Alzheimer's Disease Neuroimaging Initiative 3 (ADNI 3)

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WE REMEMBER

- Steve Ferris 2017
- Leon Thal 2007

SUMMARY OF THIS PAST YEAR

- ADNI 3 was funded by NIA and PPSB
- ADNI 2 was completed, some hold-overs
- ADNI 3 started up
  - Site start up slow, subject enrollment slow
  - Many more sites expected to start soon

WHAT HAPPENED IN PAST YEAR?

- Negative Phase 3 studies by Lilly and Merck
  - One possible explanation is “too late”
- Greater appreciation that cognitive decline/ dementia in the elderly may be “more than AD”
  - Many autopsy studies (ADNI) showed mixed patholgy
- Emerging tau PET data shows
  - Rate of tau accumulation slows with age
  - Comparison of ADNI and UCSF tau PET

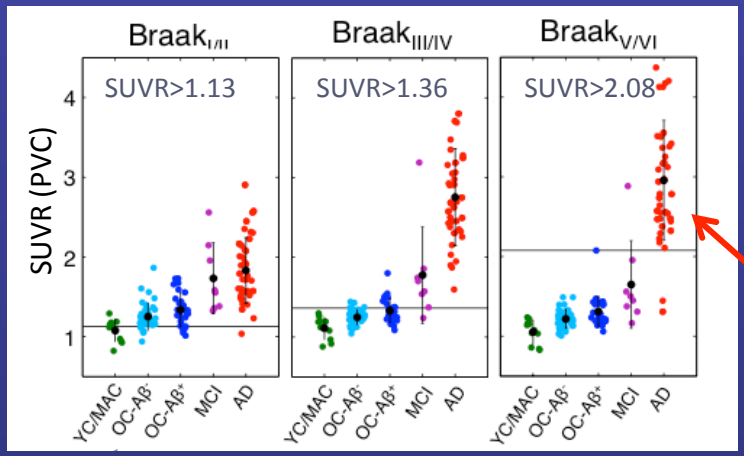
YC/MAC
Young controls/middle aged controls
Mean Age = 39

OC
Old controls (Aβ+ and Aβ-)
Mean age = 78

MCI Mean age = 70
AD Mean age=63

AD
Old controls (Aβ+ and Aβ-)

Berkeley/UCSF



Higher cortical uptake in younger UCSF AD patients

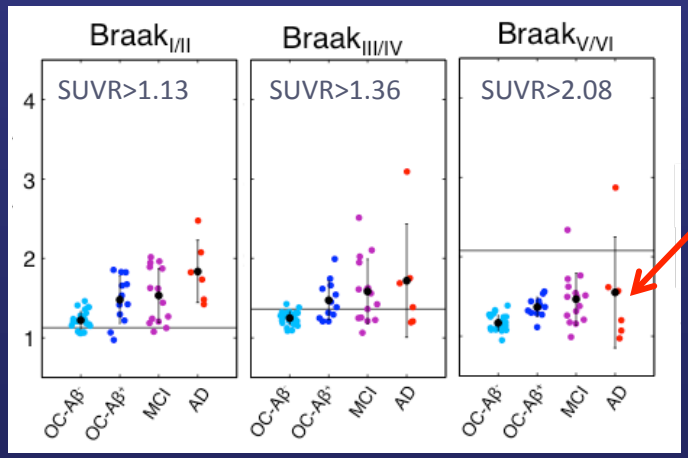
OC

Mean age = 73

MCI
Mean age = 80

AD
Mean age = 80

ADNI



IMPLICATIONS

- We are still in the early days of tau PET.
- These finding emphasize the importance of ADNI. The only large observational study using tau PET, in which data and biosamples are widely shared
- Is it possible that lack of anti AB treatment effects in LOAD are due to mixed pathology?

