The Australian Imaging Biomarkers and Lifestyle Flagship Study of Ageing

aibl

(AUSTRALIAN ADNI)

July 2011 UPDATE – Imaging

Christopher Rowe MD – *Neuroimaging stream leader*

CSIRO

THE UNIVERSITY OF MELBOURNE

NNF NATIONAL NEUROSCIENCE FACILITY

NARI

MENTAL HEALTH Research Institute

ECU EDITH COWAN UNIVERSITY

Alzheimer's Australia Living with dementia

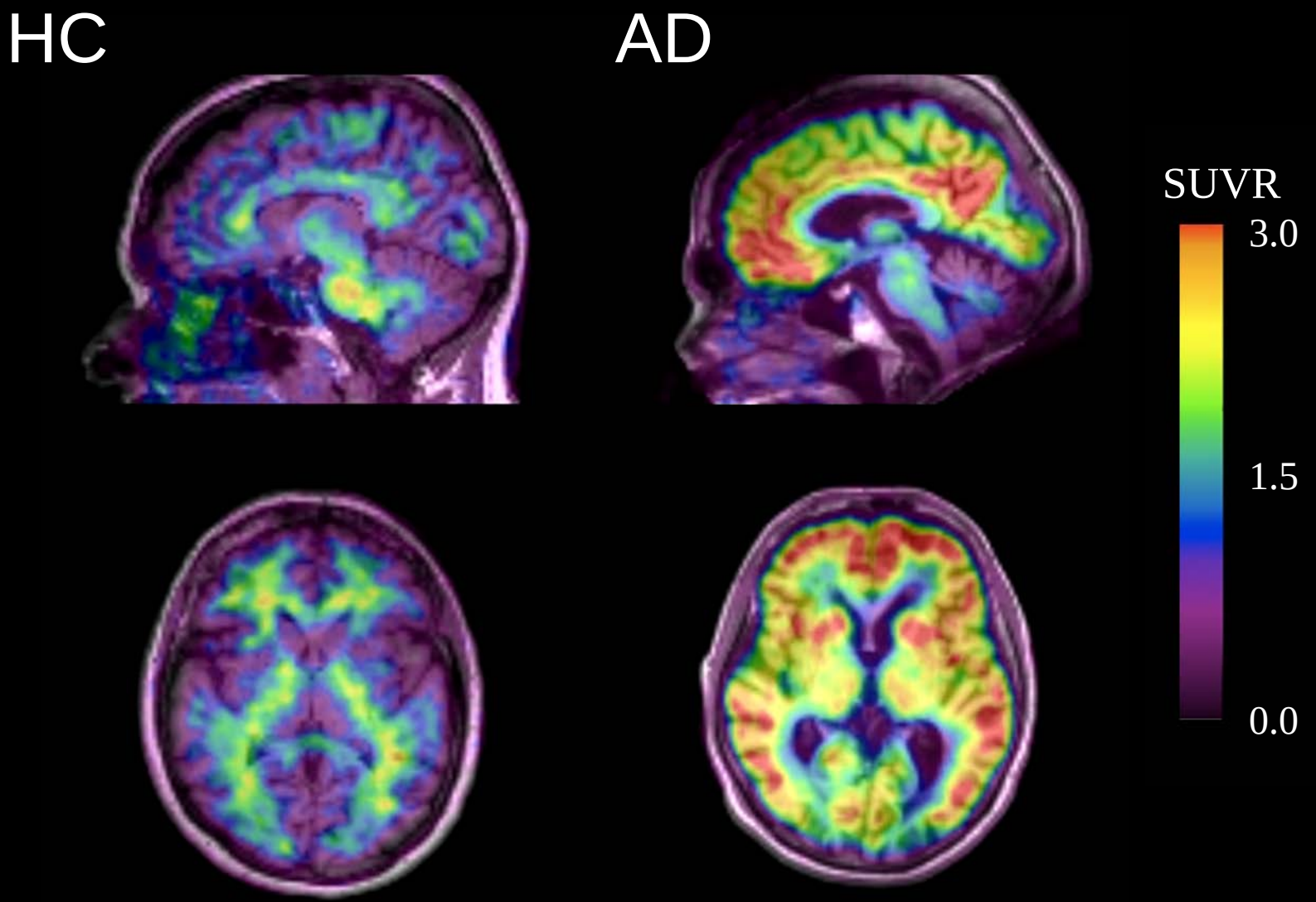
THE UNIVERSITY OF WESTERN AUSTRALIA

CogState

Austin Health

MACQUARIE UNIVERSITY SYDNEY ~ AUSTRALIA

^{11}C-PiB PET commenced at Austin Health in 2004 and expanded in 2006 through the AIBL study of aging



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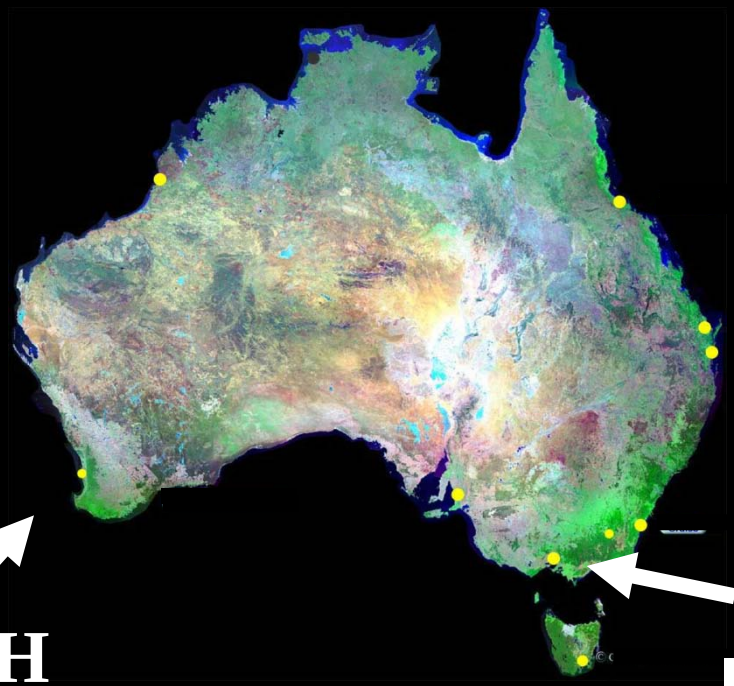
1000 subjects
(25% imaged with PiB PET and MRI)



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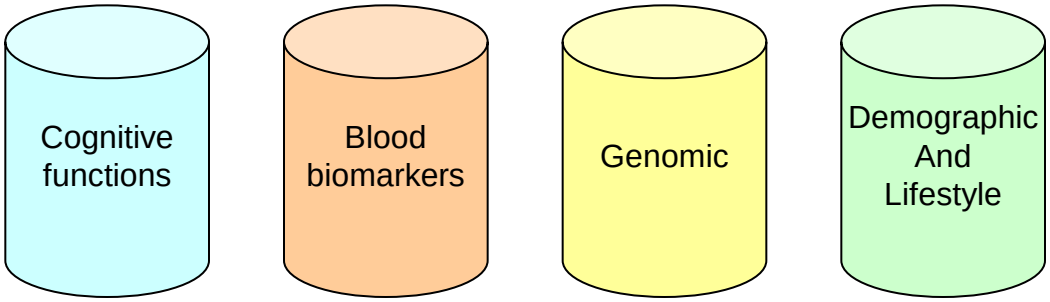
The Australian Imaging Biomarkers and Lifestyle Flagship Study of Ageing.

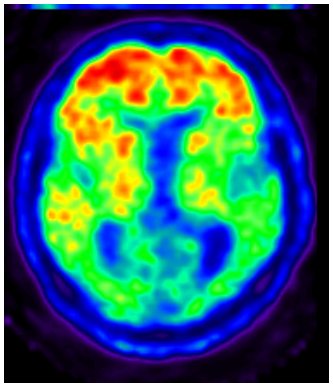
A multimodality clinical study

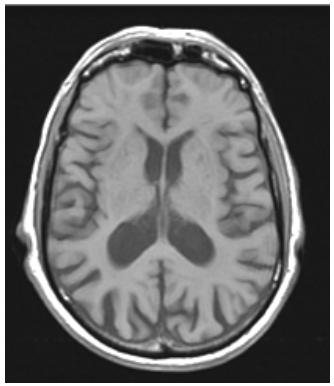
Databases



PET-PiB

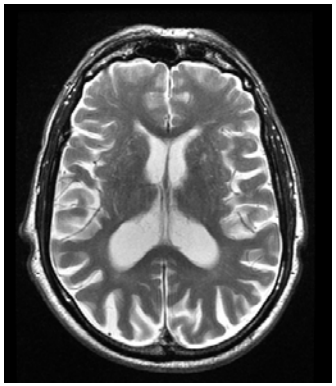
Amyloid beta load





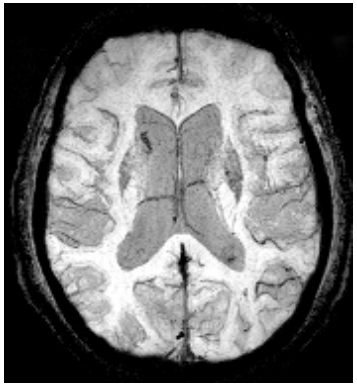
T1W

Anatomy



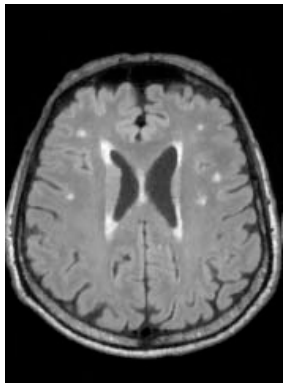
T2W

CSF and structures



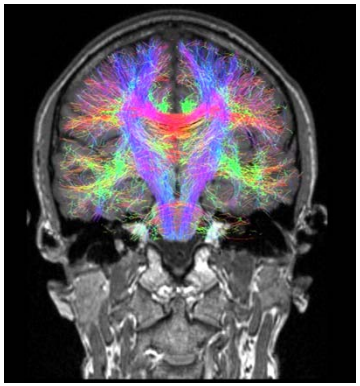
SWI

Venous tree



FLAIR

White matter lesions



DWI

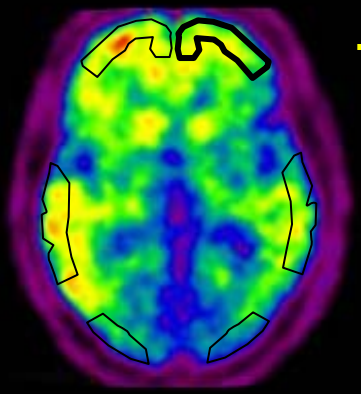
White matter connection

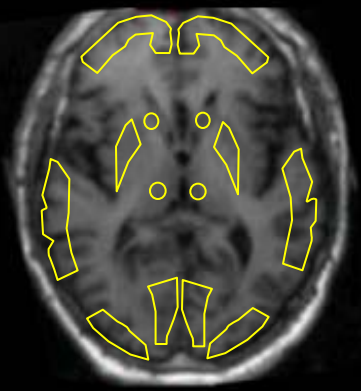
Methods

- 366 Participants
- Neuropsychology: CDR, MMSE, LM, CVLT-II, Rey Figure, etc
- MRI: 3D MP-RAGE, FLAIR, +/- SWI, DTI
- PET: Equilibrium imaging at 40-70 min after 300 MBq of ^{11}C-PiB
- Image Analysis:
  - PiB PET: Standard uptake value ratios (SUVR) i.e. cortex ROIs : cerebellar grey matter
  - MRI: 3 tissue segmentation using expectation maximization probability maps

