Imaging the Brains of Centenarians

Never Stand Still | Medicine | Psychiatry

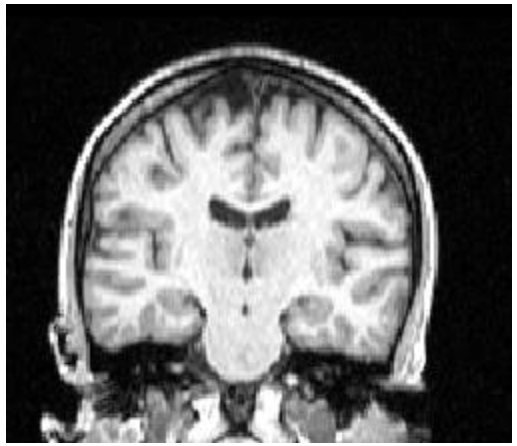
Perminder Sachdev

Centre for Healthy Brain Ageing (CHeBA)
School of Psychiatry, UNSW &
Neuropsychiatric Institute, Prince of Wales Hospital, Sydney

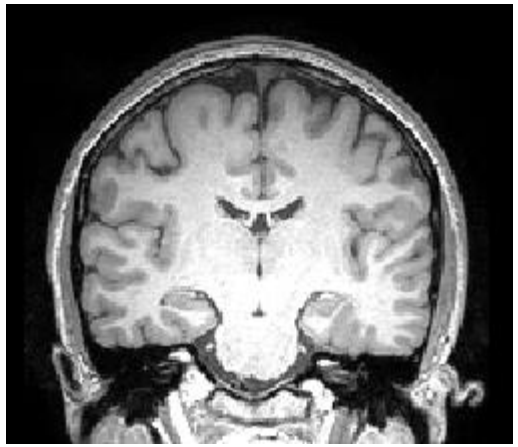
Overview

1. How does the brain change with 'normal' ageing up to the 10th and 11th decades of life?
    a. Volumes of brain structures, both cortical and subcortical
    b. Brain networks
2. What does neuroimaging tell us about the accumulation of pathology in the ageing brain?
    a. White matter abnormalities
    b. Cerebral infarctions
    c. Cerebral microbleeds
    d. Alzheimer-type pathology, esp. with amyloid imaging
    e. Hippocampal sclerosis
3. Present data from the Sydney Centenarian Study on brain imaging
4. How does brain pathology on neuroimaging relate to brain function?

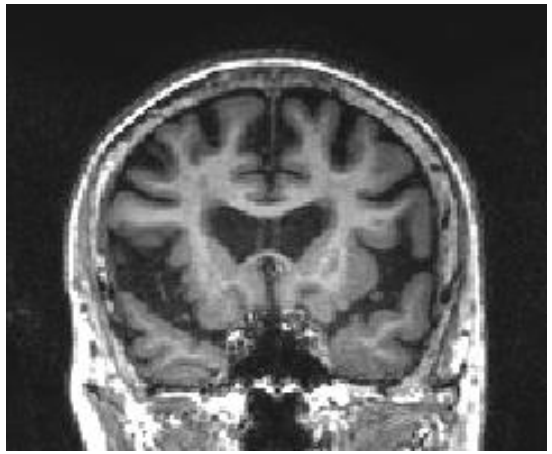
MRI - Atrophy



A 20 year old



A 40 year old



A 100 year old

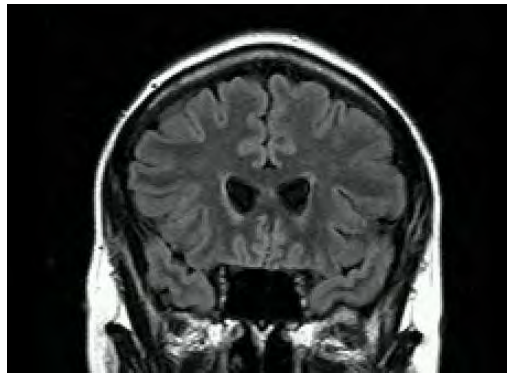
Brain changes with age:

- Atrophy of gyri
- Widened sulci
- Enlarged ventricular system

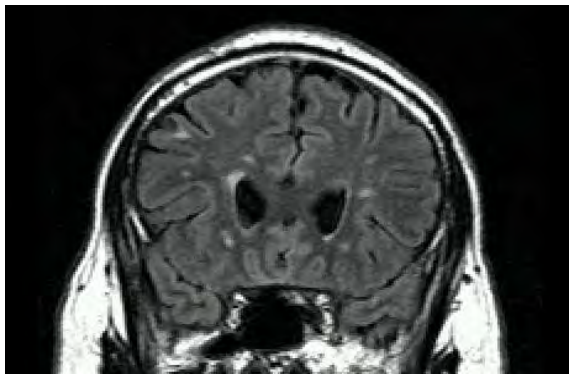
Brain weight shrinks:

- 5% by 70 years
- 10% by 80 years
- 20% by 90 years

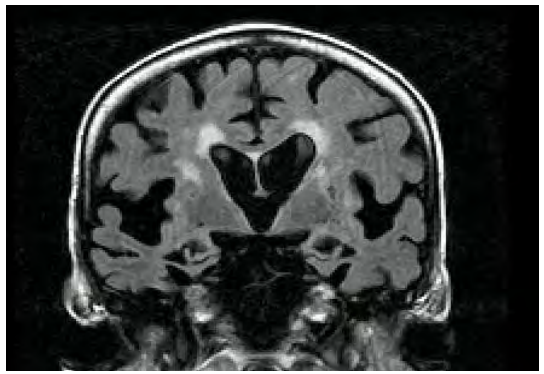
MRI – White Matter Hyperintensities (WMH)



