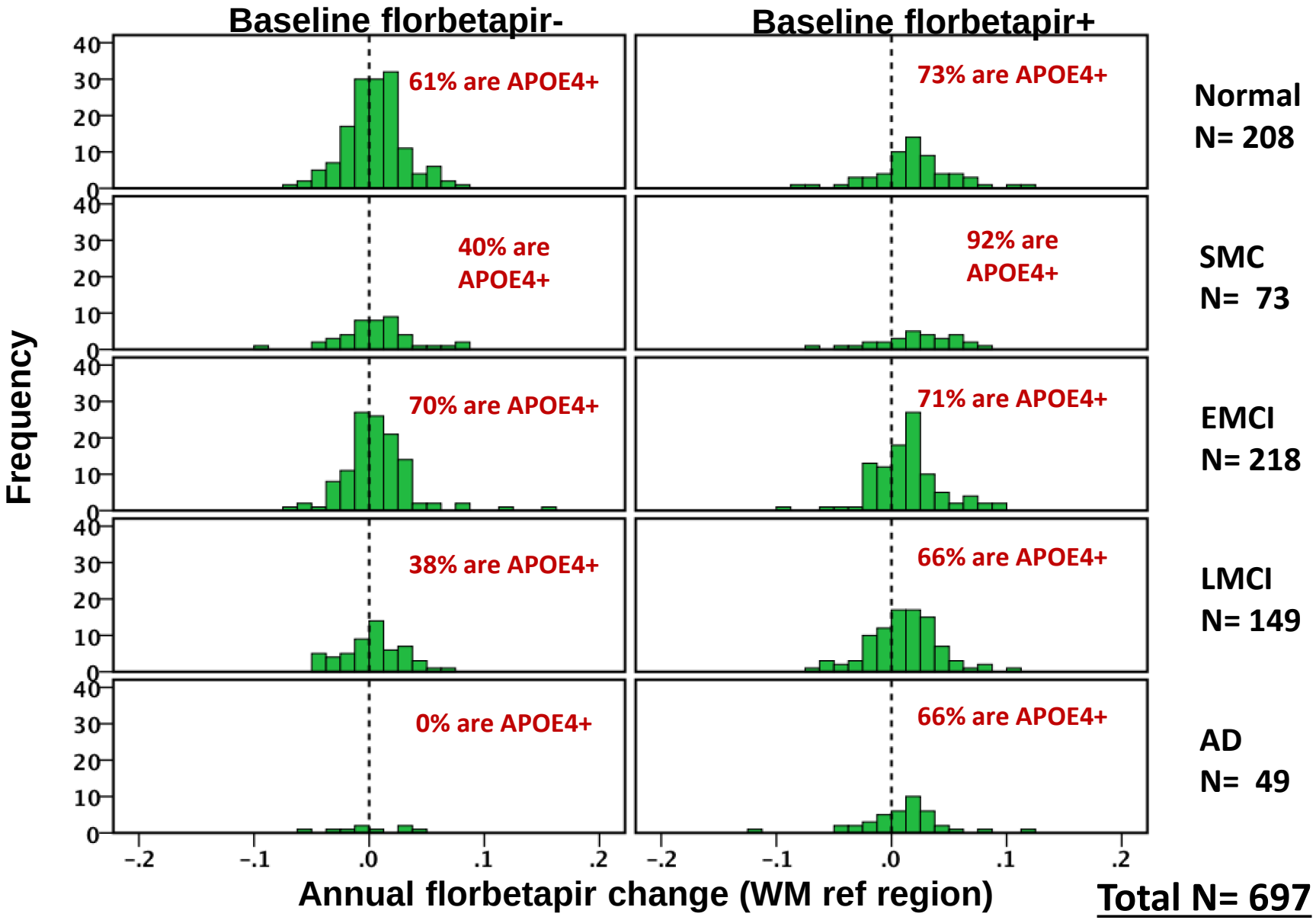
Rate of Decline Plateaus at ~ SUVR 1.25

Proportion of subjects positive at 1.25 = 50% (MCI), 35% (EMCI), 15% (N)