^{11}C-PIB – Image Quantification

Regions





Neocortical $SUVR_{40\text{-}70}$

= cortical activity / cerebellar grey matter activity from 40 to 70 minutes post injection

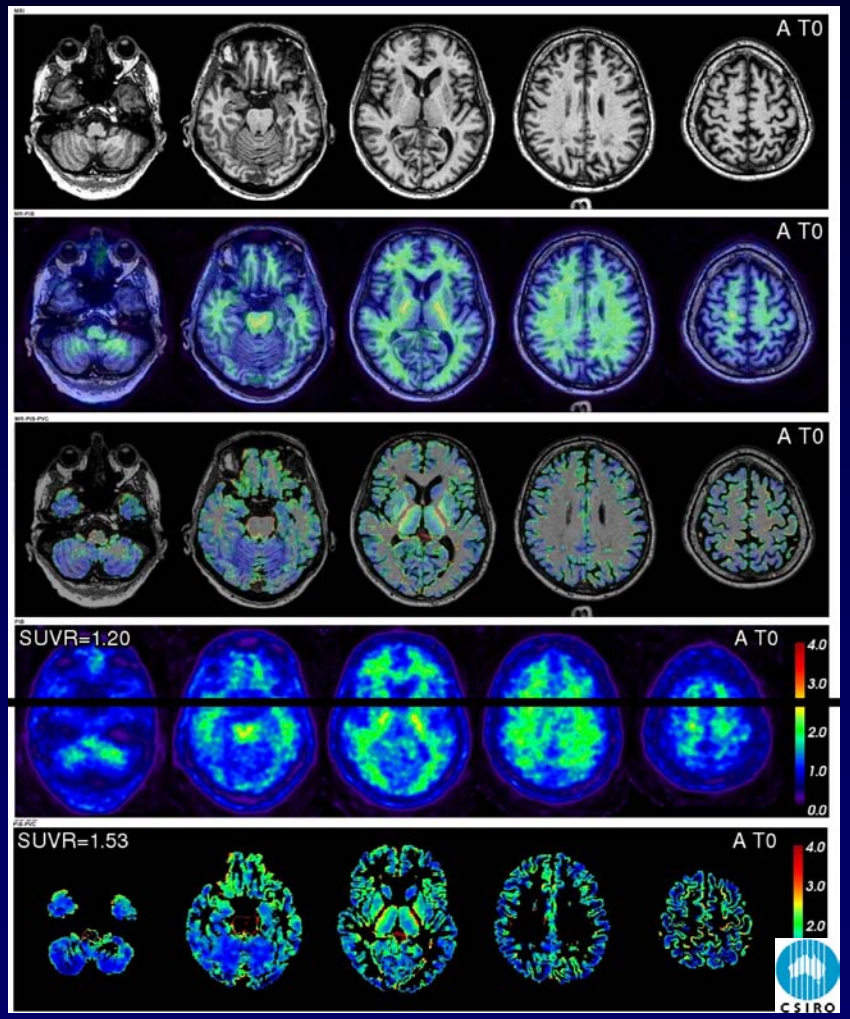
Negative is <1.5

Follow-up PiB co-registered to baseline and saved prior ROI set used.

Single operator for all PiB scans.

Image Analysis

2. Automatic: co-registration + MRI segmentation (GM, WM, CSF) + AAL template + PVC

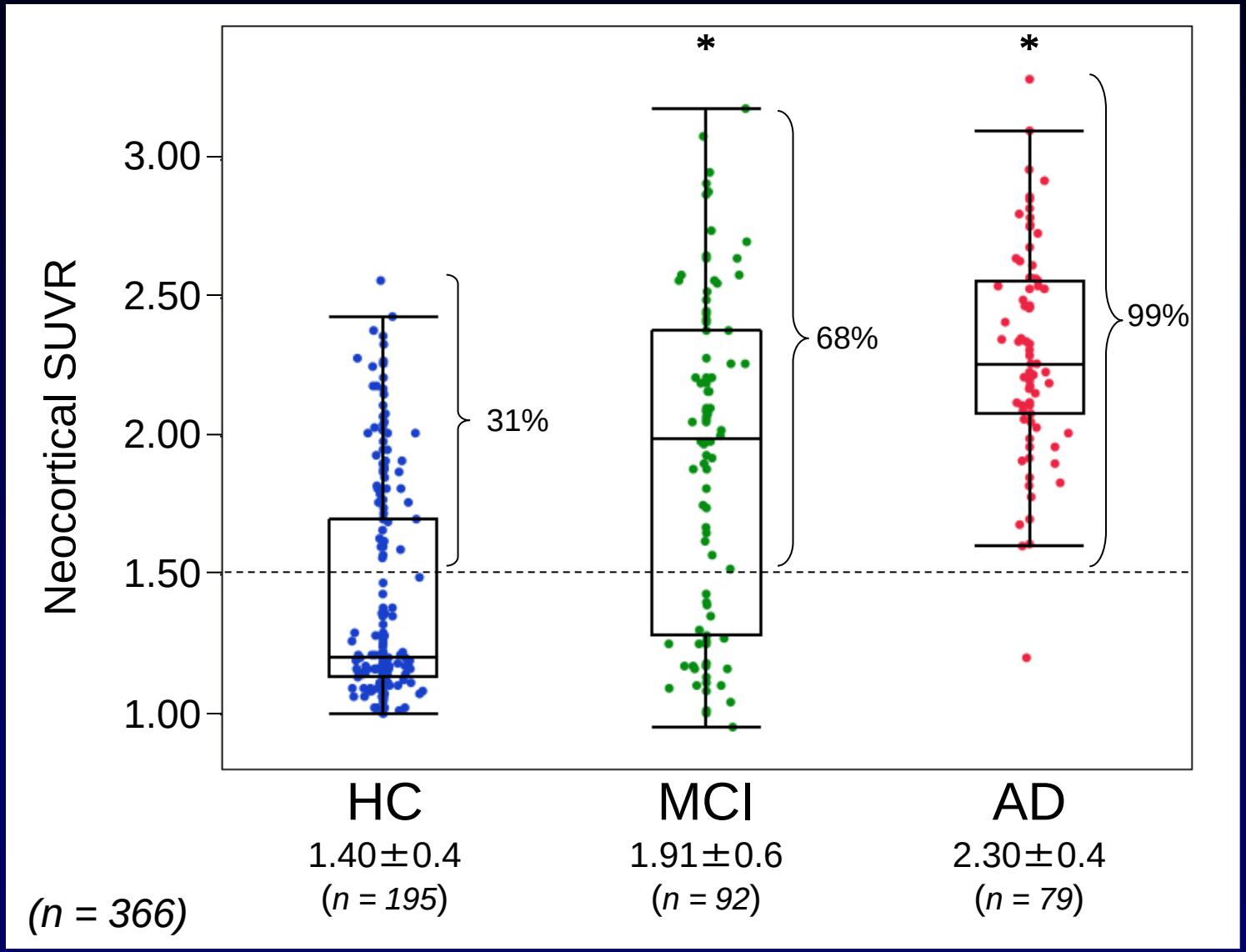


Imaging Cohort Demographics

	HC (n=195)	MCI (n=92)	AD (n=79)
Age	72	74	73
Gender (M:F)	47%	50%	50%
MMSE	29	27	21
CDR	0.0	0.5 ± 0.2	1.0 ± 0.5
CDR SOB	0.06 ± 0.2	1.25 ± 0.9	4.36 ± 1.7
% ApoE ε4	41%	61%	65%
Years of Education	13.4	12.5	12.4