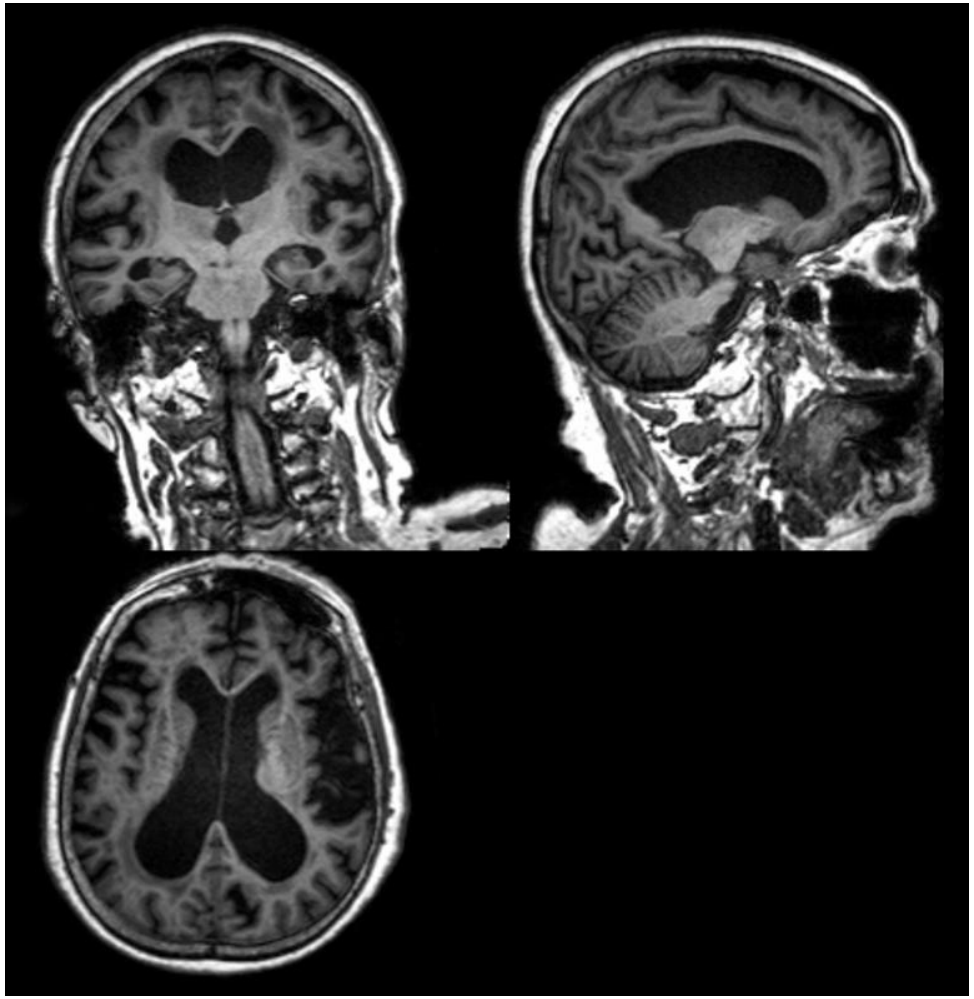
A 40 year old

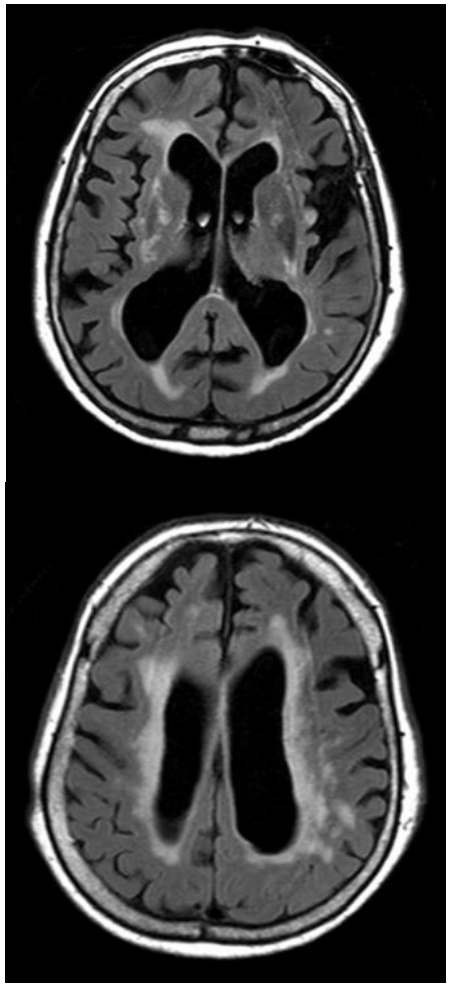


A 60 year old

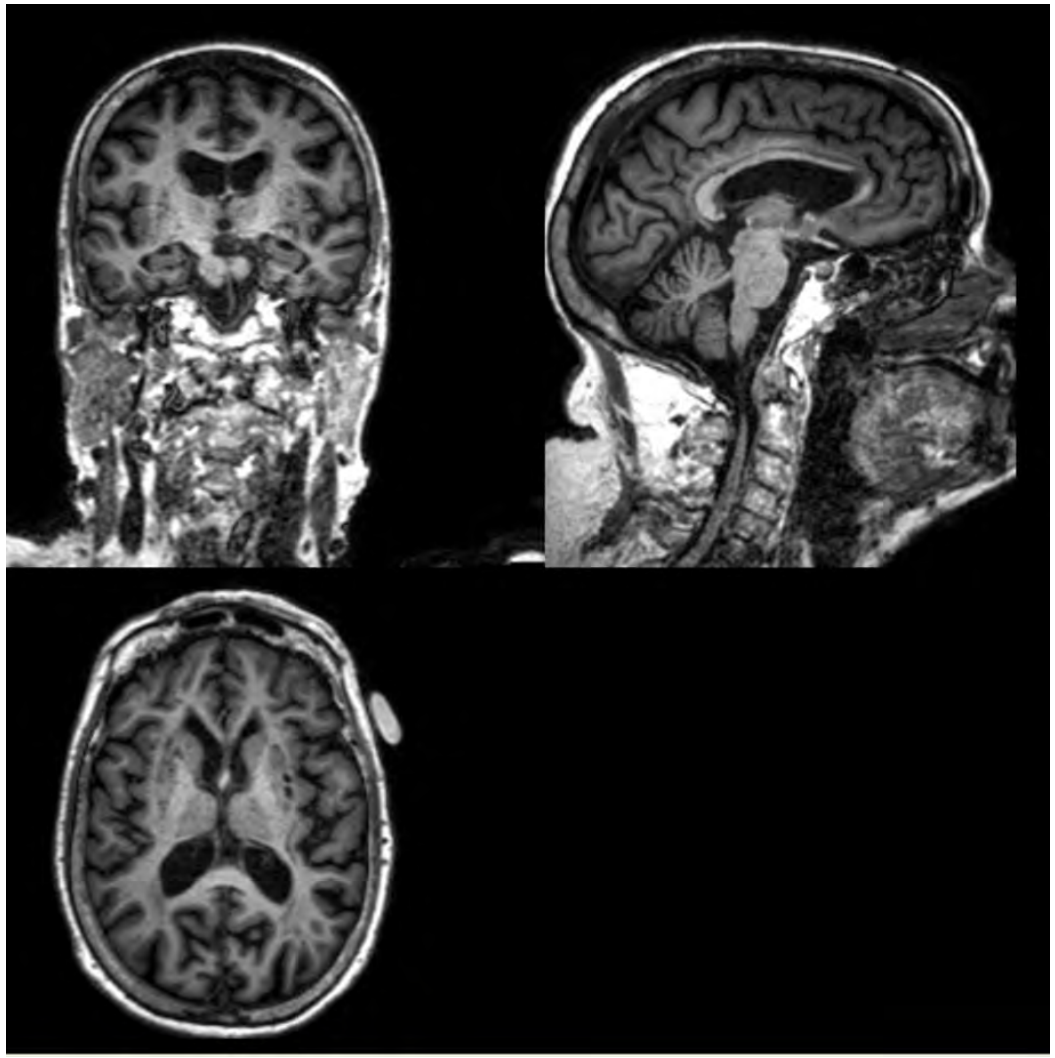


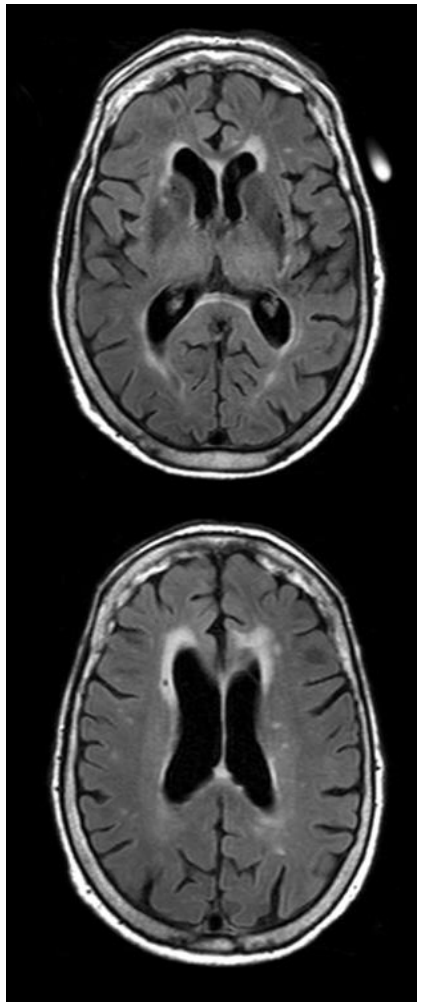
A 100 year old



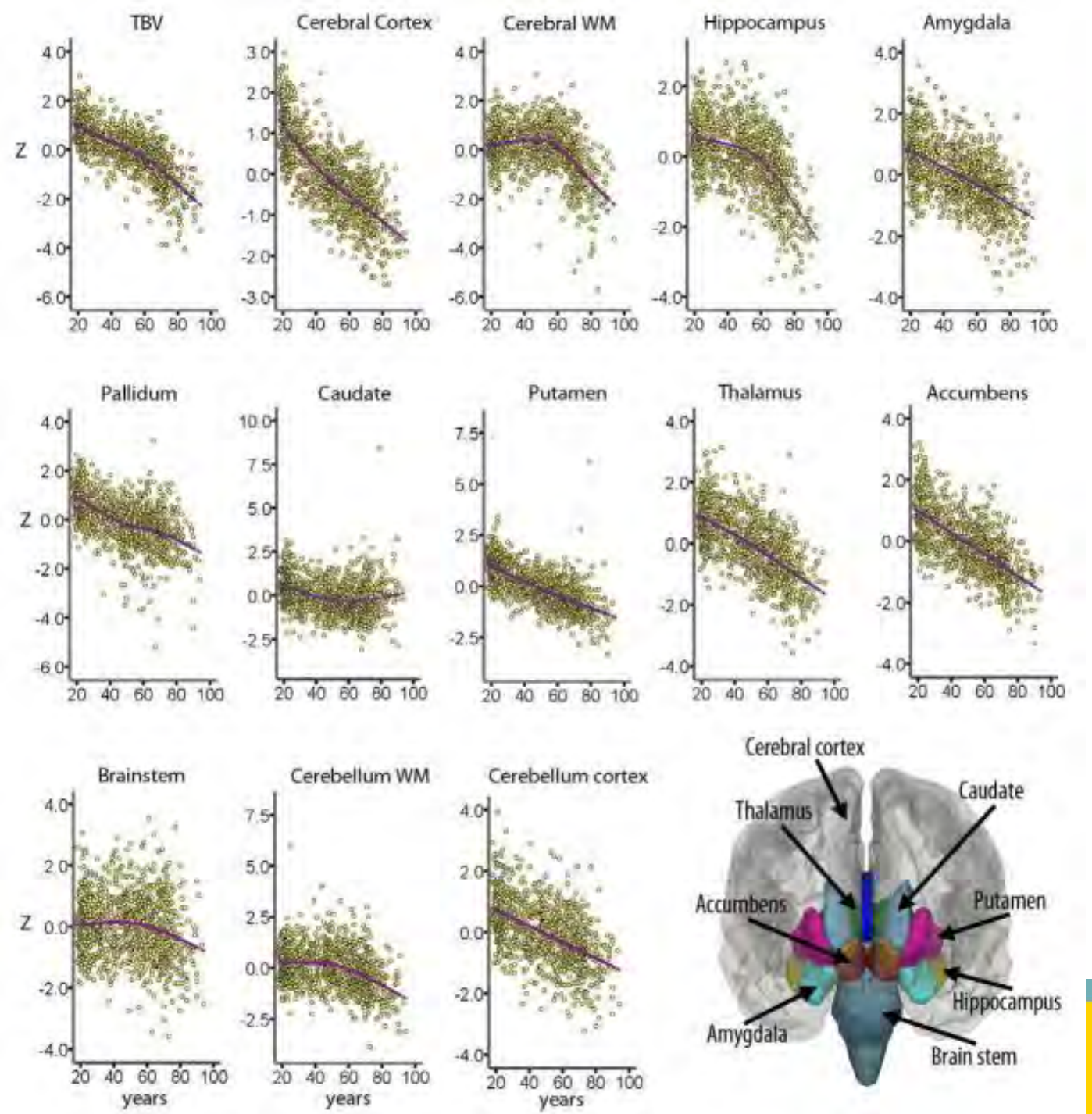


101 years F,11 years education,
MMSE 19/30 (unadjusted), ACER 58/100





101 years F, 6 years education
MMSE 29/30, ACER 85/100



Scatterplots of age-brain structure relationships

A non-parametric smoothing spline approach to delineate cross-sectionally estimated age-trajectories of the volume of 17 neuroanatomical structures in 1100 healthy adults (18–94 years).