HIGHLIGHTS FROM DOD ADNI
INCIDENCE OF MCI
(Total 174 participants)

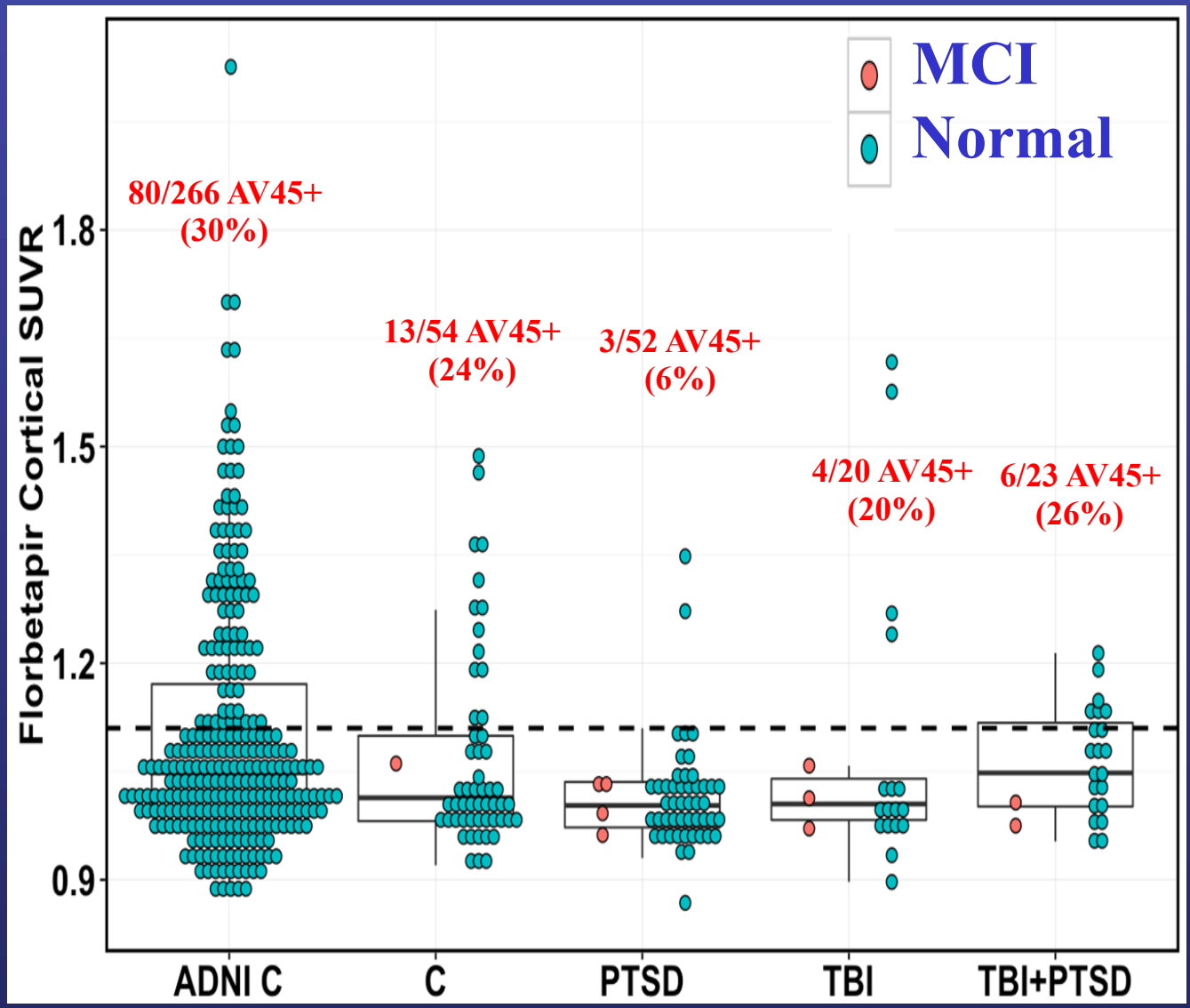
- Healthy Controls 3%
- PTSD subjects 15%
- TBI subjects 10%
- PTSD+TBI subjects 21%