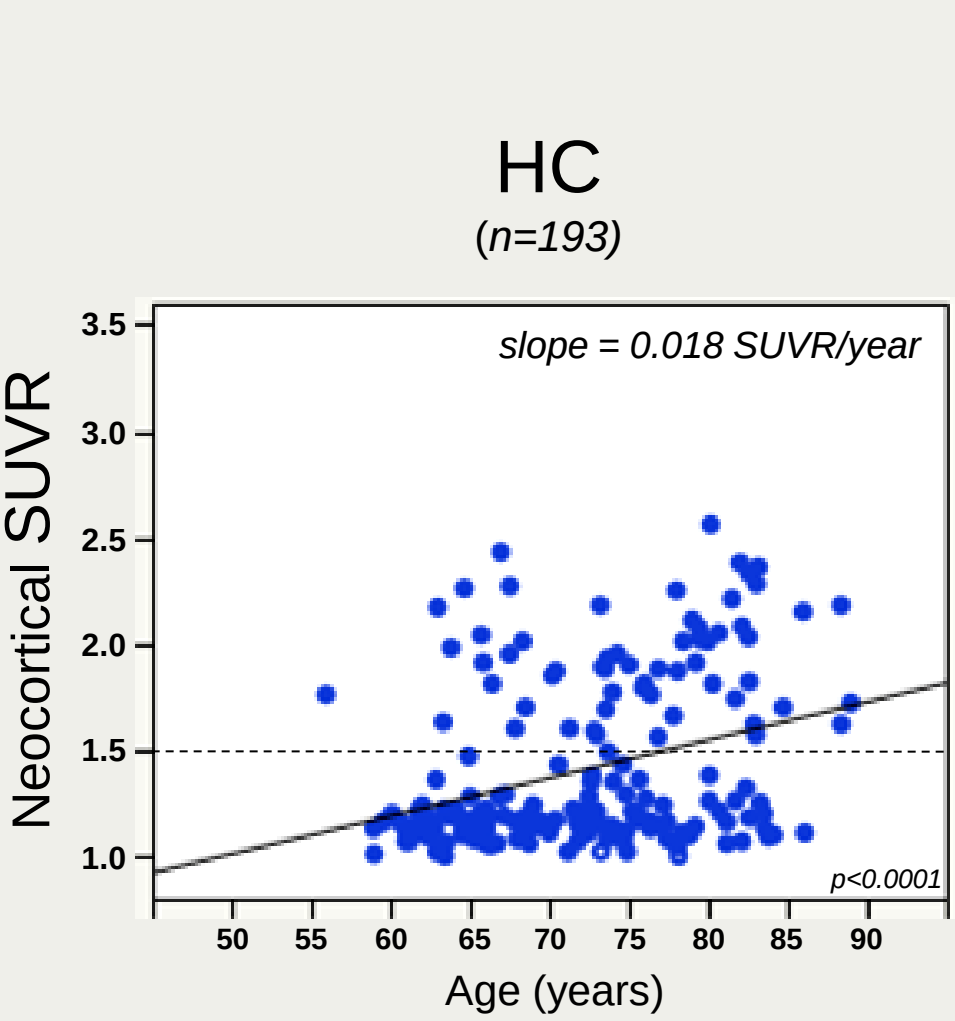
Baseline Imaging Findings

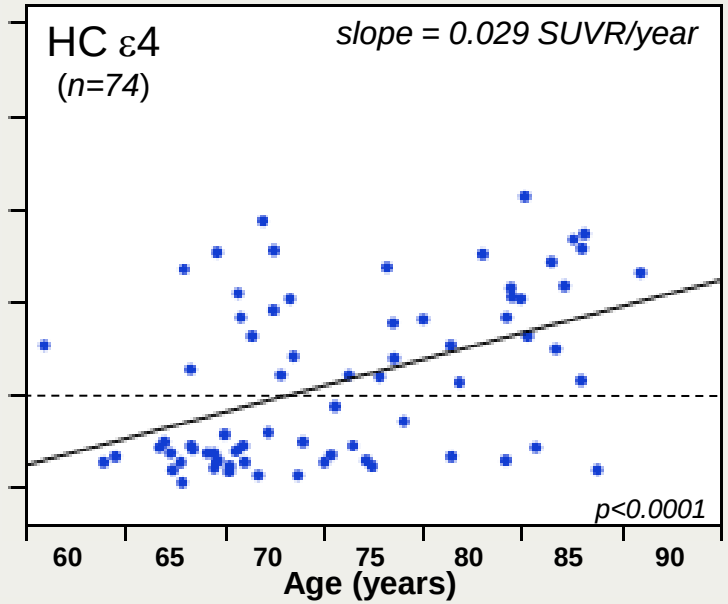
PiB neocortical SUVR in AIBL+

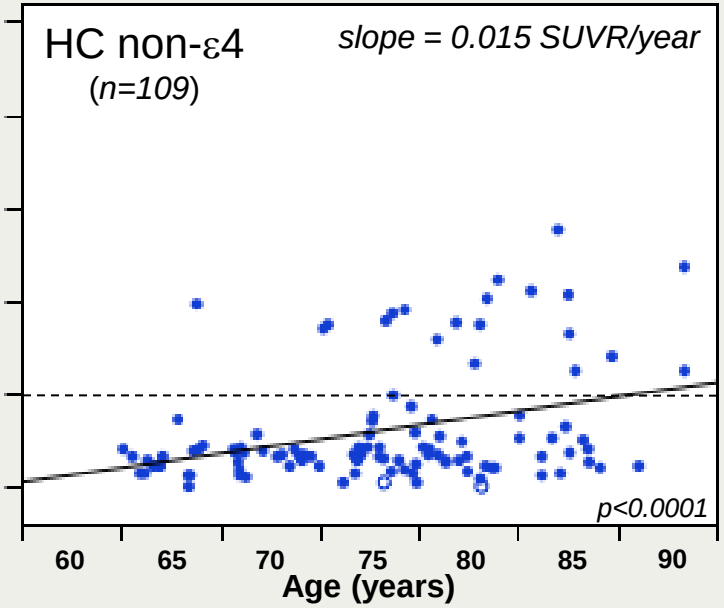


*Statistically significant results compared to controls (p< 0.0001)