Subjects with >1.5 yr AVLT followup

Linear mixed effects models, adjusting for age, sex, education, and APOE4 status, with random intercept and slope

Florbetapir annual change distribution



≥2 yr Florbetapir Trajectories

Baseline florbetapir -
Baseline florbetapir +

Nonaccumulators

78% of Florbetapir+ are Accumulators

N= 208

51% of Florbetapir- are Accumulators (15% convert to +)

76% of Florbetapir+ are Accumulators

N= 73

59% of Florbetapir- are Accumulators (20% convert to +)

71% of Florbetapir+ are Accumulators

N= 218

58% of Florbetapir- are Accumulators (15% convert to +)

67% of Florbetapir+ are Accumulators

N= 149

58% of Florbetapir- are Accumulators (11% convert to +)

68% of Florbetapir+ are Accumulators

N= 49

44% of Florbetapir- are Accumulators (0% convert to +)

Florbetapir SUVR annual change

60 70 80 90 100

Age

Total N= 697

≥4 yr Florbetapir Trajectories

Baseline florbetapir -
Baseline florbetapir +

Nonaccumulators

91% of Florbetapir+ are Accumulators

N= 80

56% of Florbetapir- are Accumulators (17% convert to +)

77% of Florbetapir+ are Accumulators

N= 90

63% of Florbetapir- are Accumulators (23% convert to +)

76% of Florbetapir+ are Accumulators

N= 44

58% of Florbetapir- are Accumulators (5% convert to +)

33% of Florbetapir+ are Accumulators

N= 5

50% of Florbetapir- are Accumulators (0% convert to +)