Neurobiol Aging. 2013 Oct;34(10):2239-47

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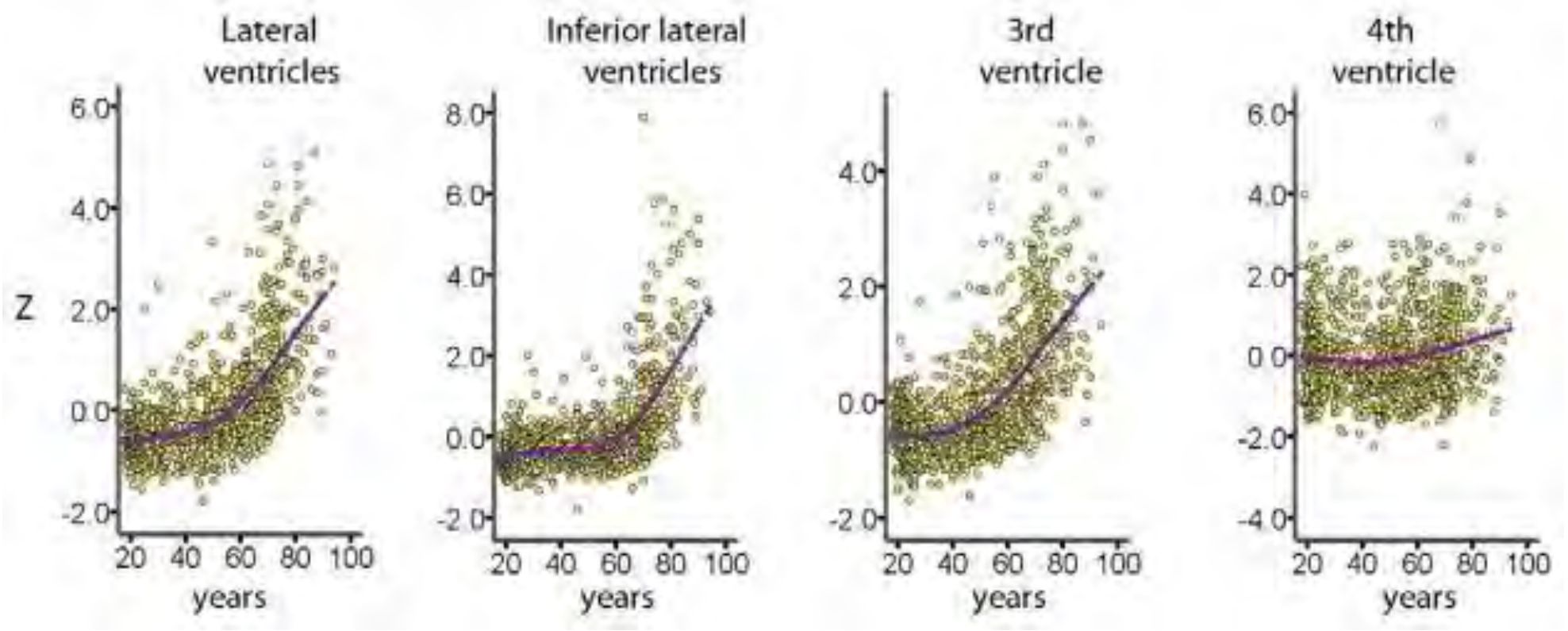
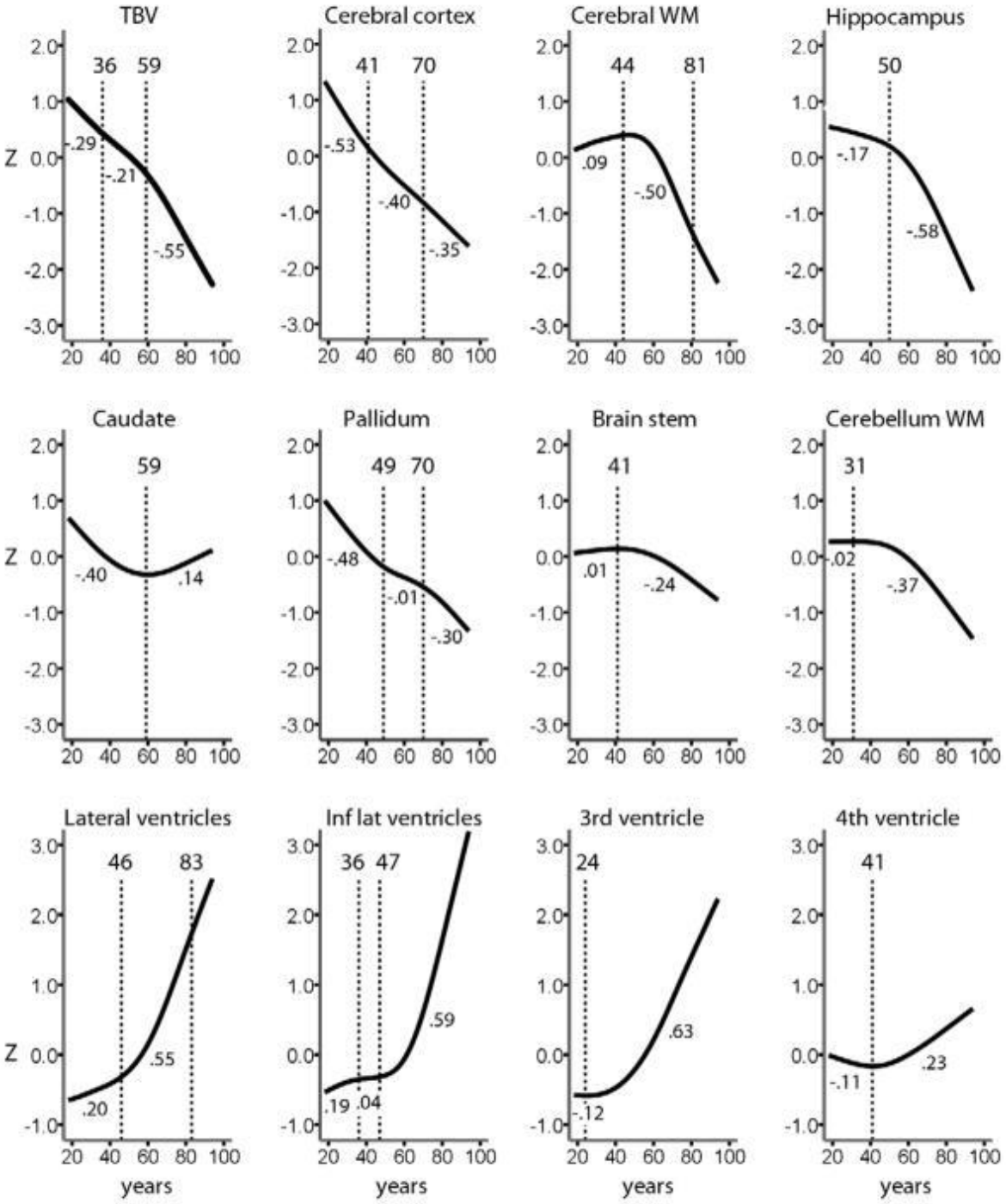
Scatterplots of age - ventricular system relationships

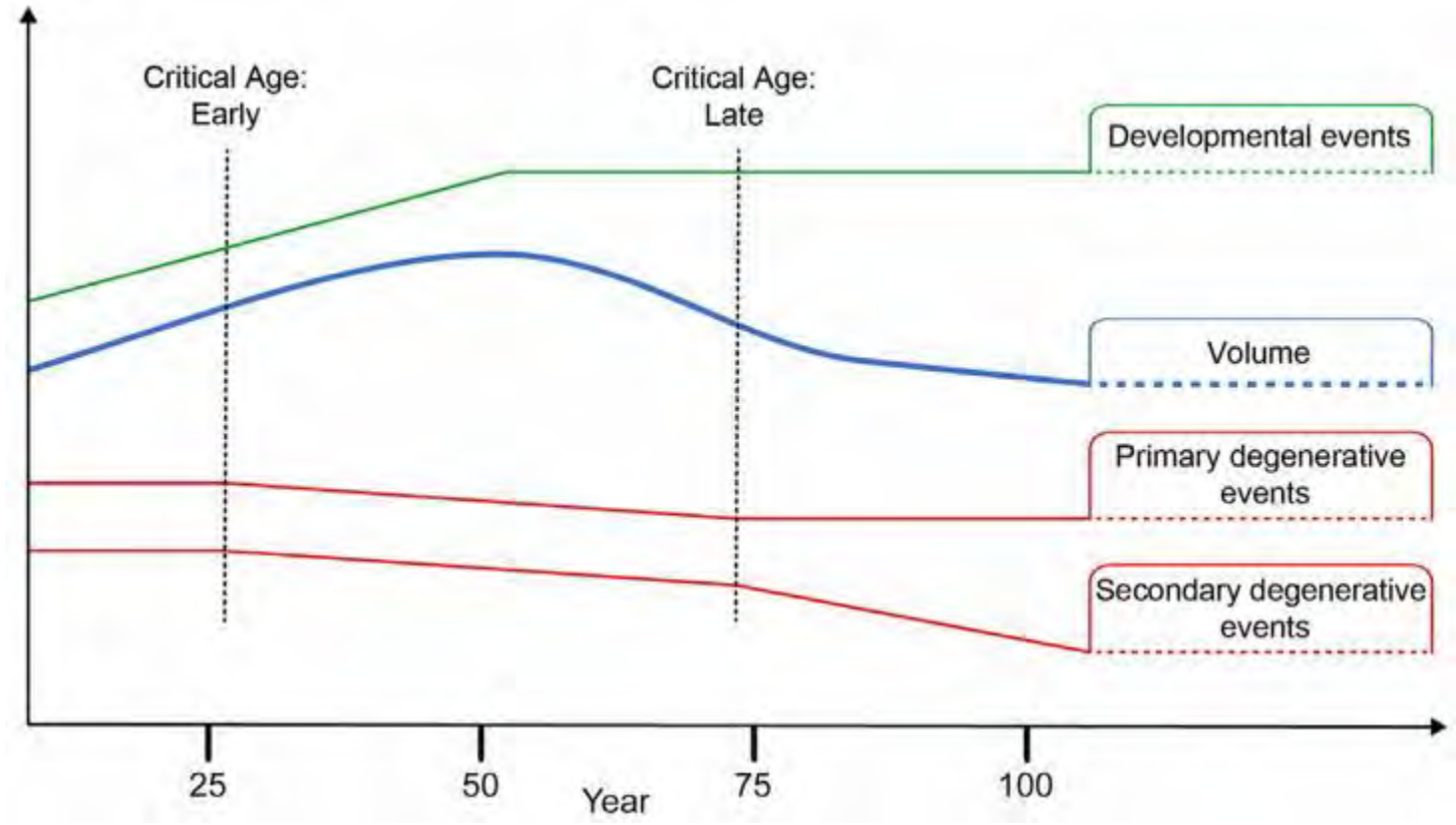


Neurobiol Aging. 2013 Oct; 34(10): 2239–2247.



Estimated age-trajectories and critical ages

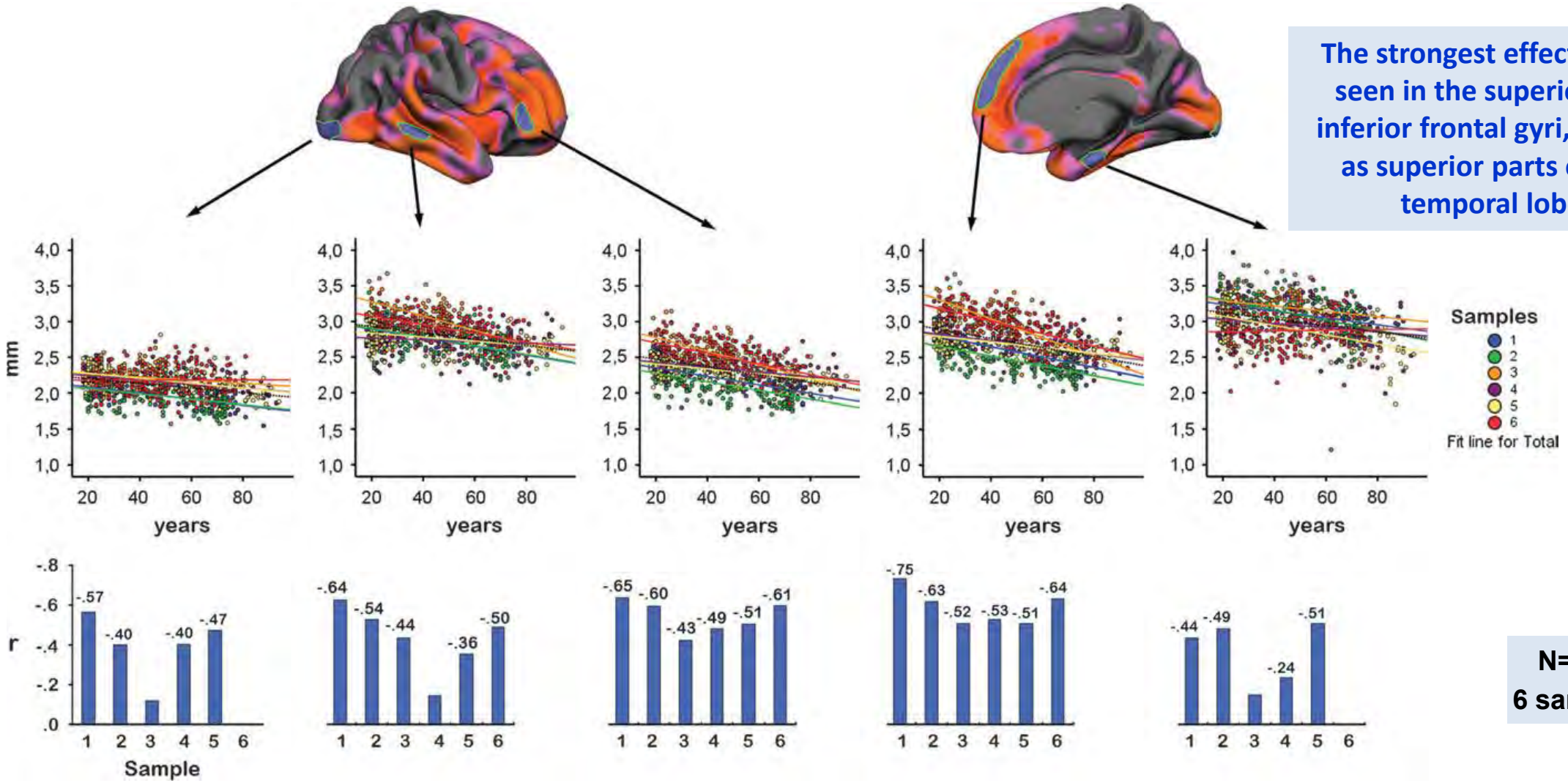
A hypothetic model for discontinuous change in rate of atrophy