Relation between ApoE, age, and Aβ burden

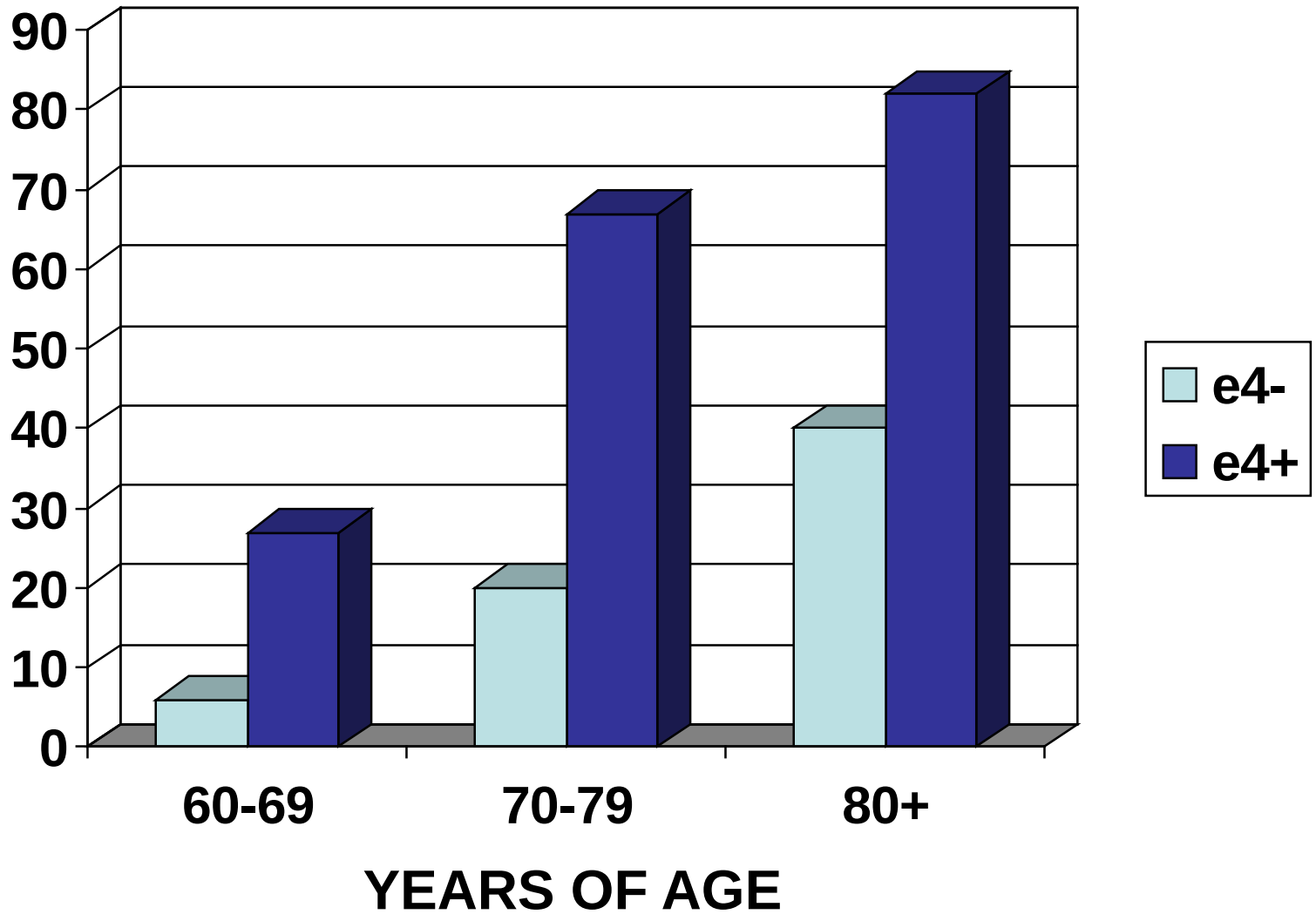






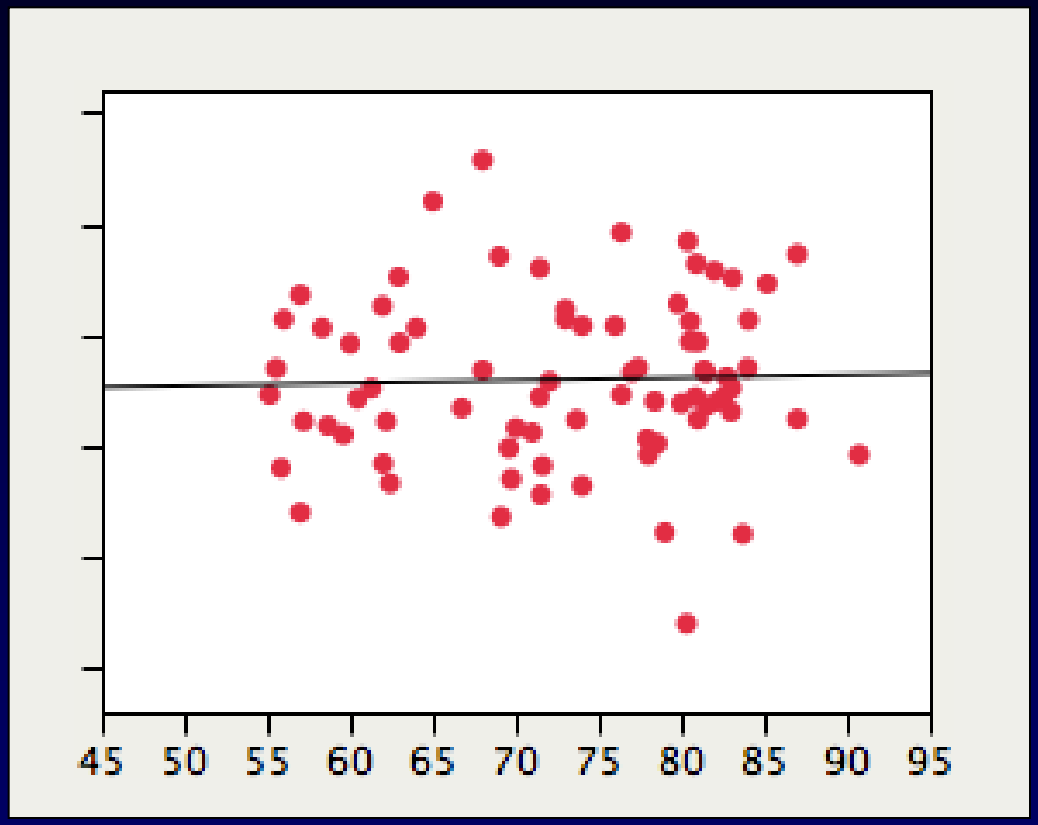
aibl+

% Healthy Elderly PiB+ve



Aβ burden vs Age

Older AD do not have less PiB binding



aibl+

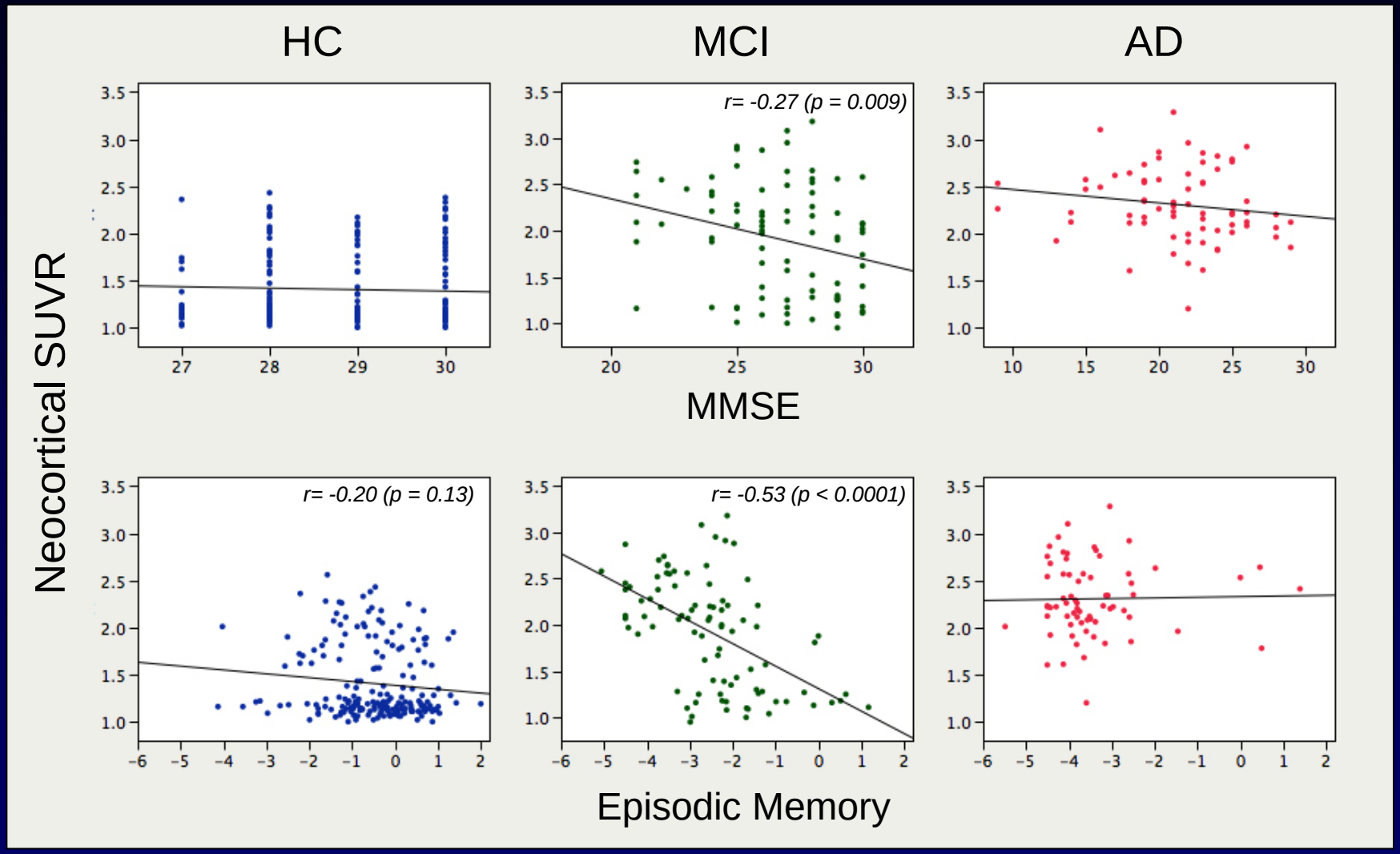
Calculated accuracy for PiB (AD vs HC)

HC PiB+: **11% in 60's, 32% in 70's, 51% in 80's**

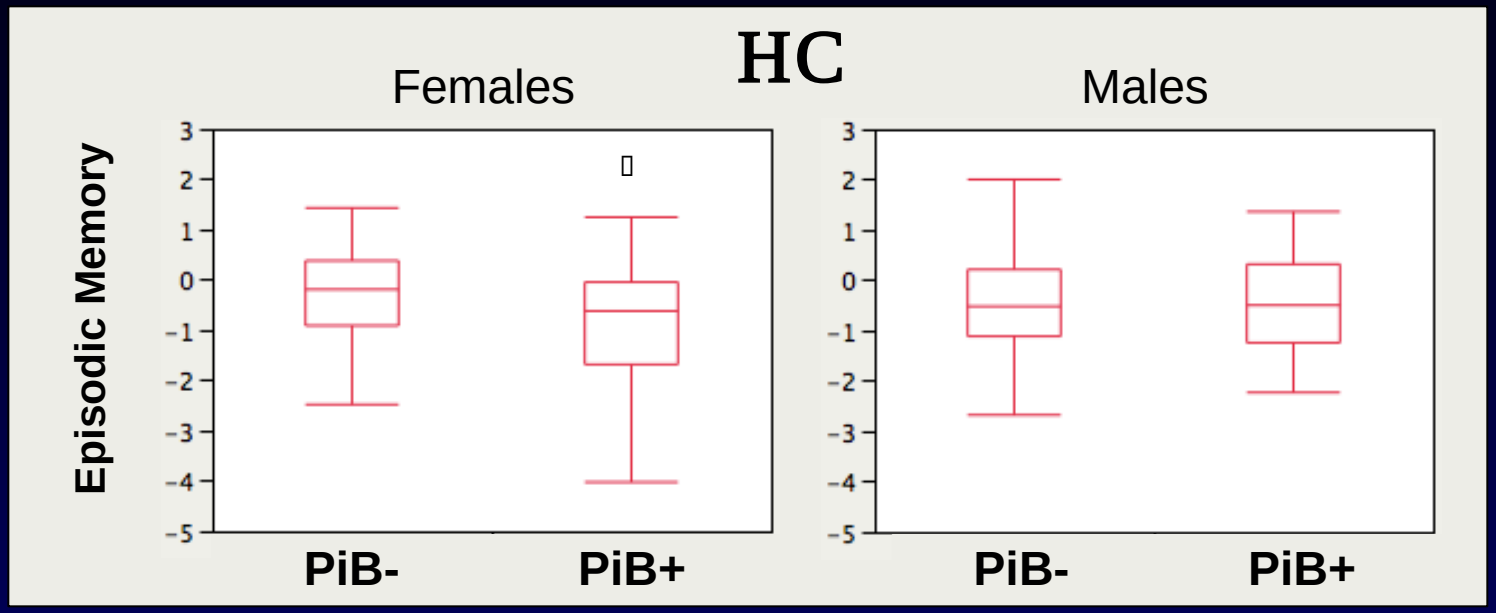
(e4 prevalence corrected)

Age	Sens.	Specif.	Accuracy	PPV	NPV
60-69	95	88	**92**	89	95
70-79	95	68	**84**	75	93
80+	95	49	**78**	65	91