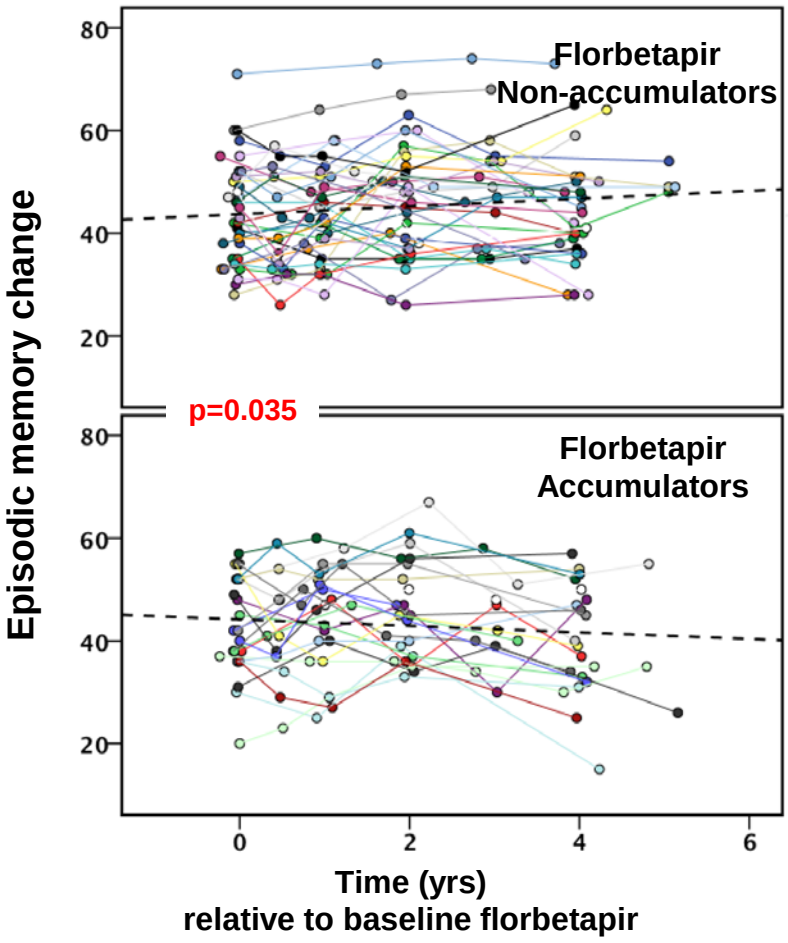
Florbetapir SUVR annual change

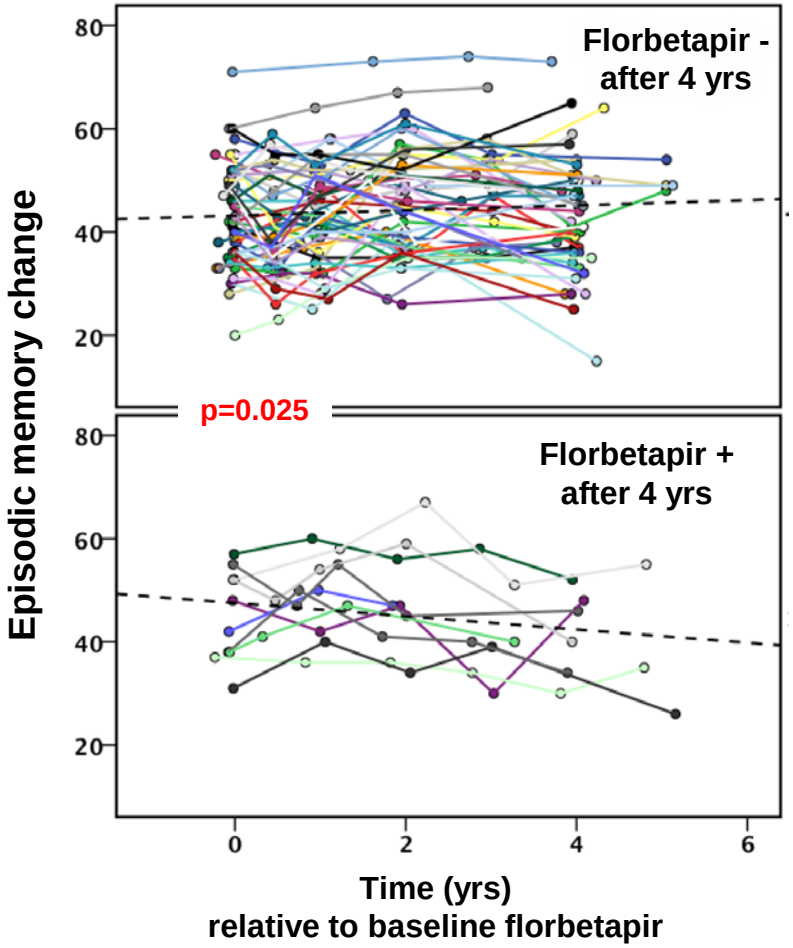
80 90 100 60 70 80 90 100

Age

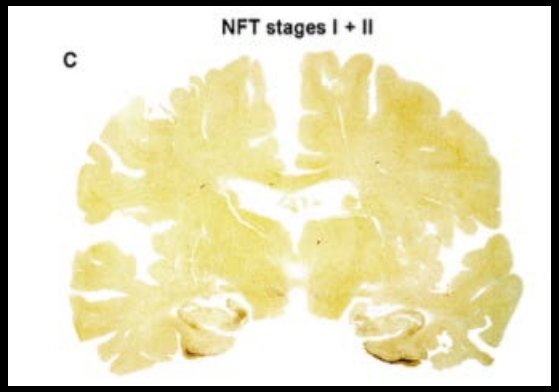
Total N= 219

Negative normal subjects who accumulate florbetapir more likely to decline cognitively