- **No sex differences in age trends except for the caudate were observed.**
- **No evidence of neuroprotective effects of larger brain size or educational attainment.**

N=140
5 year FU in 129

Raz et al. Cerebral Cortex November 2005;15:1676--1689



The strongest effects were seen in the superior and inferior frontal gyri, as well as superior parts of the temporal lobe

N=883
6 samples

Scatter plots of mean thickness in selected cortical areas

Cerebral Cortex September 2009;19:2001--2012

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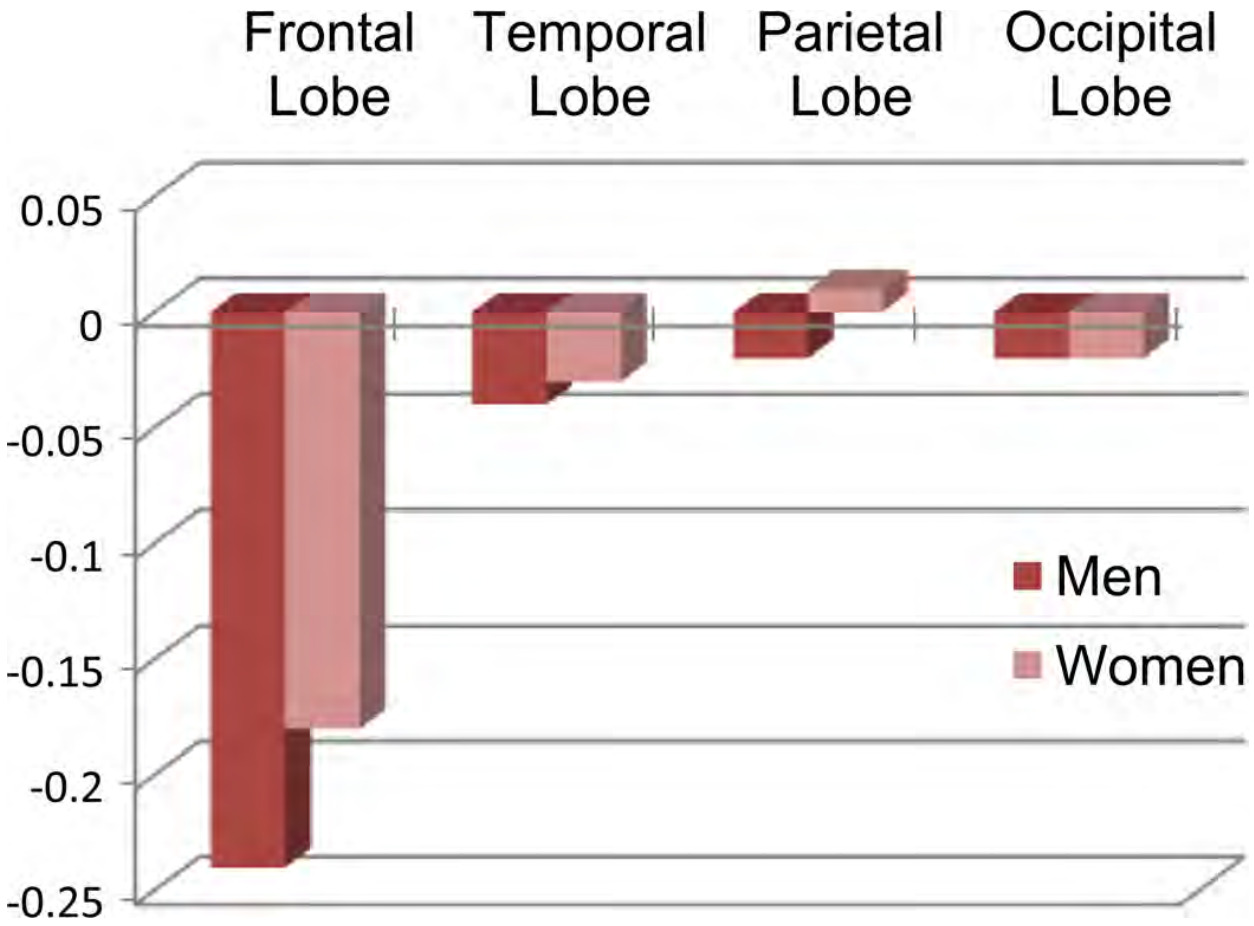
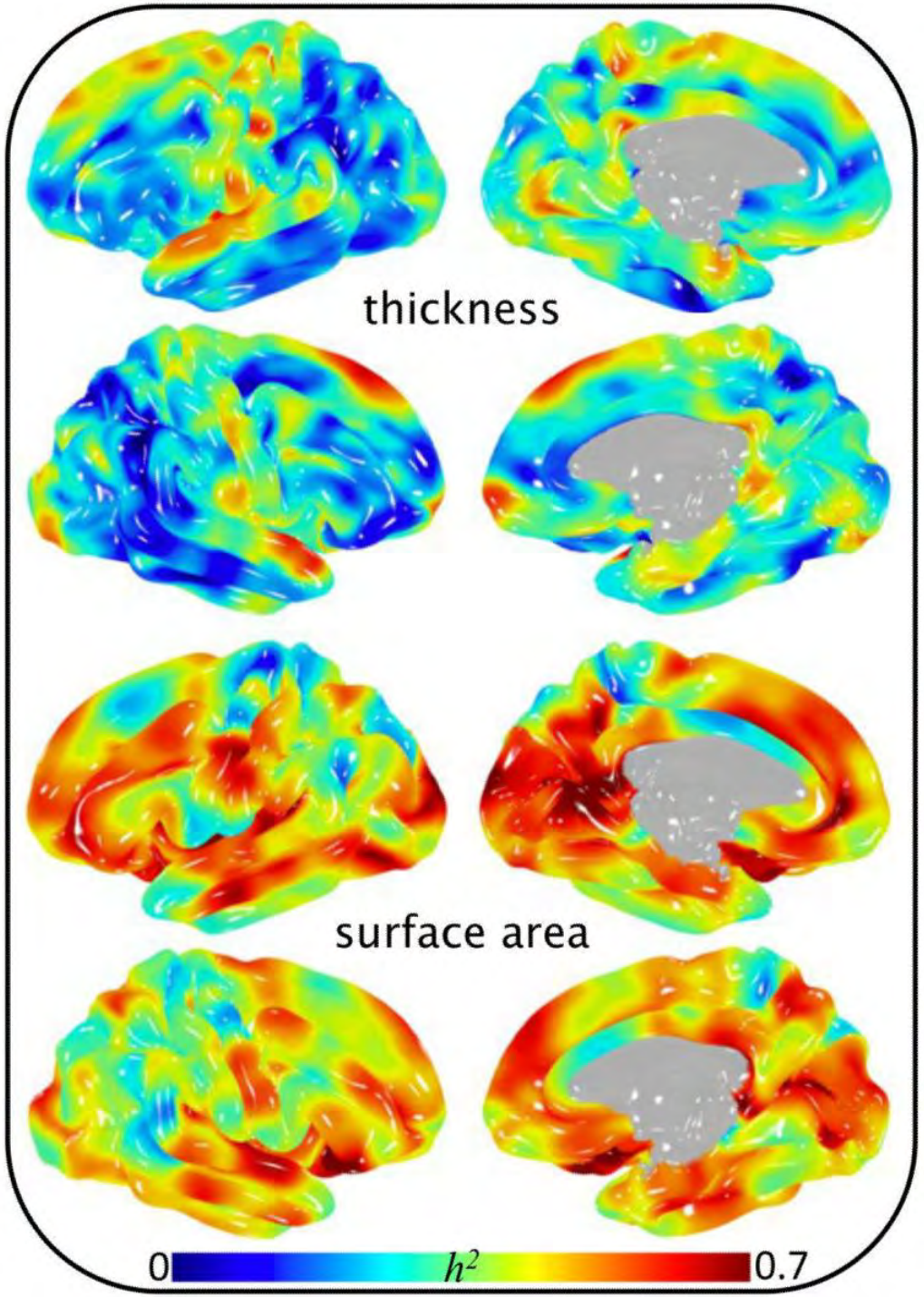


Cross-sectional estimates of yearly differences in lobar brain volumes as a percentage of head size for men and women of the Framingham Heart Study. Significant differences are seen for Frontal and Temporal lobar brain volumes, but not Parietal or Occipital

Neuropsychol Rev. 2014 Sep; 24(3): 271–289



Heritability of 40,962 pointwise cortical phenotypes in 838 subjects.

Brain Imaging Behav. 2014 June ; 8(2): 143–152.

Cross-sectional MRI Study

- Objective: brain changes in aging and in dementia
- Subjects
  - Sydney Centenarian Study: 95-103 years
  - Sydney Memory and Ageing Study: 71-94 years
- Dementia consensus
- Brain MRI: T13D and FLAIR