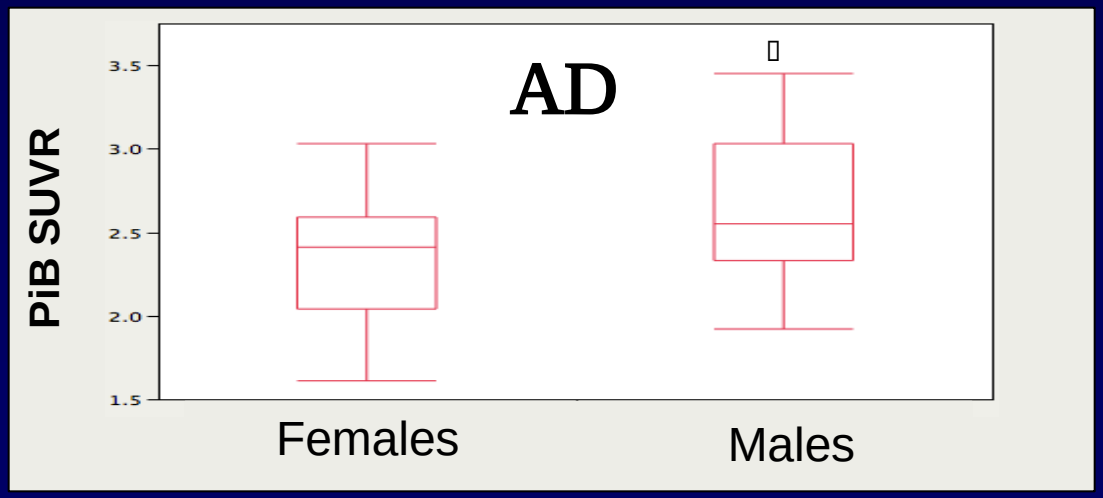
Aβ burden vs cognition



Gender Differences

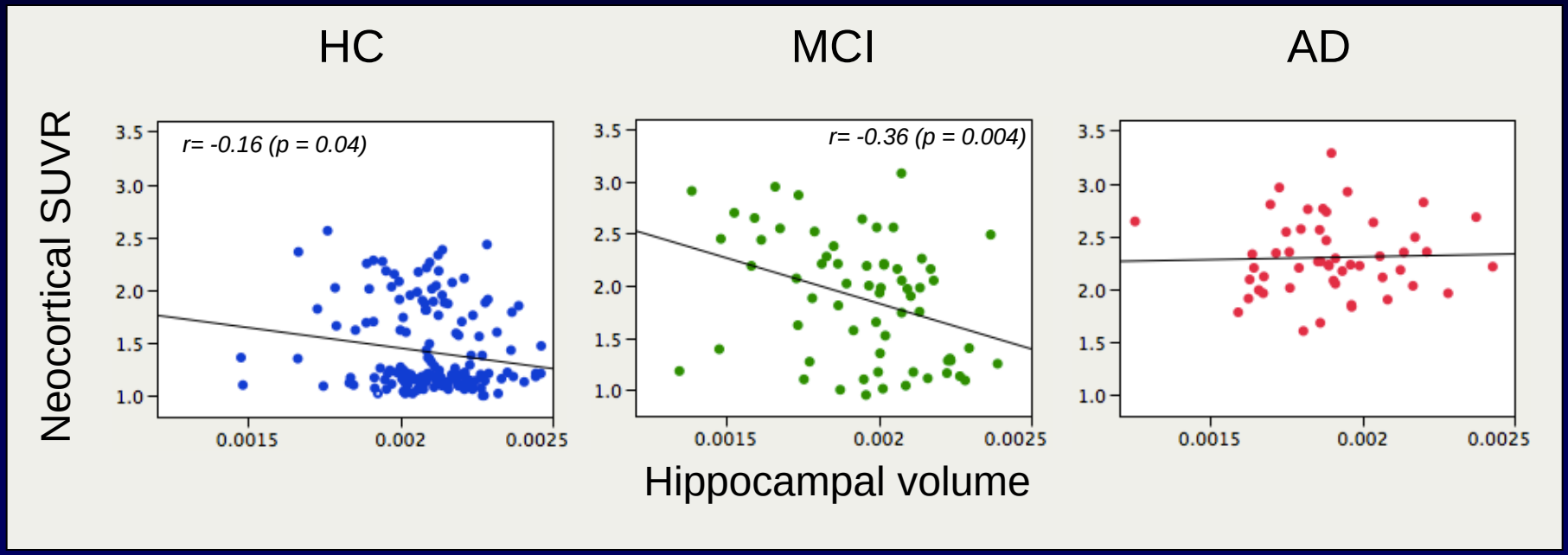


Female but not male PiB+ HC have lower memory scores



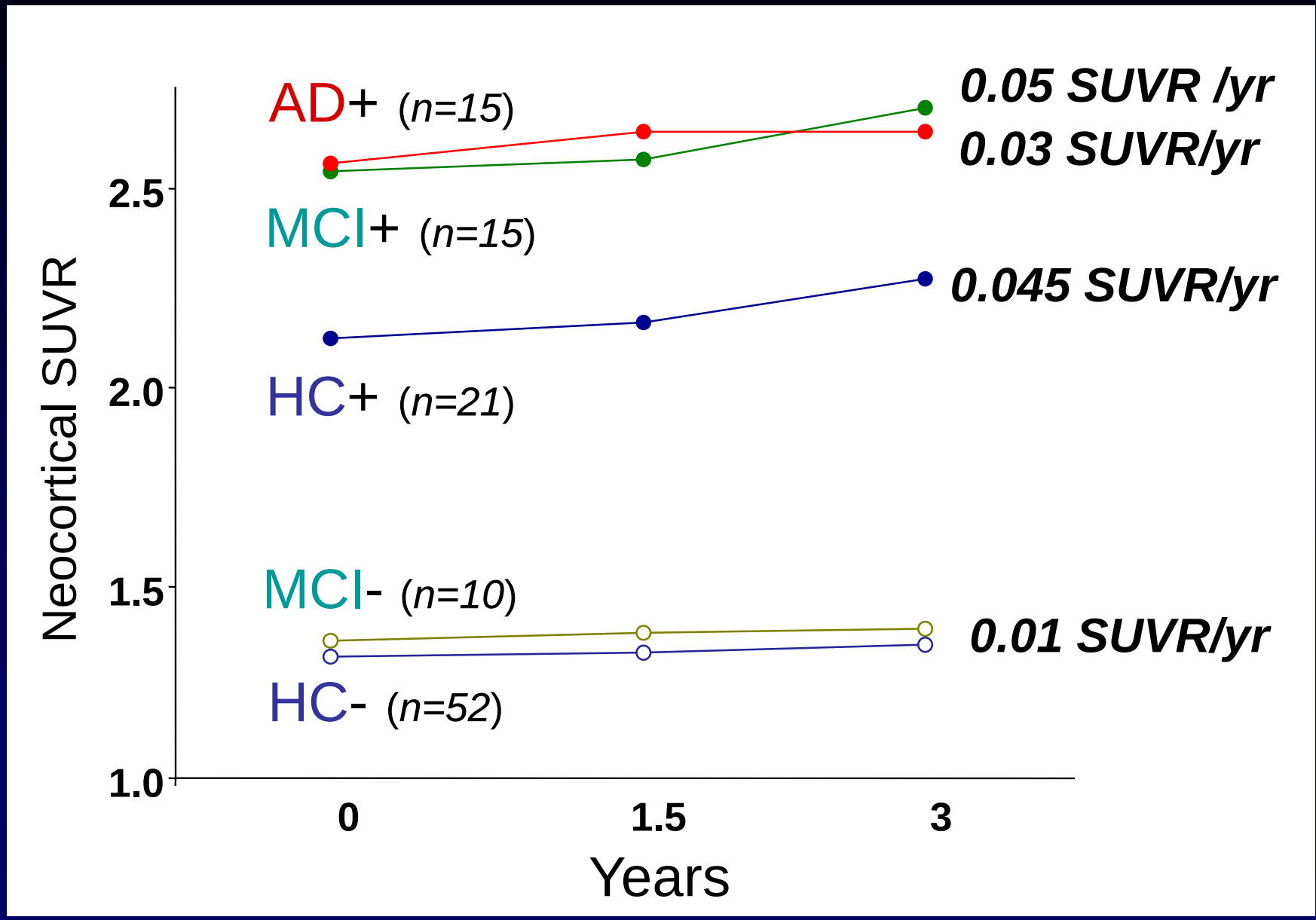
Male AD have higher PiB

Aβ burden vs hippocampal volume