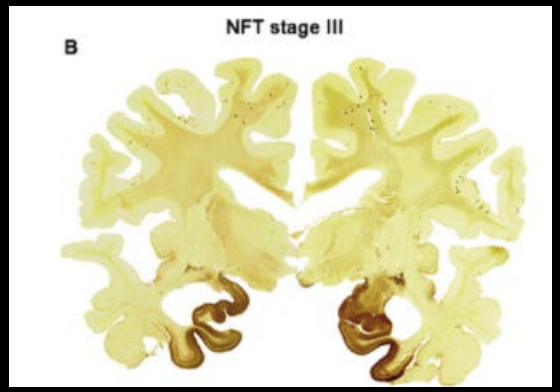




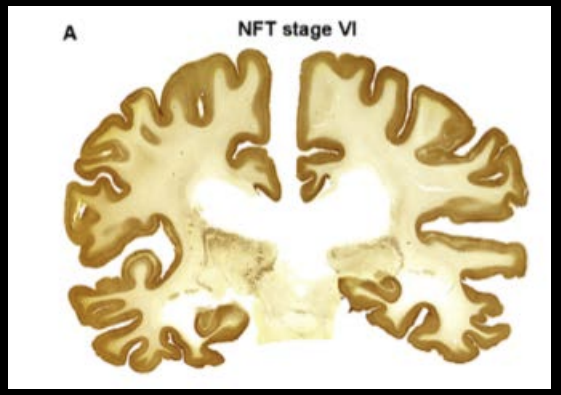
Braak staging



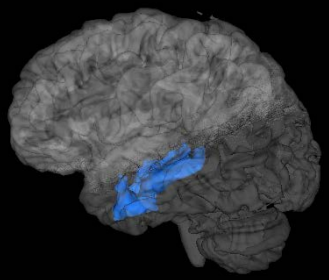
Braak I/II
(blue)

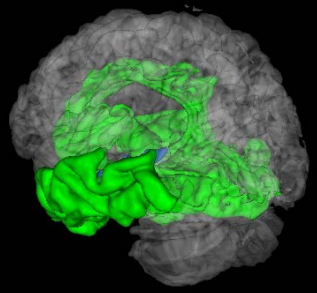


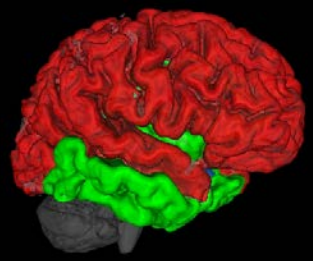
Braak III/IV
(green)