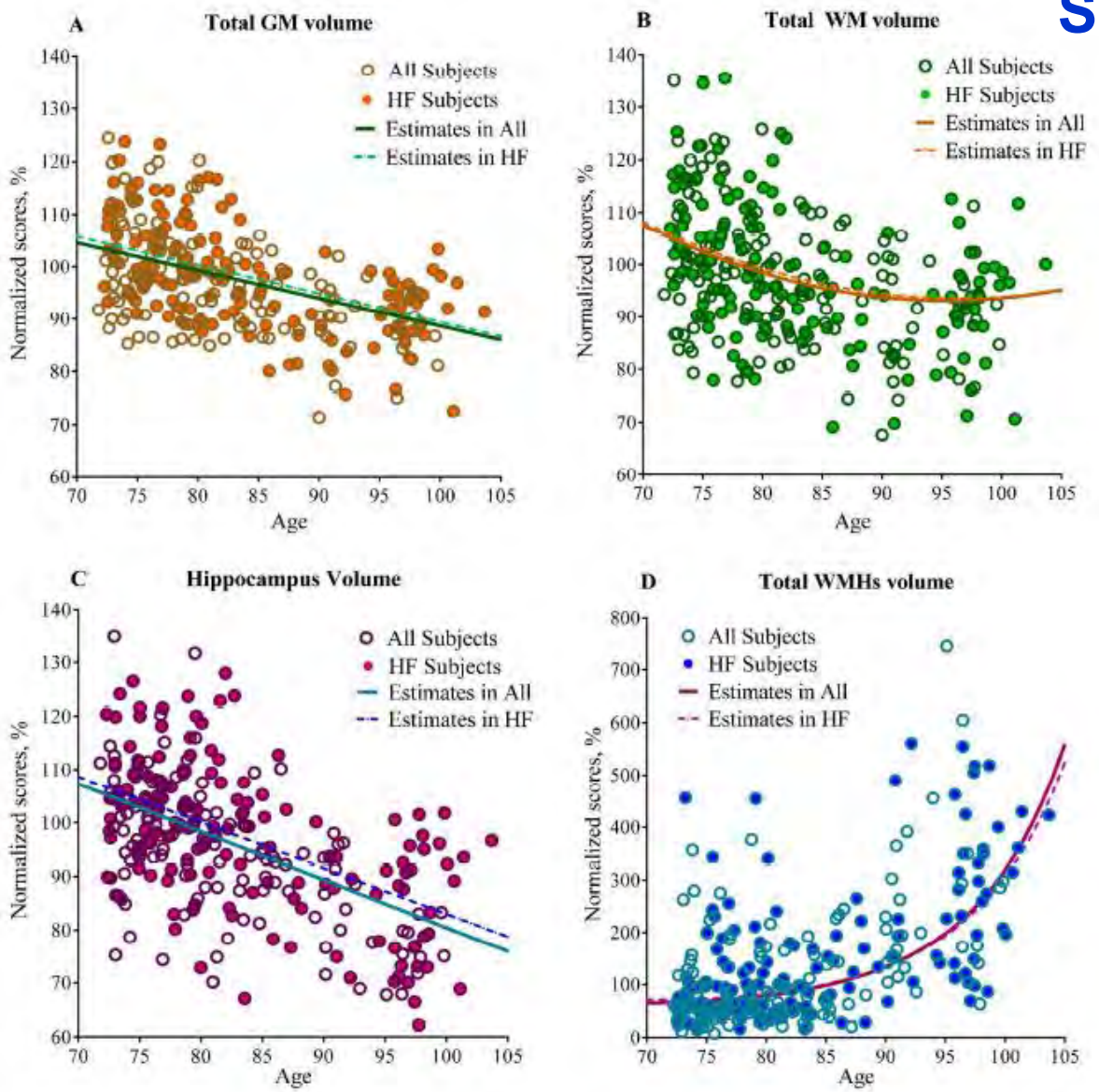
Sachdev et al. 2010, 2013

Non-demented

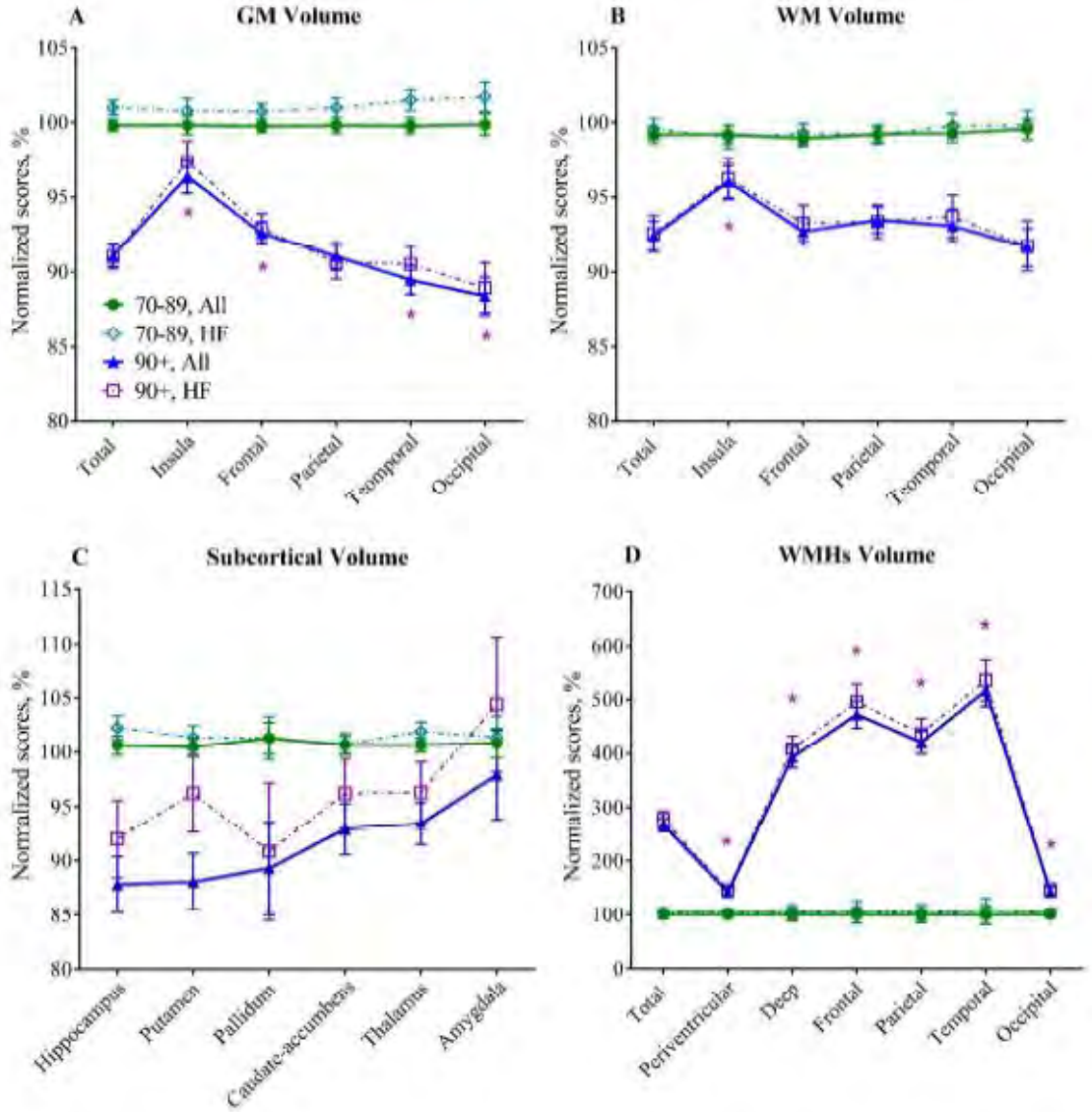
Demographics of participants in different decades of age.					
Age range, years	70-79	80-89	90-99	100+	p[a]
Non-demented, N	134	73	65	5	-
High-functioning %	58.2%	53.4%	58.5%	100%	-
Age, years (mean ± SD)	75.9 ± 2.3	83.7 ± 2.6	94.9 ± 3.1	101.4 ± 1.4	<0.001
Female %	50.7%	56.2%	50.8%	20%	0.446
MMSE (mean ± SD)	28.4 ± 1.4	27.8 ± 1.6	27.2 ± 2.0	28.4 ± 0.6	<0.001
APOE ε4 carriage %	25%	22.2%	16.1%	0%	0.380

[a]p value of Fisher's Exact Test or analysis of variance.

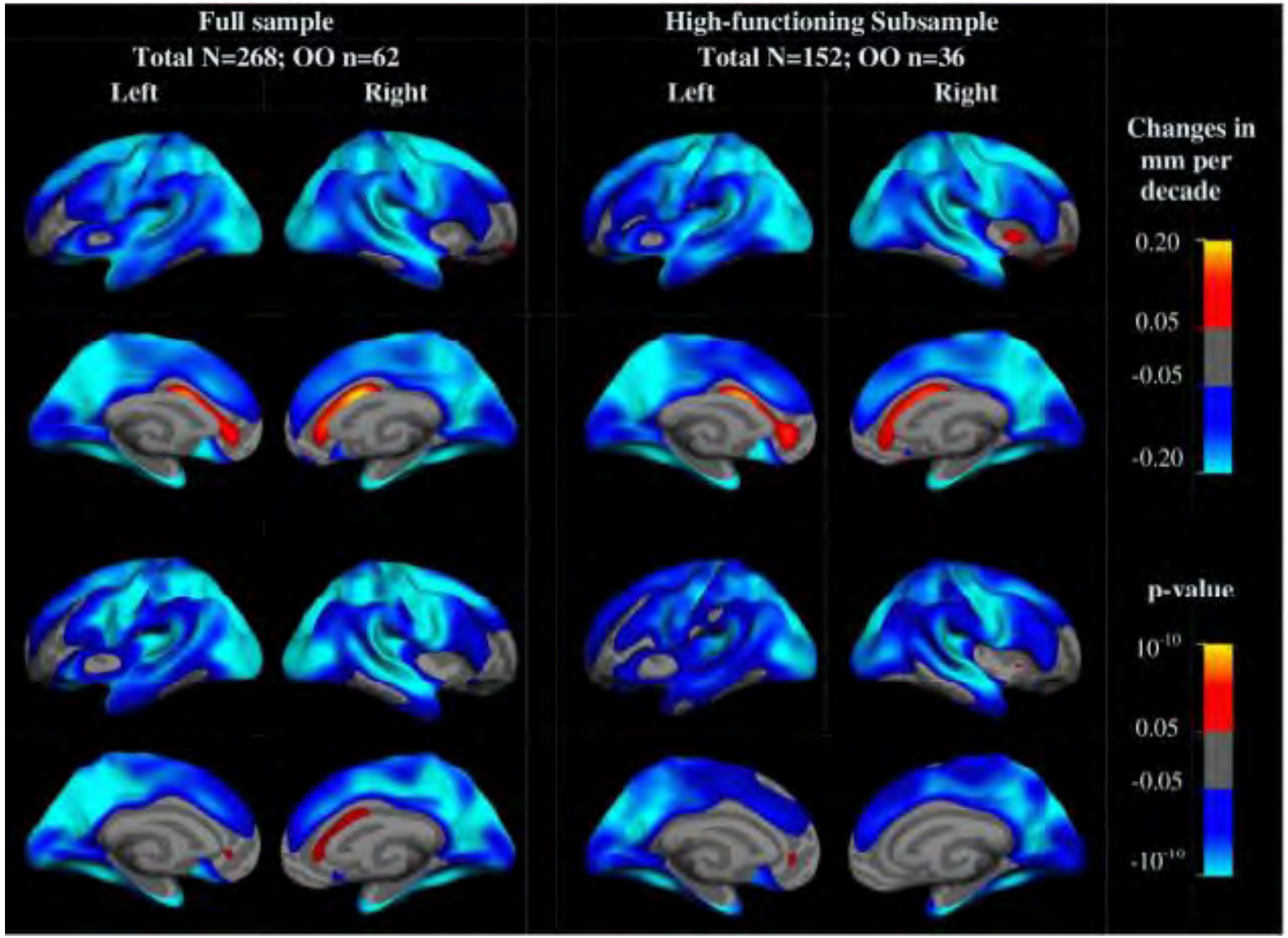
SCS



Relationship of age with total brain volumes from 71 to103 years



Group comparison of brain volumetrics between the young old (YO, 70-89 years) and oldest old (OO, 90+ years).