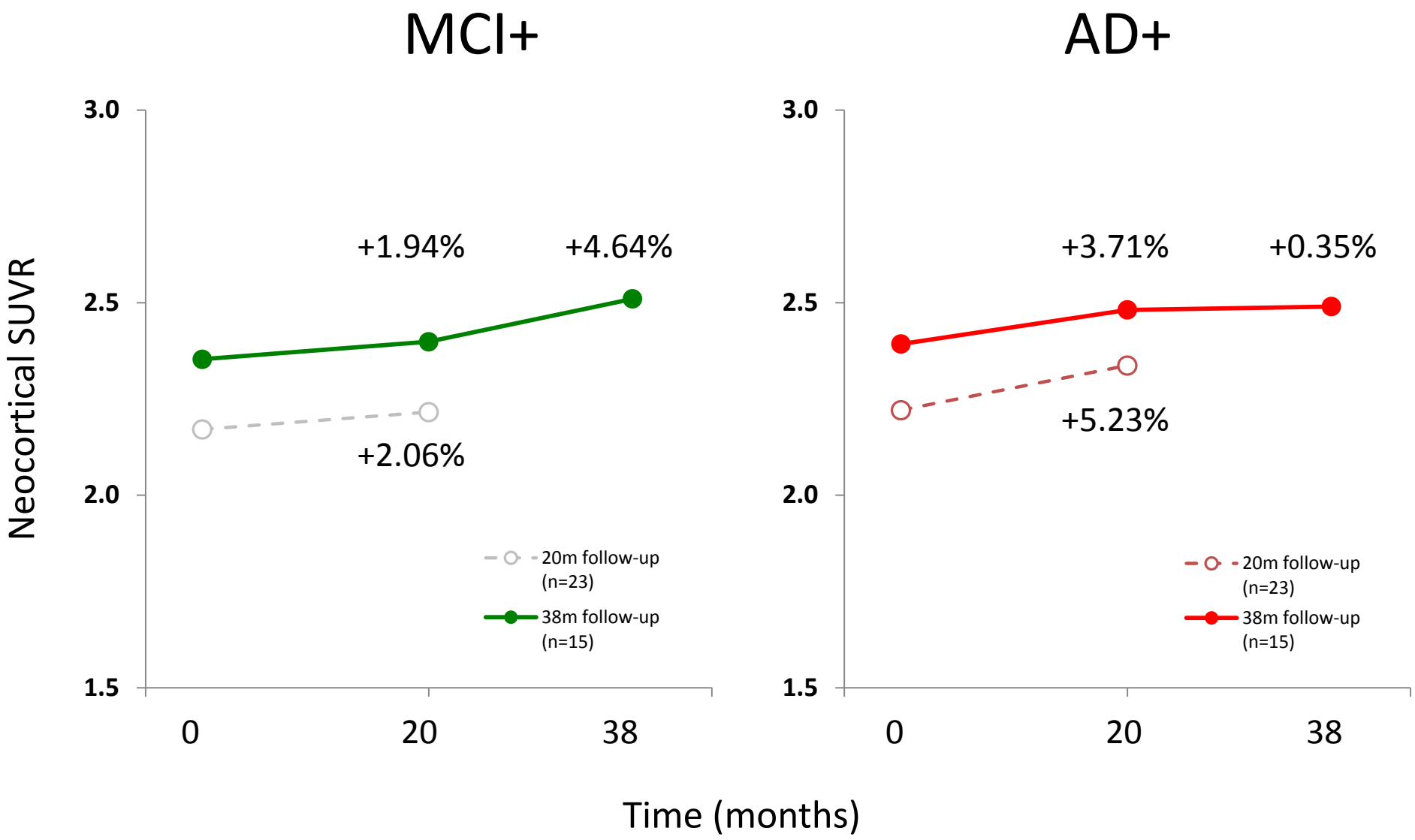


Follow-up Data

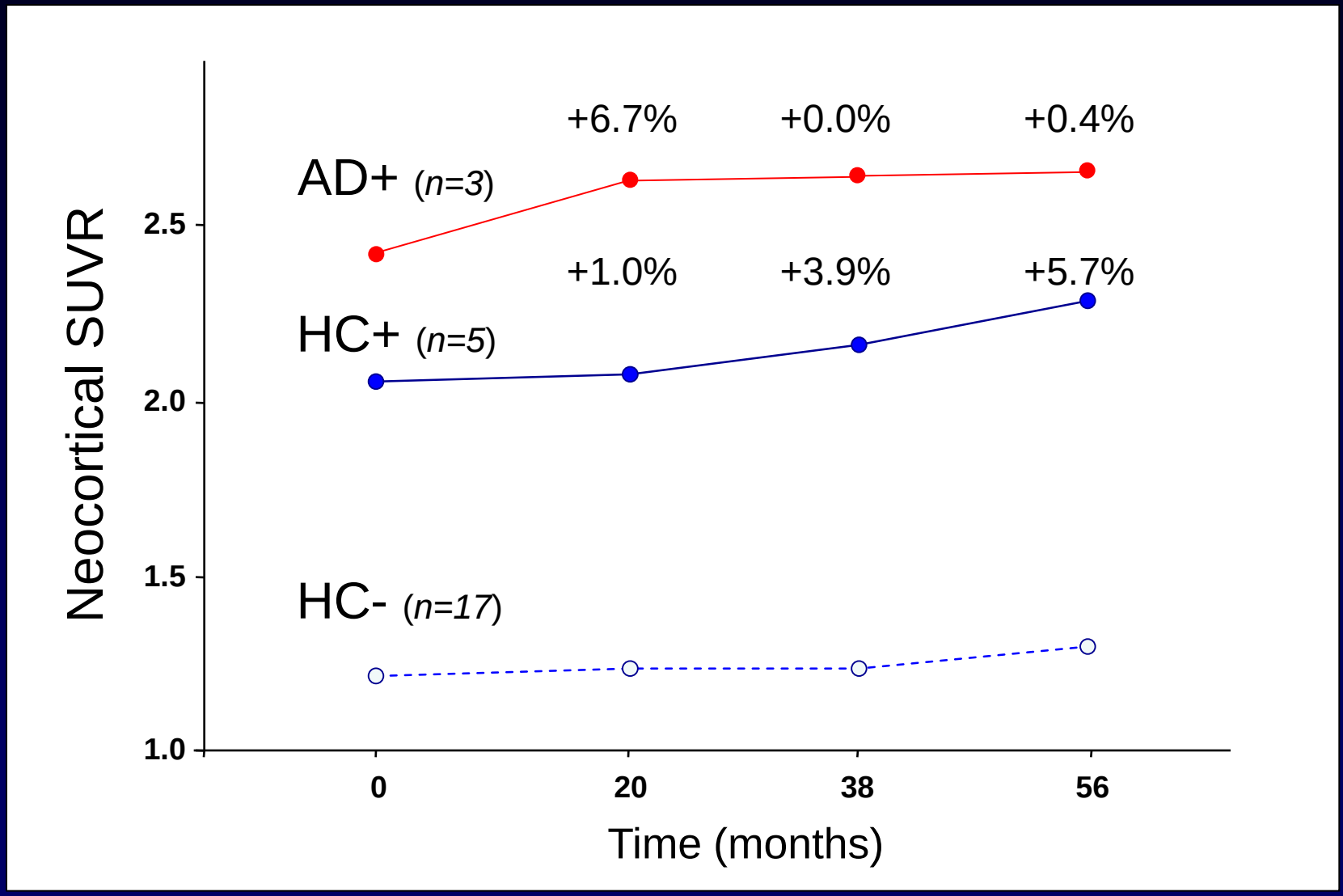
3 year PiB PET



Note: Atrophy correction did not change shape of graphs

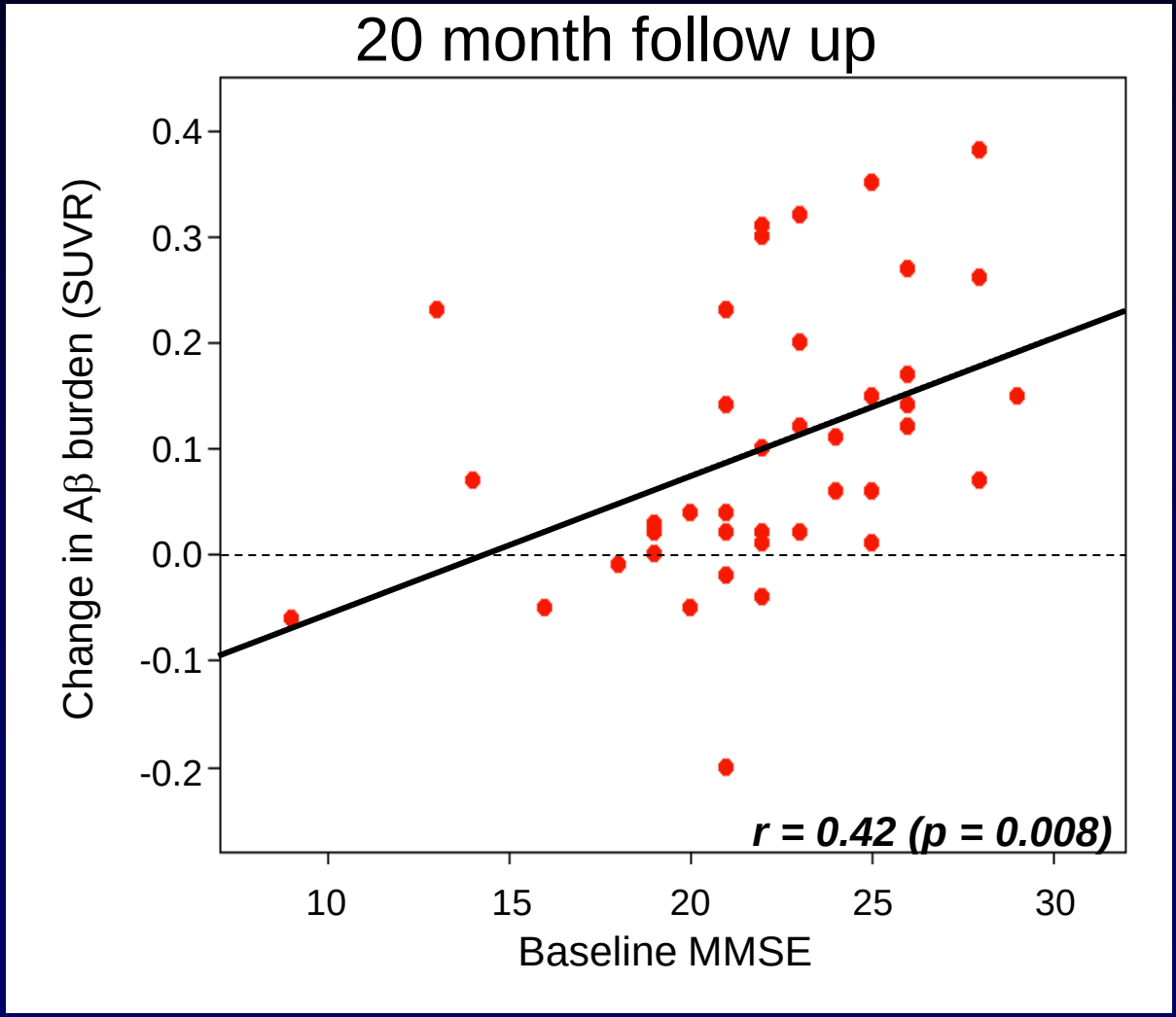


5-year follow-up

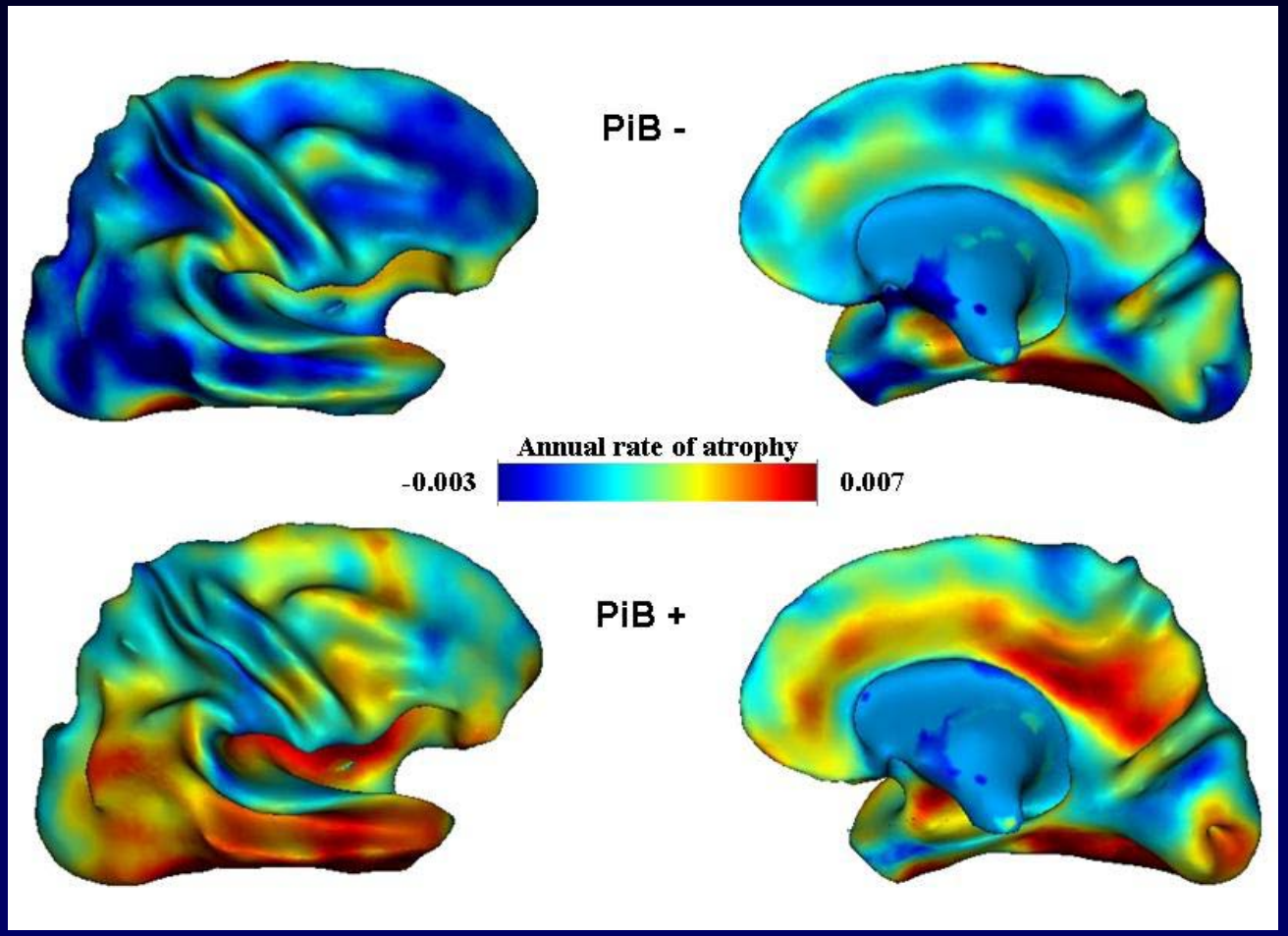