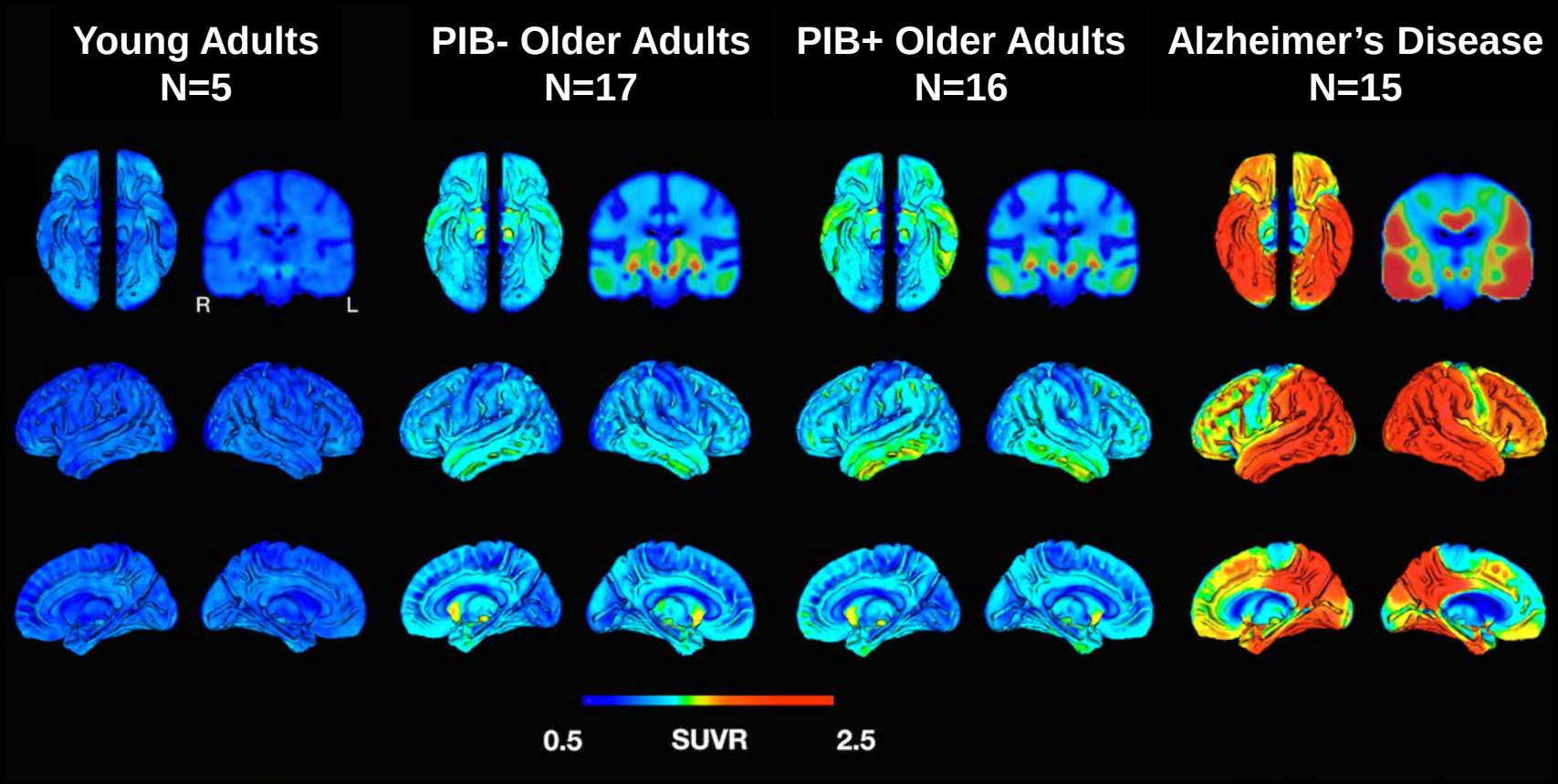
Braak V/VI
(red)