DOD ADNI: Imaging and CSF Results

	Control	TBI	PTSD	TBI &PTSD
Hippocampal volume (% of ICV)	52 0.51 (0.06)	16 0.52 (0.05)	37 0.53 (0.06)	15 0.51 (0.08)
WMH	58 5.6 (5.5)	19 5.0 (5.3)	53 4.3 (3.7)	25 4.5 (5.0)
AV45 (Berkeley)	55 1.07 (0.14)	24 1.08 (0.18)	56 1.02 (0.08)	29 1.08 (0.16)
CSF A-beta	27 218.7 (53.9)	10 222.7 (56.7)	24 237.6 (29.6)	7 229.5 (41.2)
CSF Tau	26 54.7 (27.0)	10 45.8 (9.4)	24 46.4 (16.8)	7 44.4 (13.7)
CSF pTau	27 32.1 (22.1)	10 26.0 (6.7)	24 27.7 (13.6)	6 36.1 (20.6)
MS A-beta 42	37 1091.8 (412.7)	15 1148.9 (487.0)	43 1412.9 (517.4)	20 1305.6 (533.3)
MS A-beta 40	37 7326.5 (2469.1)	15 7404.3 (1695.9)	43 8039.9 (2890.7)	20 7721.9 (2306.8)
MS A-beta 38	37 1627.9 (532.8)	15 1726.5 (396.1)	43 1801.6 (633.6)	20 1712.1 (531.9)

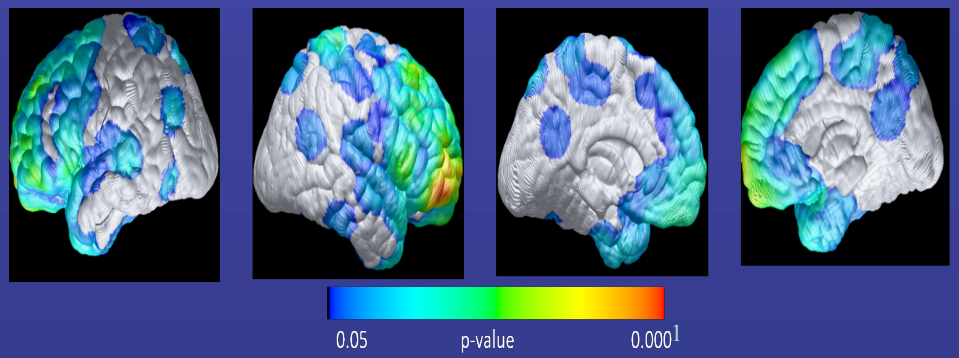
Sample size and mean (standard deviation) is presented, due to differences in processed scans/samples across labs. Control refers to those with neither TBI nor PTSD. Hippocampal volume is generated using FreeSurfer from the Weiner lab. WMH is white matter hyperintensities from the DeCarli lab. AV45 (Berkeley) is the summary SUVR measure from the Jagust/Landau lab.

Florbetapir Amyloid PET: Individual data by group and cognitive status

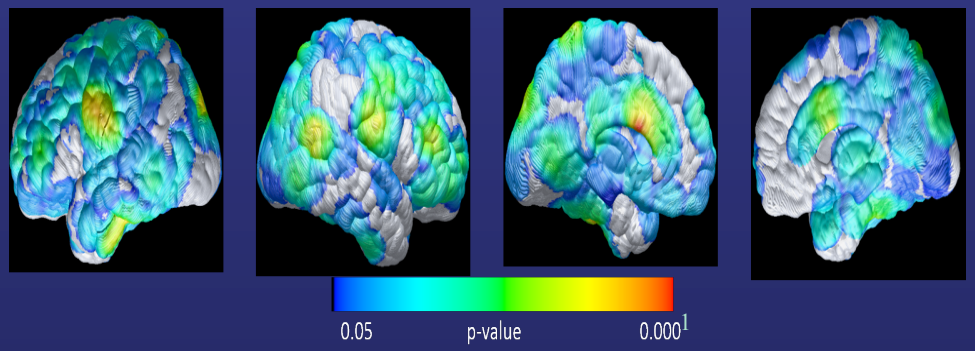


	ADNI C	C	PTSD	TBI	TBI+PTSD	Total N
N	266	54	52	20	23	149
Age	75.6	70.6	67.7	67.5	68.1	
% ApoE4+	26%	28%	27%	37%	38%	

Lower Florbetapir SUVRs in cognitively impaired PTSD Subjects (n=43) than in controls (n=47) , p=0.05 uncorrected (Kewei Chen, Eric Reiman, Banner Inst)



Lower Florbetapir SUVRs in in CU PTSD Subjects with SSRI Use (n=16) than in CU PTSD Subjects without SSRI Use (n=27) p=0.05 uncorrected