Surface analysis of age effects on cortical thickness

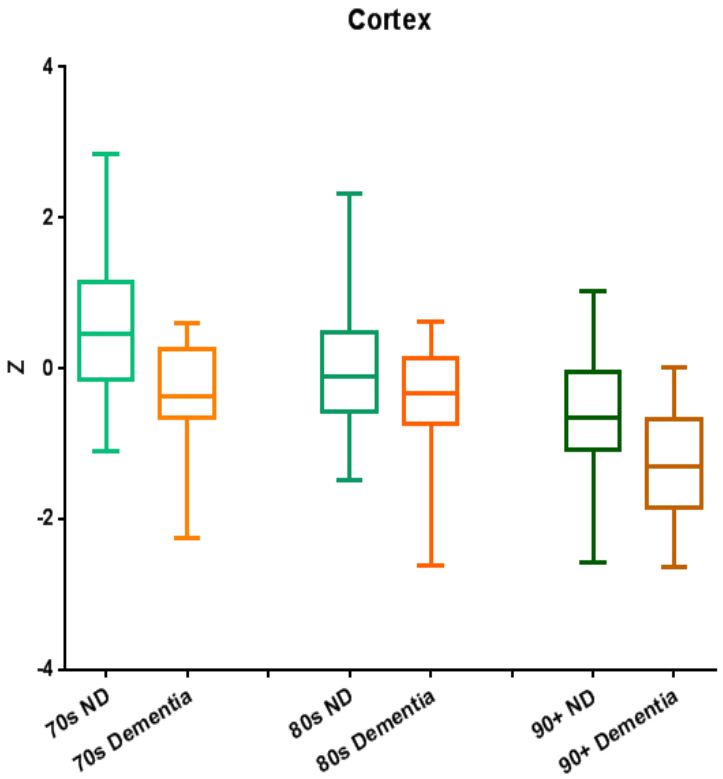
Yang et al. Neurobiol Aging 2016; 40:86-97

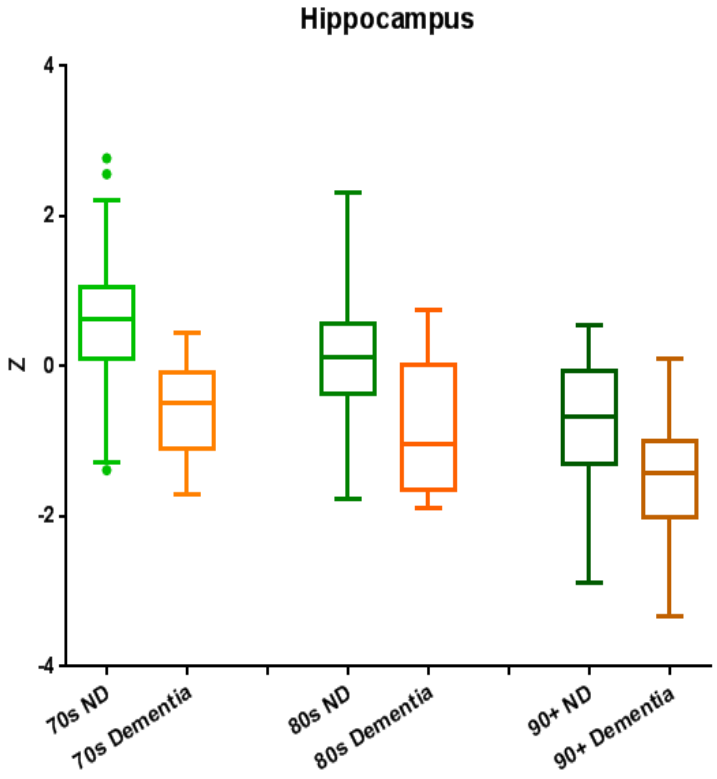
Demented

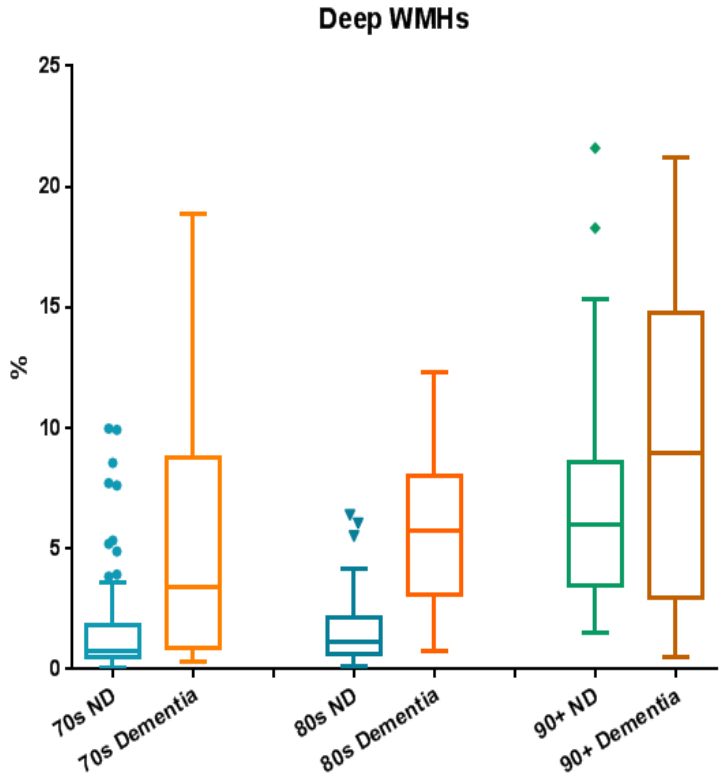
Demographics of participants in different decades of age.					
Age range, years	70-79	80-89	90-99	100+	p[a]
N	10	16	10	4	-
Age, years (mean ± SD)	78.1 ± 1.5	86.6 ± 2.0	94.9 ± 2.5	101.5 ± 0.6	<0.001
Female %	50.0%	37.5%	70%	100%	0.100
MMSE (mean ± SD)	24.4 ± 2.3[c]	22.6 ± 4.1[d]	22.1 ± 2.9	16.5 ± 4.2[c,d]	0.005[c,d]
APOE ε4 carriage %	50.0%	37.5%	11.1%[e]	0%[d]	0.219

[a]p value of Fisher's Exact Test or analysis of variance.

Cortex, hippocampus and deep WMHs

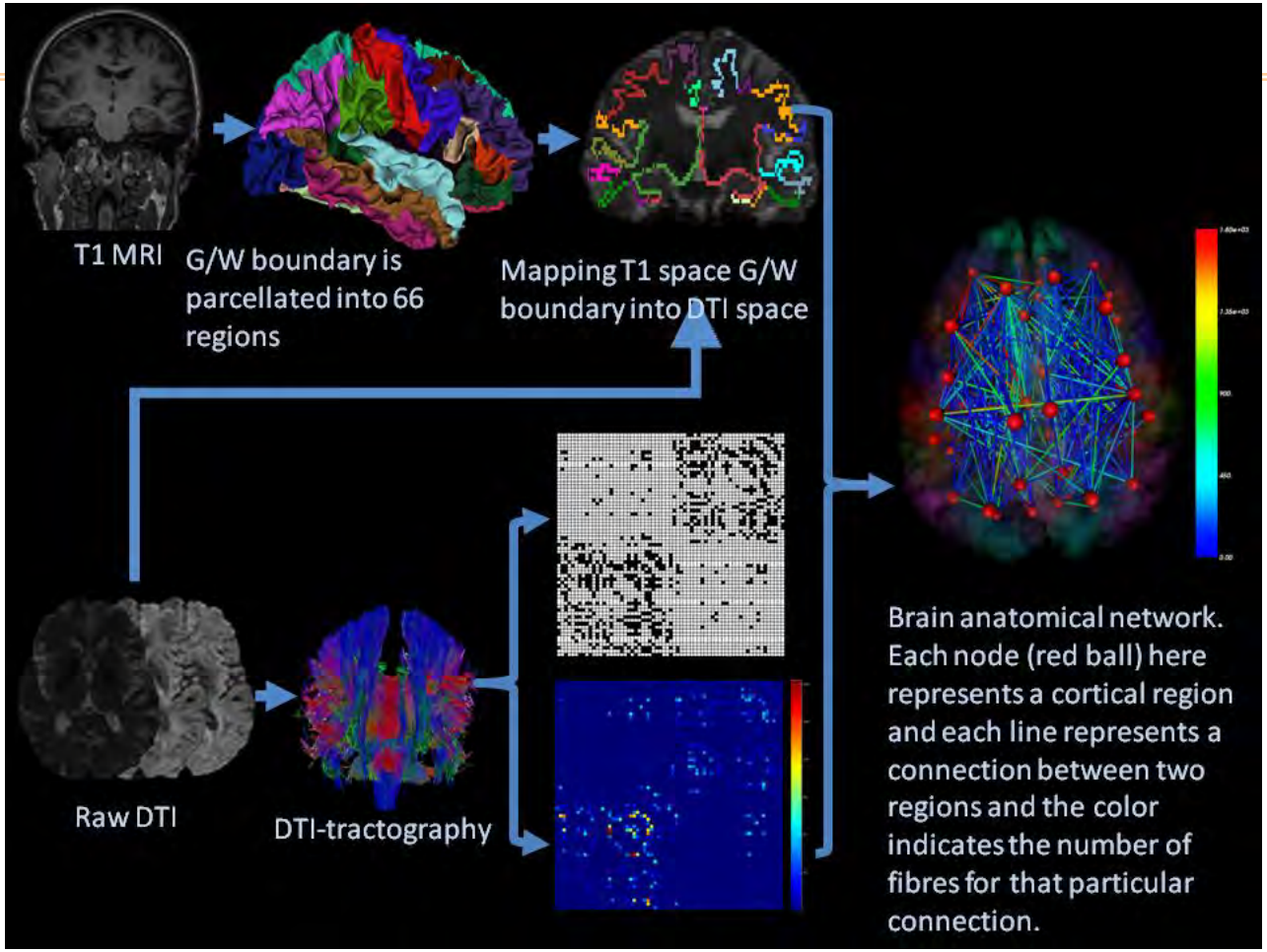




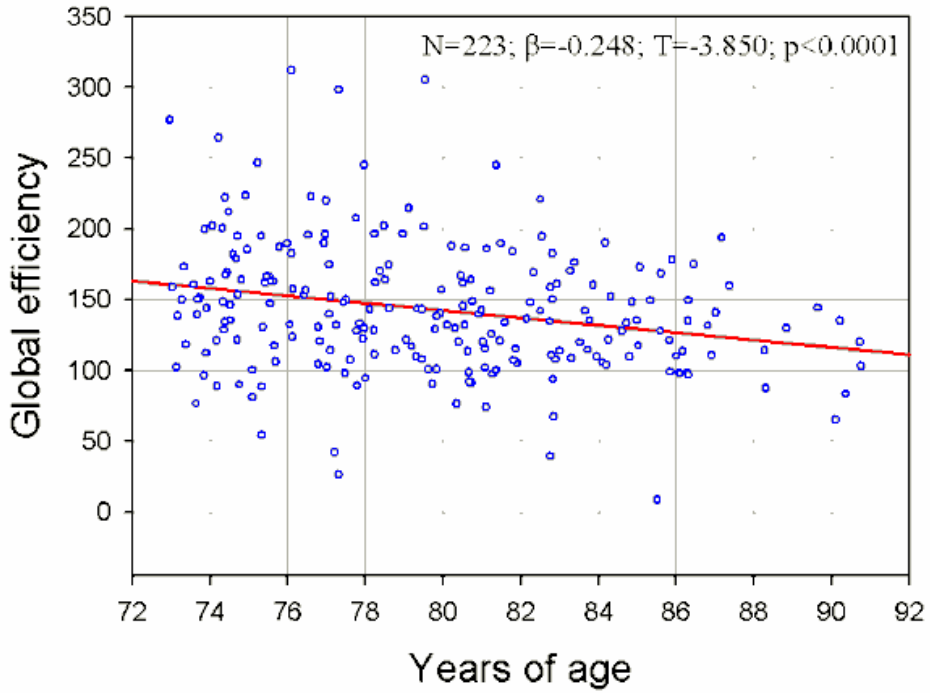


Logistic Regression	OR (95% CI) at 80 years	OR (95% Ci) at 95 years	p-value (age*MRI)
Cortex, Z	12.26 (4.65 – 32.38)	7.57 (2.61 – 21.91)	0.320
Hippocampus, Z	6.37 (3.13 – 12.98)	3.39 (1.15 – 7.45)	0.204
Deep WMHs, 5%	5.21 (2.45 – 11.07)	1.70 (1.02 – 2.84)	**0.010***