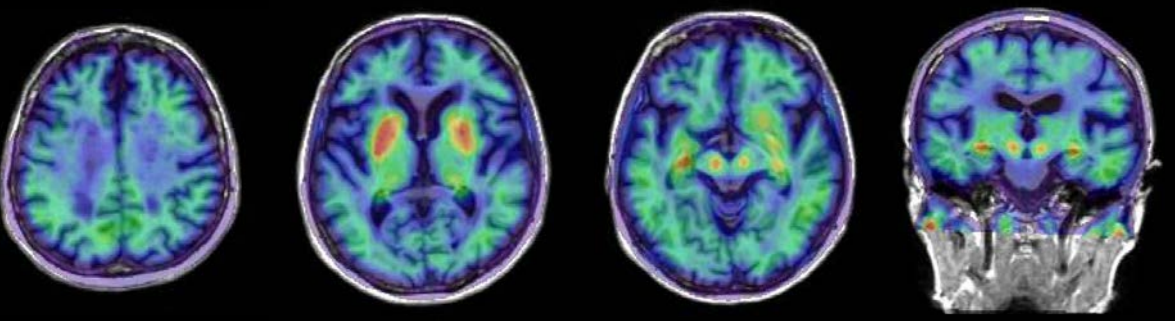


AV-1451 mean images

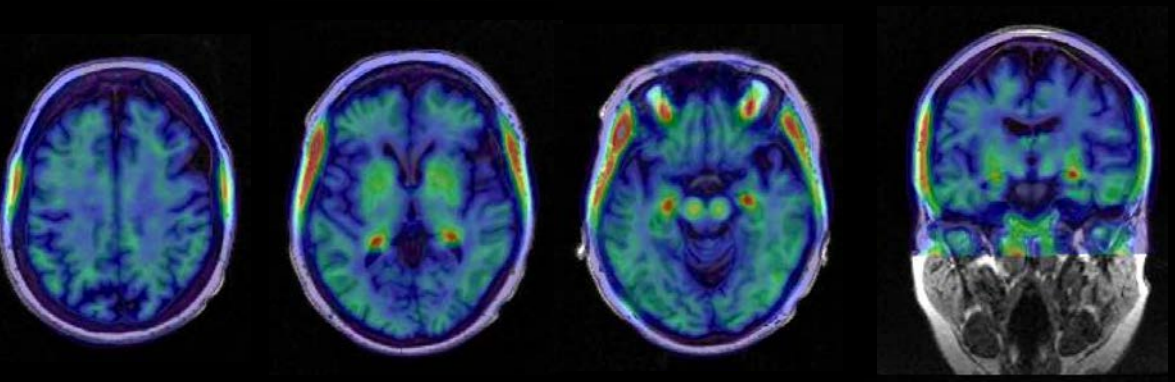


Schöll, Lockhart et al, *Neuron* 2016

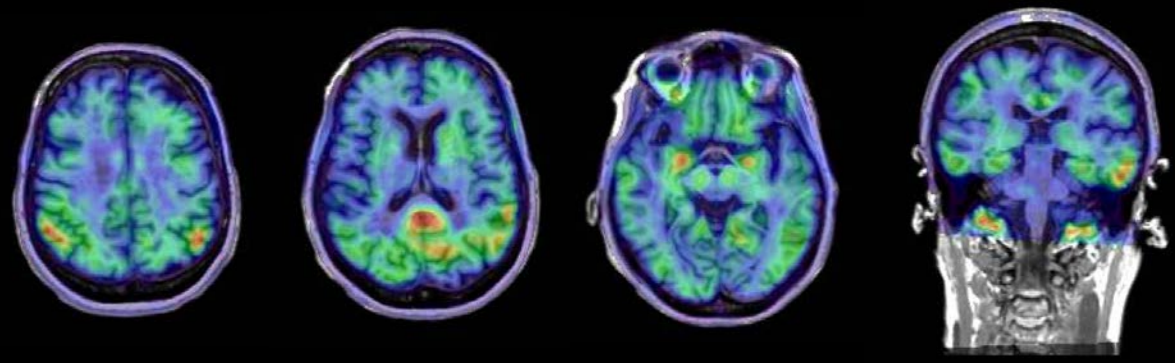
Example AV1451 scans



81yo EMCI Female
Braak1/2 = 1.18
Braak3/4= 1.17
Braak 5/6= 1.08



77yo EMCI Female
Braak1/2 = 1.32
Braak3/4= 1.18
Braak 5/6= 1.11



74yo AD Female
Braak1/2 = 2.00
Braak3/4= 1.81
Braak 5/6= 1.78

SUVR Threshold = 0.5 - 2.5

ADNI AV1451 summary

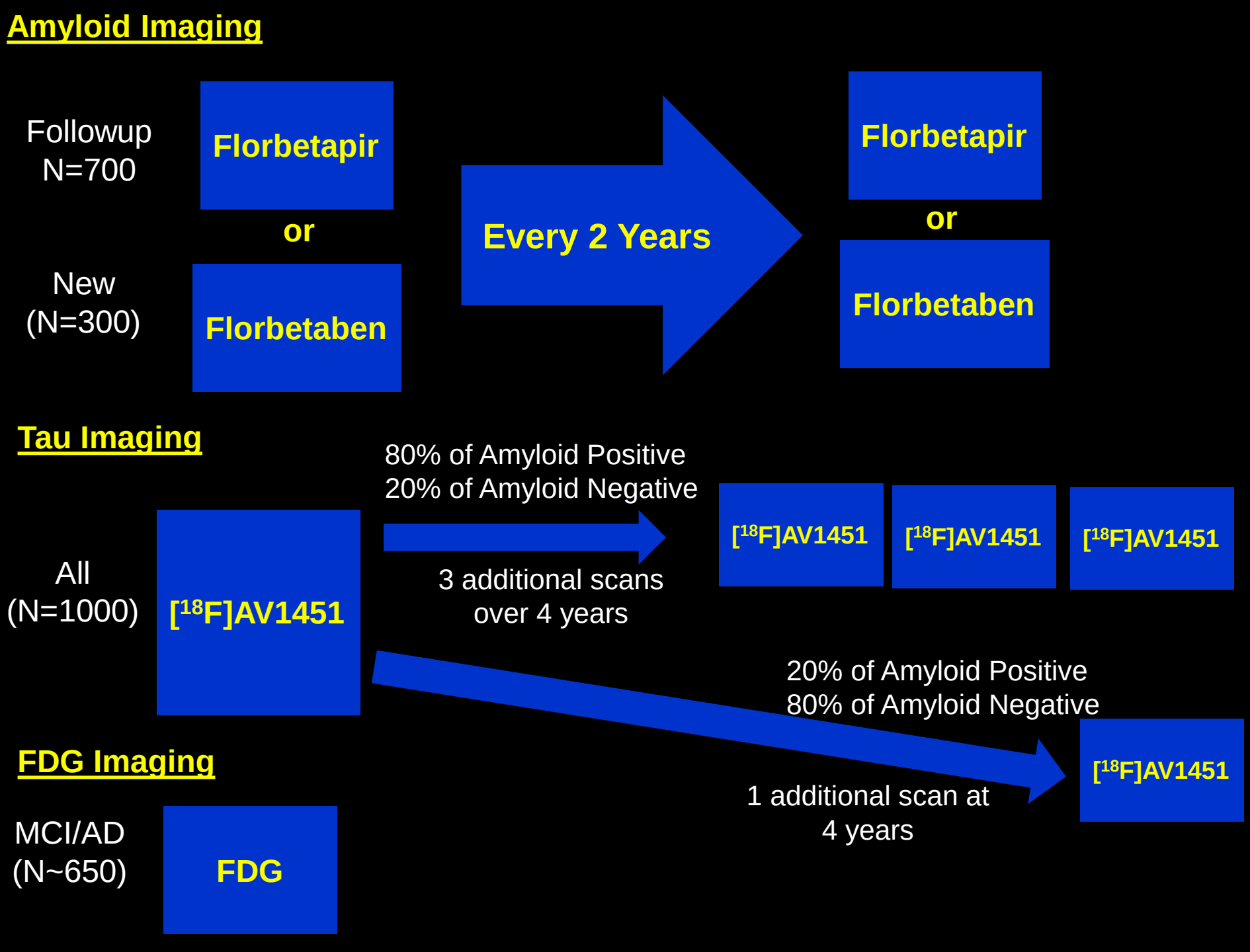
Baseline florbetapir -

Baseline florbetapir +

AV1451 tau and cognitive performance

Baseline florbetapir -

Baseline florbetapir +


Amyloid Imaging
Followup
N=700
Florbetapir
or
New
(N=300)
Florbetaben
Every 2 Years
Florbetapir
or
Florbetaben
Tau Imaging
80% of Amyloid Positive
20% of Amyloid Negative
All
(N=1000)
[18F]AV1451
3 additional scans
over 4 years
[18F]AV1451
[18F]AV1451
[18F]AV1451
20% of Amyloid Positive
80% of Amyloid Negative
1 additional scan at
4 years
[18F]AV1451
FDG Imaging
MCI/AD
(N~650)
FDG

Crucial Points

We want to retain as many “rollover” subjects as possible

Projections for ~300 new subjects with florbetaben

Many sites will be scanning new subjects with florbetaben, returning subjects with florbetapir

Amyloid PET will guide tau scan frequency

Subjects randomly selected based on the 80%/20% stratification

A second (or third?) tau tracer in ADNI?

Strong commitment to adding a second tau tracer to ADNI3 - As of today, no additional tracers available for summer 2016 startup

<u>Requirments for a tau tracer</u>

- Preclinical/clinical supportive data
- Regulatory pathway
- Manufacture at no cost to ADNI
- Distribution to a substantial proportion of sites

1 or more additional tracers could be available late 2016/early 2017?