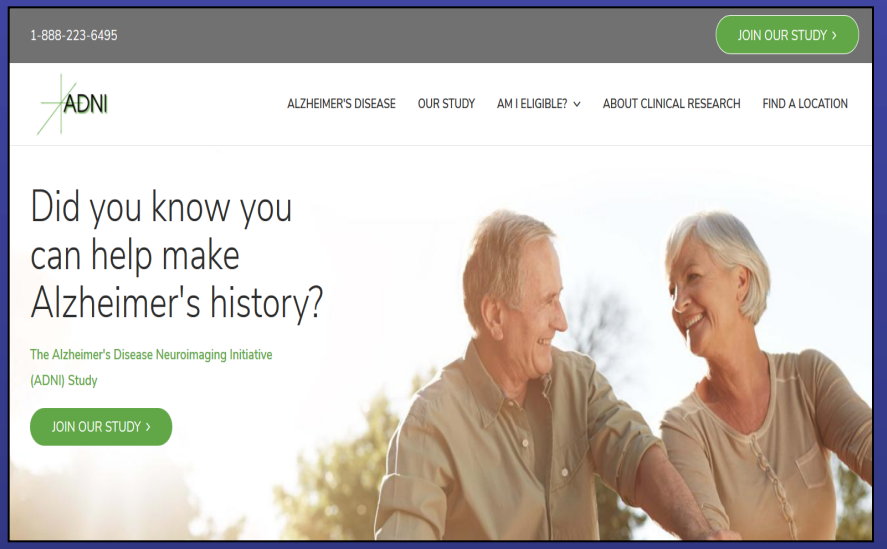


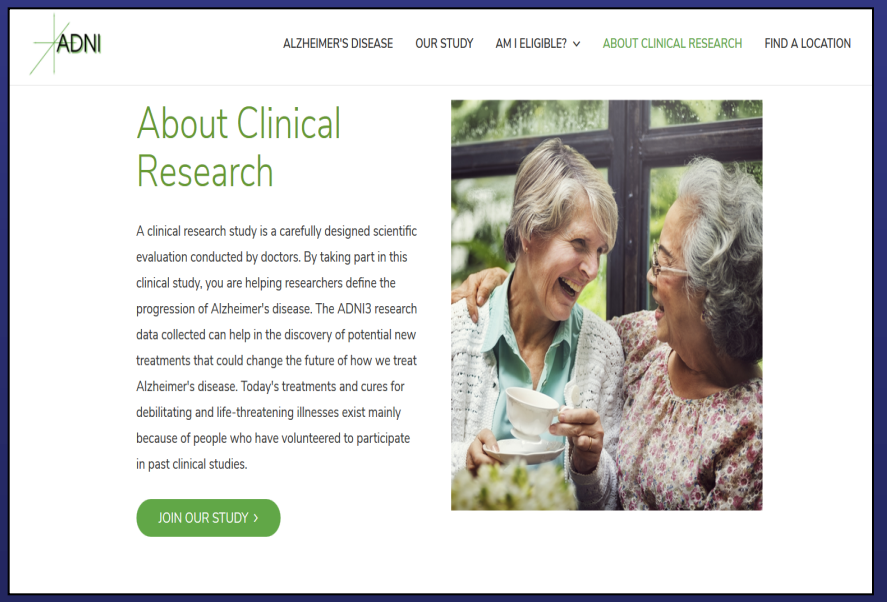
All analyses were w/ Age, Education, APOE status and MMSE corrected, but findings remained w/o.

Monte Carlo simulation (N=1000) showed that # of voxels in the displayed direction is significantly greater than # of voxels in the opposite direction ($p<0.001$).

ADNI3 WEBSITE FOR RECRUITMENT

- Recruitment website for ADNI3
- Three main paths for potential participants
  1) Call 800 number
  2) Take eligibility screener
  3) Find a location
- Tracking





ACCOMPLISHMENTS OF ADNI

- Validation of "amyloid phenotyping"
- Large scale longitudinal tau PET
- Improved CSF analysis: leading to clinical use
- Over 1022 publications from ADNI
- Data widely used for design of AD clinical trials
  - Growing number of trials, problem for ADNI recruitment

THE BIG PROBLEMS

- Overall, the problem is recruitment/retention
- Importance of continuing ADNI2 rollovers
  - Please encourage subjects to continue in ADNI
- Difficulty in enrolling new subjects
  - High subject burden
  - Competing clinical trials
- Paul Aisen/Ron Petersen will discuss later this morning