AD with lower MMSE have slower PiB rise

(*n=40*)

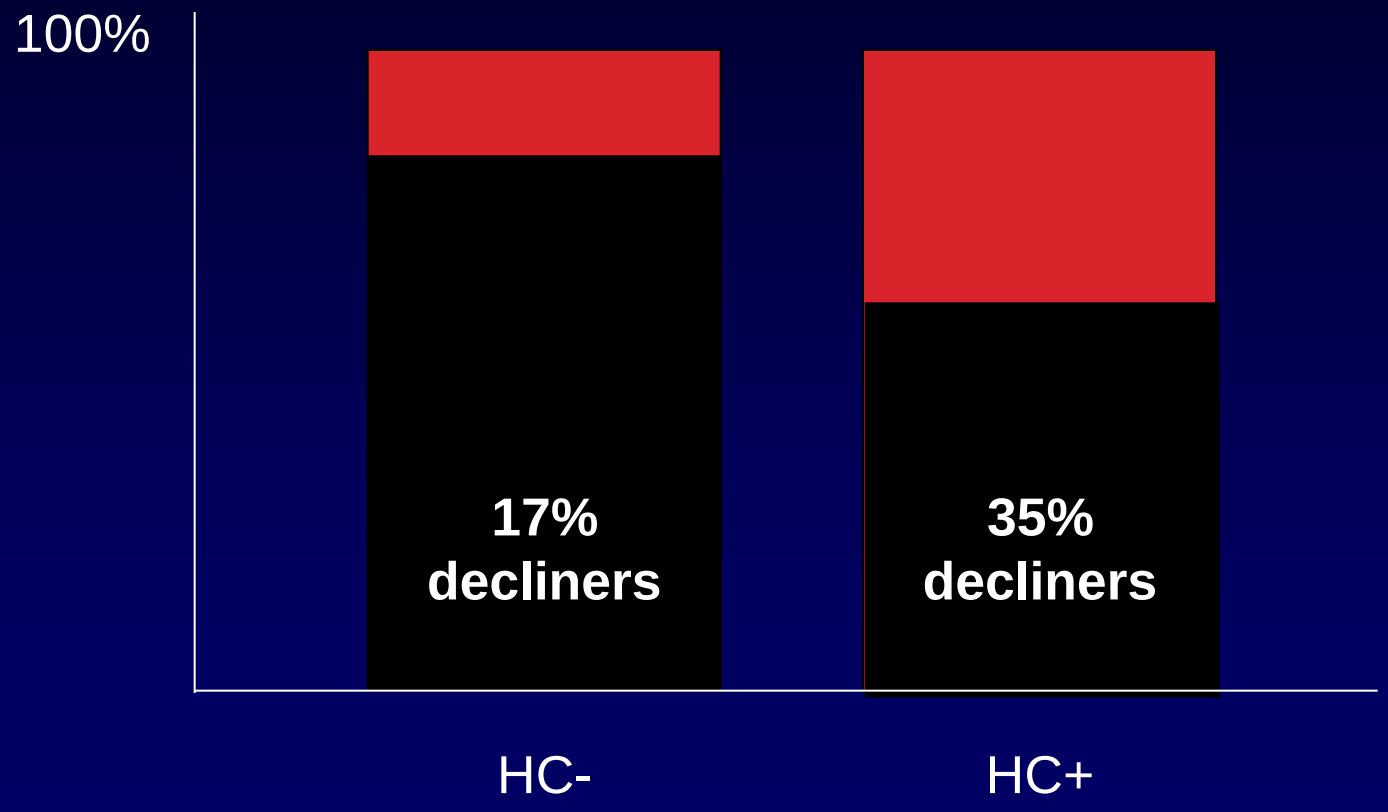


Average rate of atrophy over one year in HC PiB- vs PiB+.



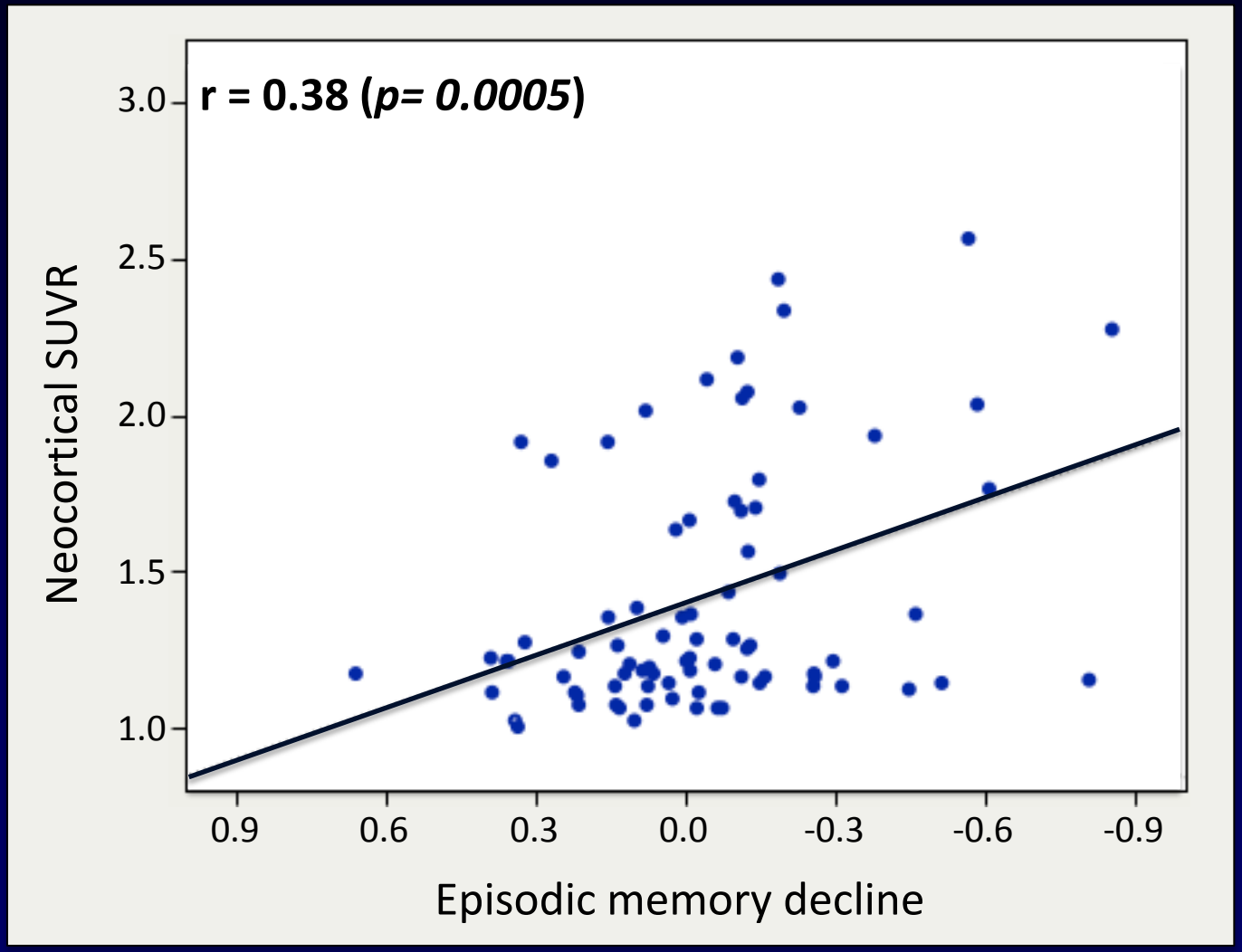
Change in memory vs Baseline PiB: Decline >*0.5 SD* in HC with a 3 year follow-up

(*n=80*)