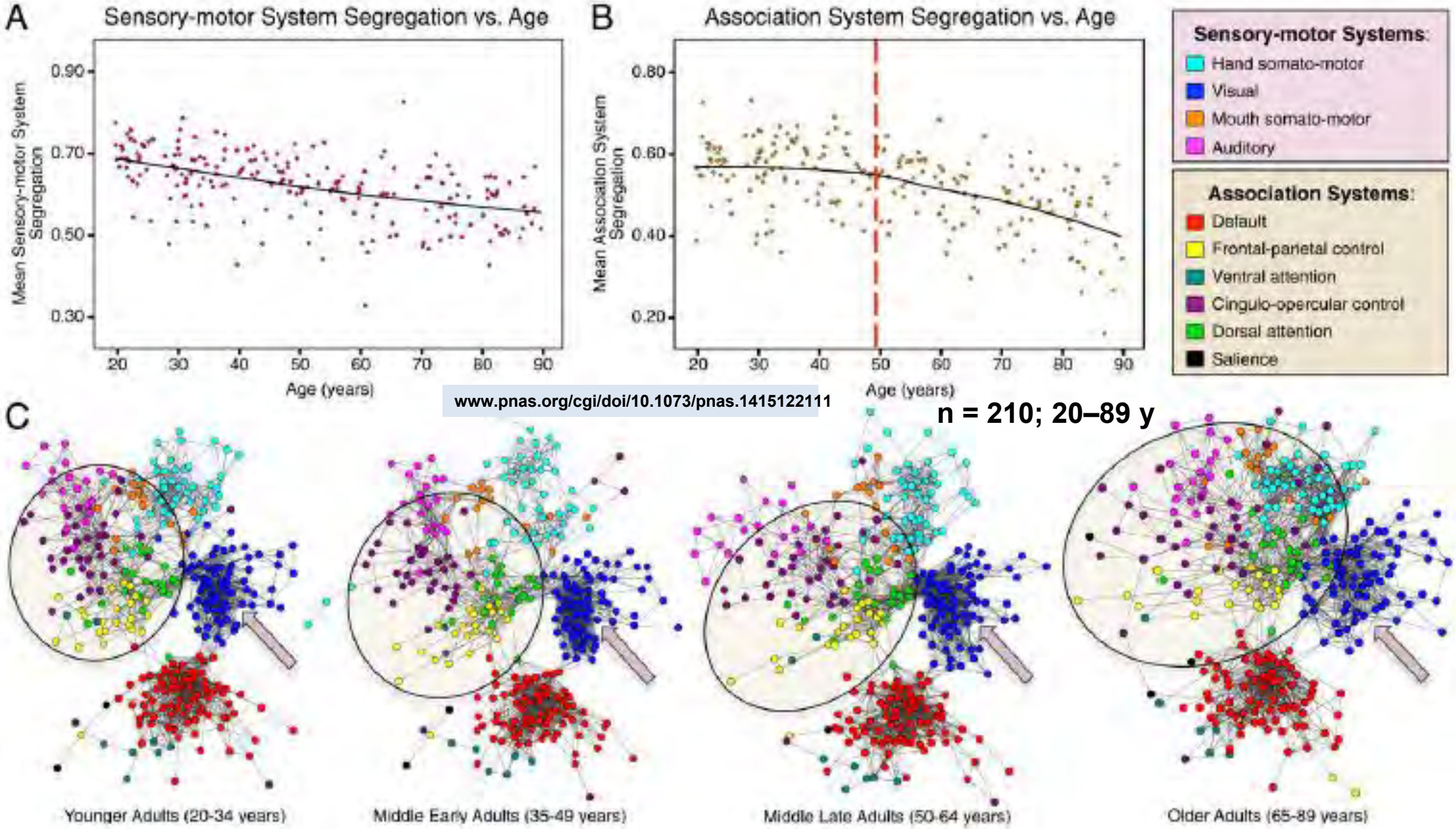
Brain network construction

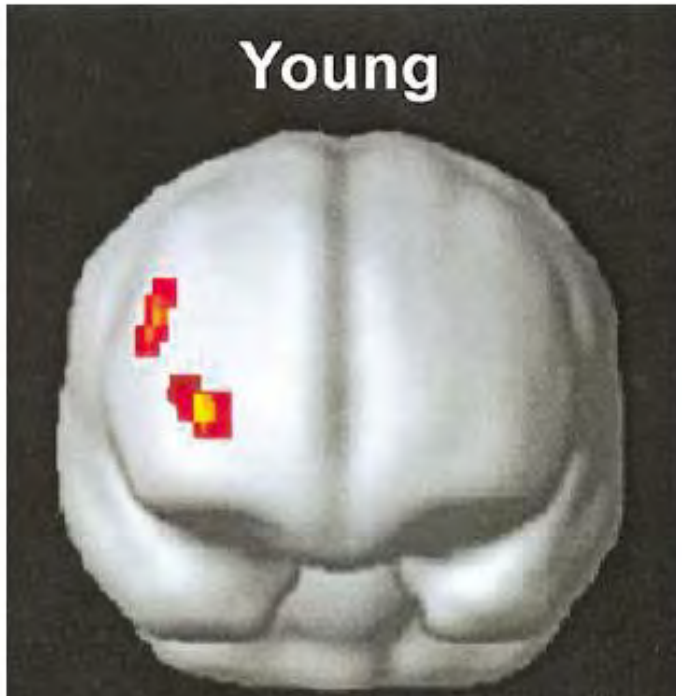


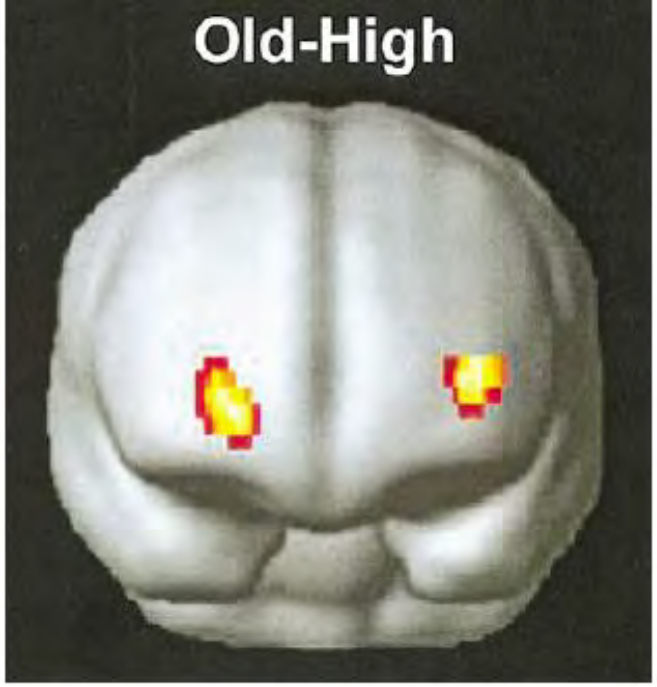
Age - anatomical networks

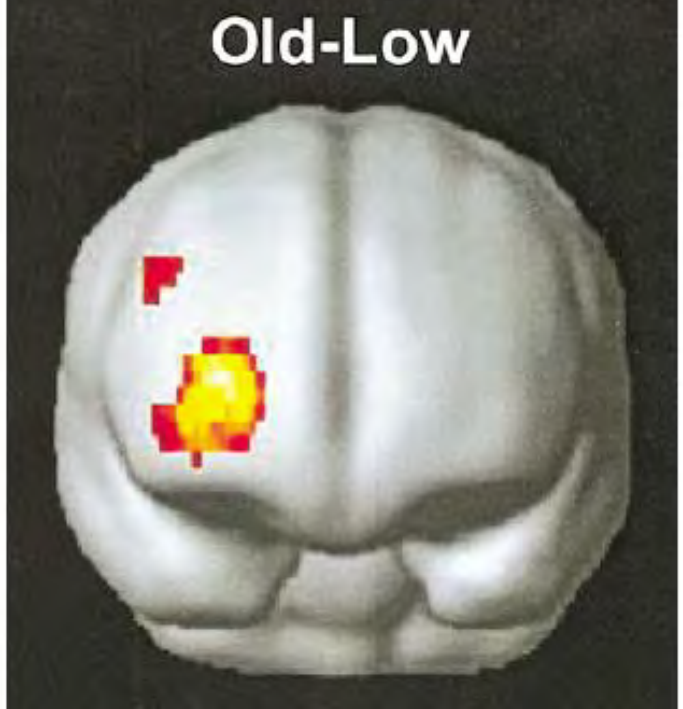


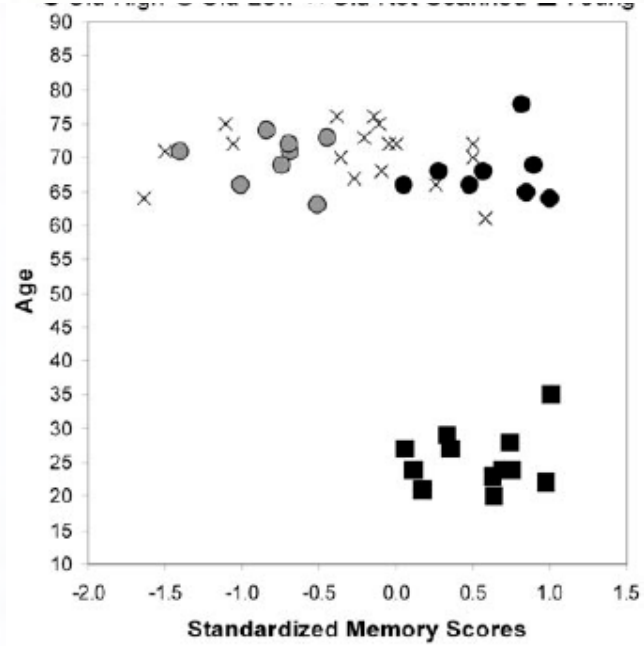
Global efficiency vs. Age: considering the connectivity of the whole brain


A
Sensory-motor System Segregation vs. Age
Mean Sensory-motor System Segregation
0.90
0.70
0.50
0.30
20
30
40
50
60
70
80
90
Age (years)
B
Association System Segregation vs. Age
Mean Association System Segregation
0.80
0.60
0.40
0.20
Age (years)
Sensory-motor Systems:
Hand somato-motor
Visual
Mouth somato-motor
Auditory
Association Systems:
Default
Frontal-parietal control
Ventral attention
Cingulo-opercular control
Dorsal attention
Salience
www.pnas.org/cgi/doi/10.1073/pnas.1415122111
C
n = 210; 20–89 y
Younger Adults (20-34 years)
Middle Early Adults (35-49 years)
Middle Late Adults (50-64 years)
Older Adults (65-89 years)