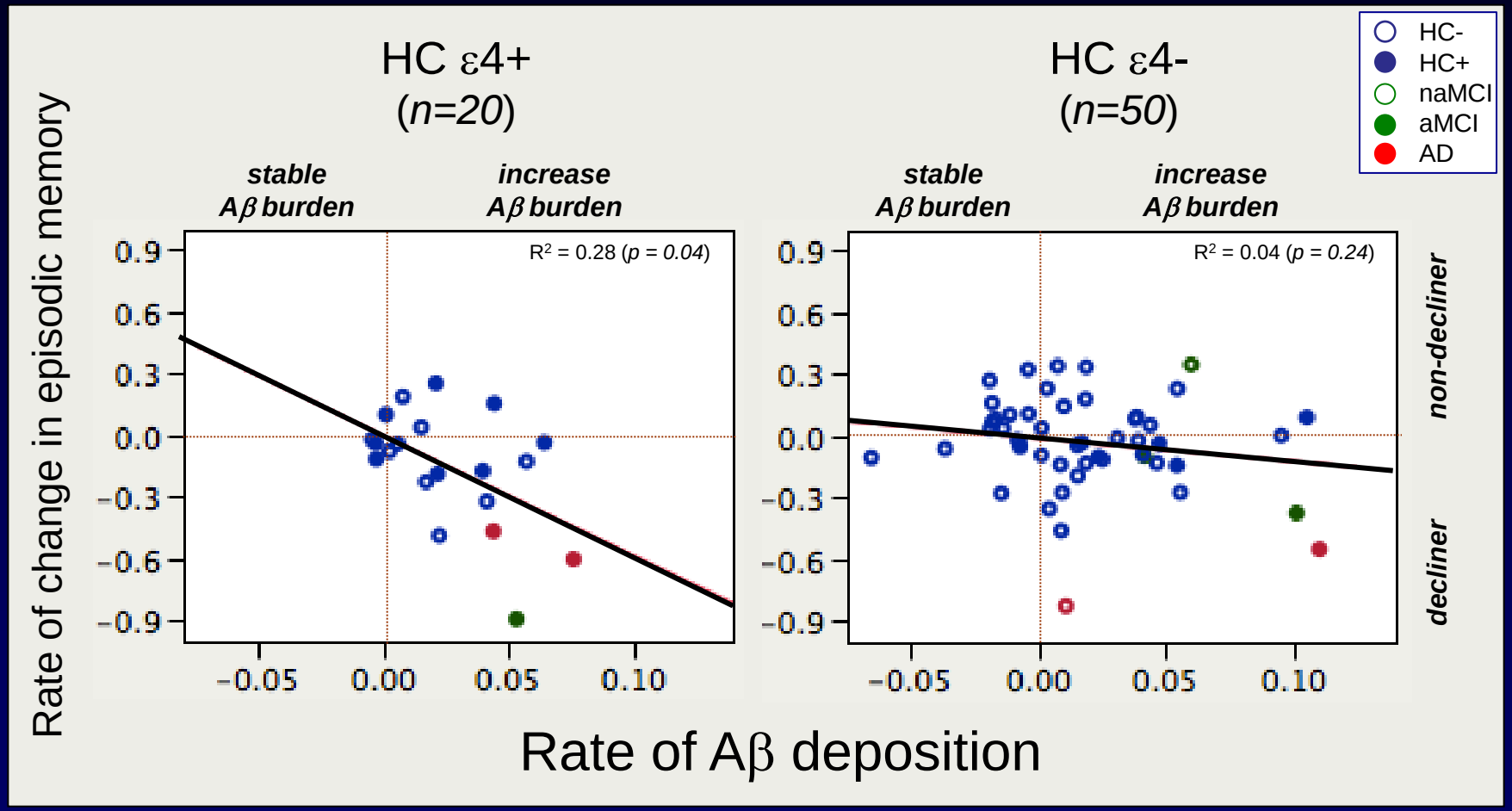
Relation between baseline Aβ burden and memory decline in healthy controls

(36 months follow-up)



Relation between rate of Aβ deposition and rate of memory decline

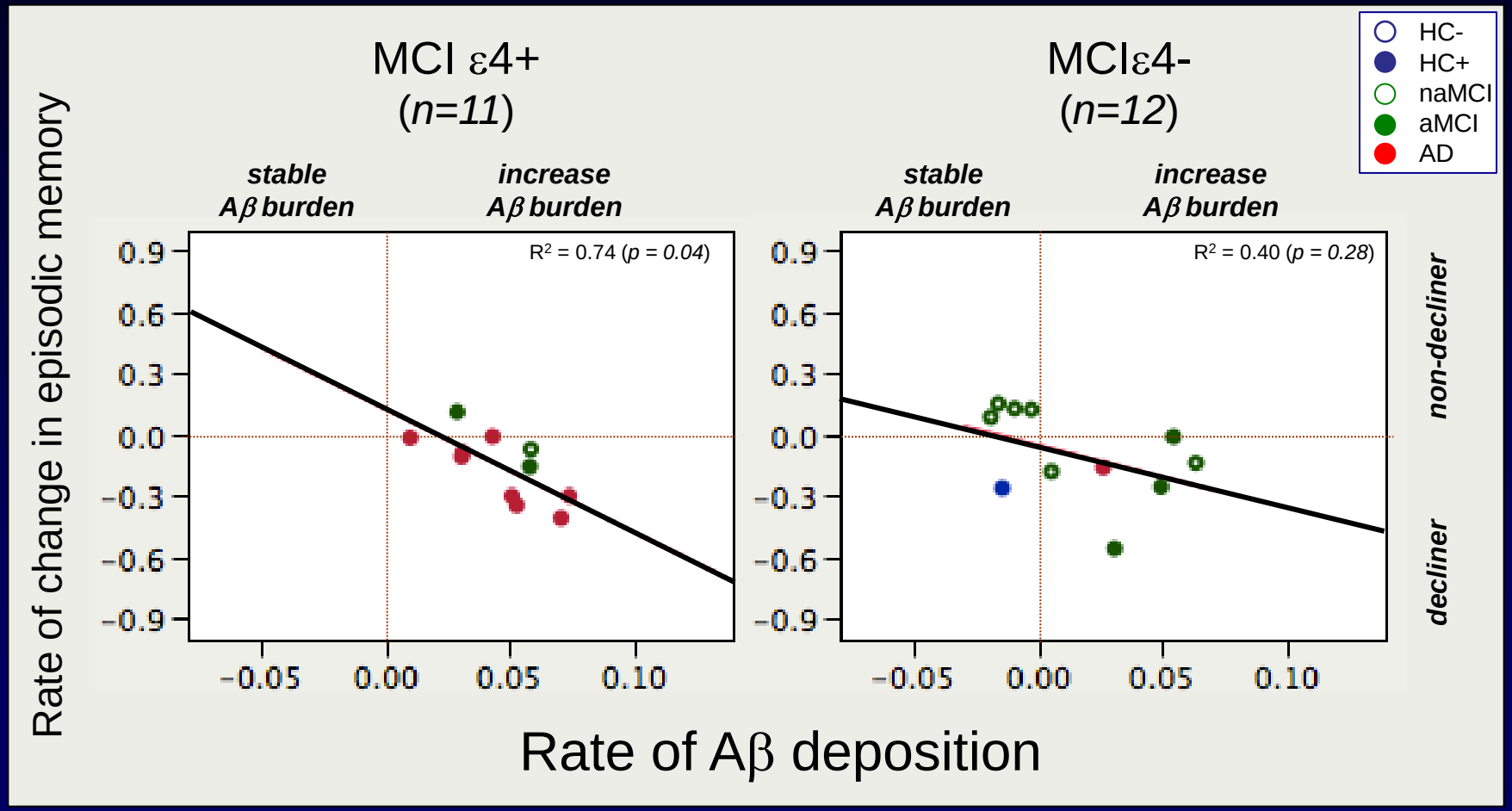
3-5 year follow-up



effect of ApoE status

Relation between rate of Aβ deposition and rate of memory decline

3-5 year follow-up



effect of ApoE status

Prediction of Progression: HC to MCI/AD

20 months
n=195

PiB-ve Subjects: 135
Converters to MCI/AD 3 (2%)

PiB+ve Subjects: 60
Converters to MCI/AD **6 (10%)**

36 months
n=178

PiB-ve Subjects: 124
Converters to MCI/AD 8 (6%)

PiB+ve Subjects: 54
Converters to MCI/AD **9 (17%)**

Prediction of Progression: HC to MCI/AD

20 months

	ACCURACY	*NPV*	***OR***
Neocortical PiB+ve (SUVR >1.5)	0.54	0.98 (CI 0.93-0.99)	**4.9**

36 months

	ACCURACY	*NPV*	***OR***
Neocortical PiB+ve (SUVR >1.5)	0.56	0.94 (CI 0.87-0.97)	**3.0**

Prediction of Progression: MCI to Dementia

	20 Months n=92	36 Months n=72
PiB -ve:	29	PiB -ve : 19
Converters to AD	2 (7%)	*Converters to AD* 3 (16%)
DLB	1 (3%)	*DLB* 1 (5%)
FTD	2 (7%)	*FTD* 2 (10%)
VaD	1 (3%)	*VaD* 1 (5%)
PiB +ve:	63	PiB +ve : 53
Converters to AD	32 **(51%)**	*Converters to AD* 39 **(74%)**

Prediction of Progression: MCI to Dementia
(at 36 months follow-up)

	ACCURACY	*Odds Ratio*	*NPV*
PiB+ve (SUVR >1.5)	0.79	15	0.83 (CI 0.58-0.96)
ApoE ε4+	0.78	11	0.77 (CI 0.50-0.92)
Composite Memory (<2.0)	0.68	5	0.64 (CI 0.36-0.86)
Hippocampal atrophy (<0.0021)	0.60	2	0.57 (CI 0.34-0.77)
PiB + Hipp Vol (n=30, ++ vs --)	0.86	>20	1.00 (CI 0.52-1.00)

Summary

AIBL+ Findings

- Aβ deposition is slow and of similar rate in PiB+ HC and MCI (2% SUVR per year).
- A plateau occurs with advancing dementia.
- Aβ is common in older HC

  11% if 60-69
  32% if 70-79
  51% if 80+ years

  and strongly related to genetics i.e. ApoE-ε4 status (risk 2-3X)

Over 3 Years

- Aβ in HC is associated with faster cognitive decline and grey matter atrophy.
- 17% of PiB+ HC develop MCI/AD *(c.f. 6% of PiB-)*
- 74% PiB+ MCI develop AD *c.f. 16% of PiB- Odds Ratio = 12 (but 20% PiB- develop other dementias)*
- Combination of biomarkers provides better prediction *(e.g. if PiB+ and hippocampal atrophy = 86% accuracy)*