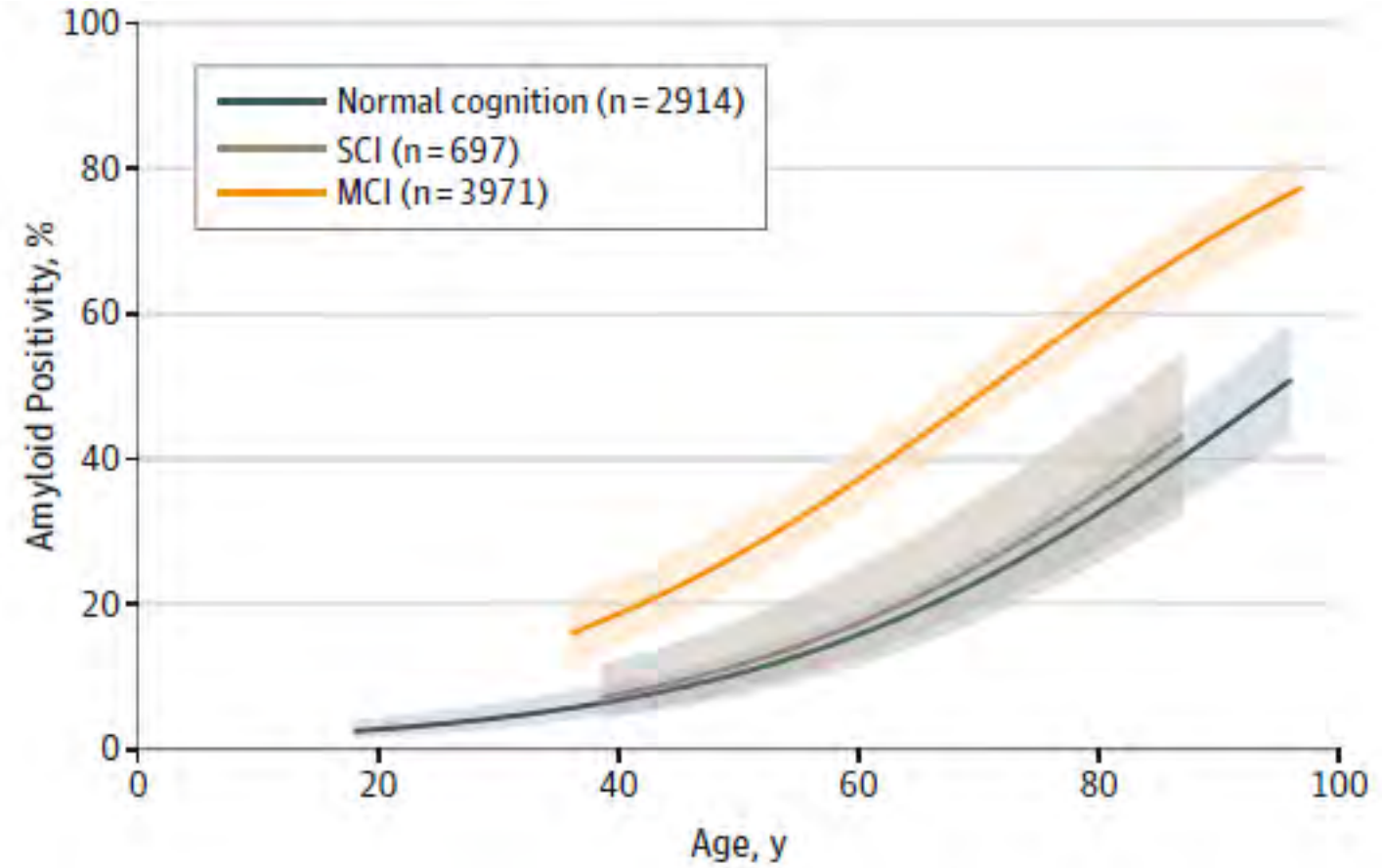






Cabeza R et al. NeuroImage 17, 1394–1402 (2002)

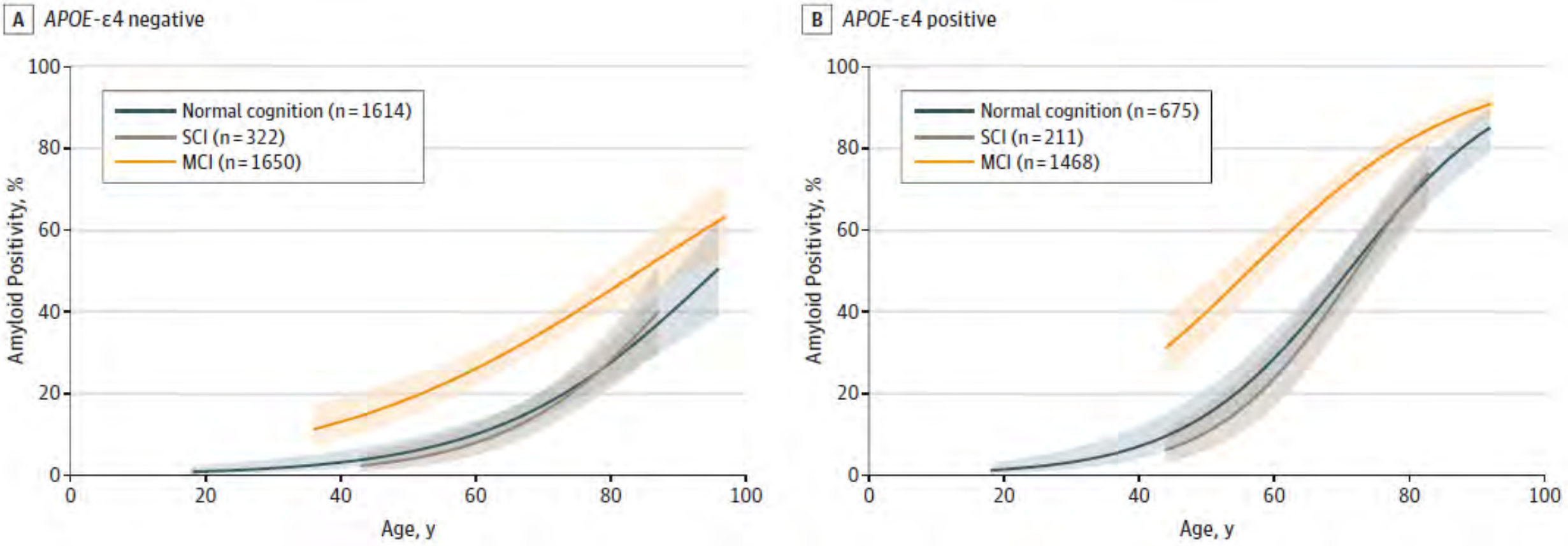
Amyloid imaging



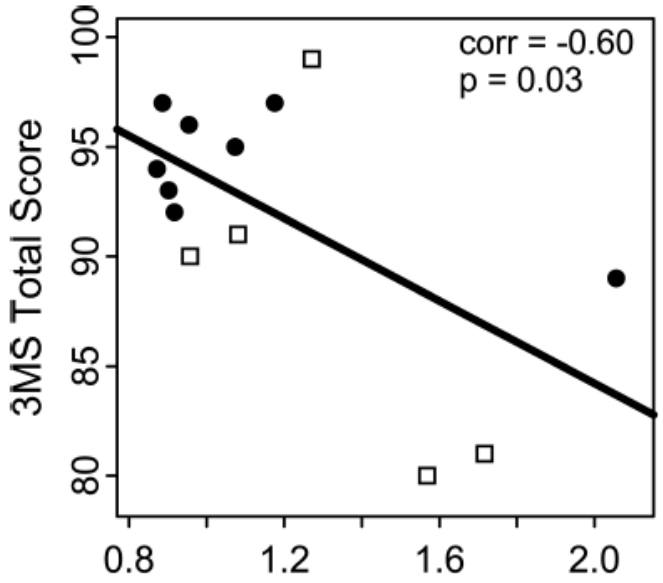
Association of Age With Prevalence Estimates of Amyloid Positivity According to Cognitive Status

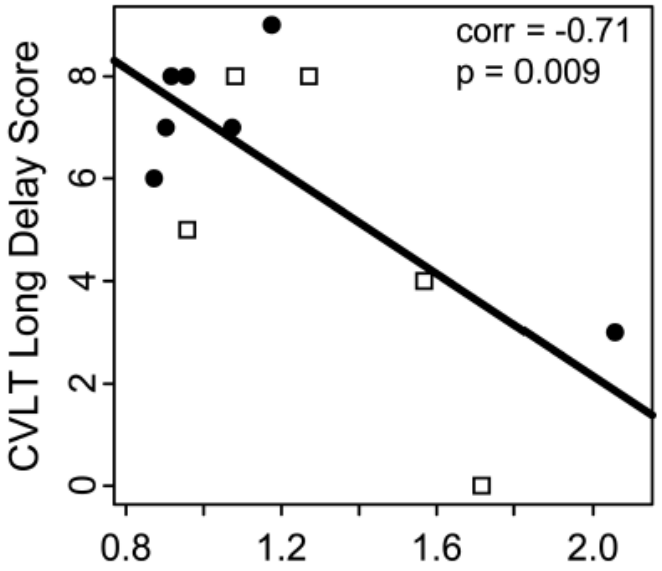
Individual records were provided for 2914 participants with normal cognition, 697 with SCI, and 3972 with MCI aged 18 to 100 years from 55 studies

JAMA. 2015;313(19):1924-1938.



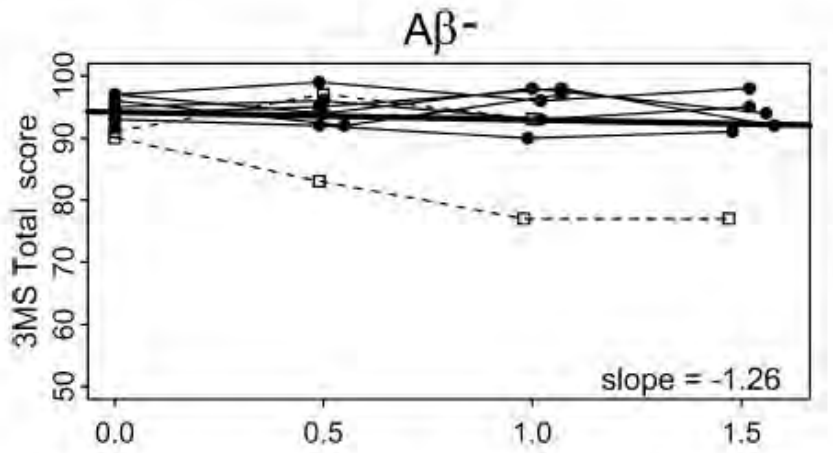
Association of Age With Prevalence Estimates of Amyloid Positivity According to Cognitive Status and Apolipoprotein E (APOE) Genotype

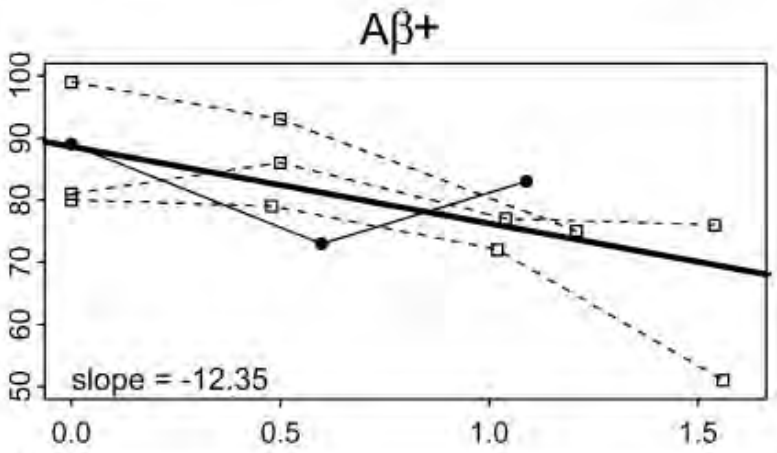




Test scores at baseline versus average cortical SUVr in non-demented participants from The 90+ Study

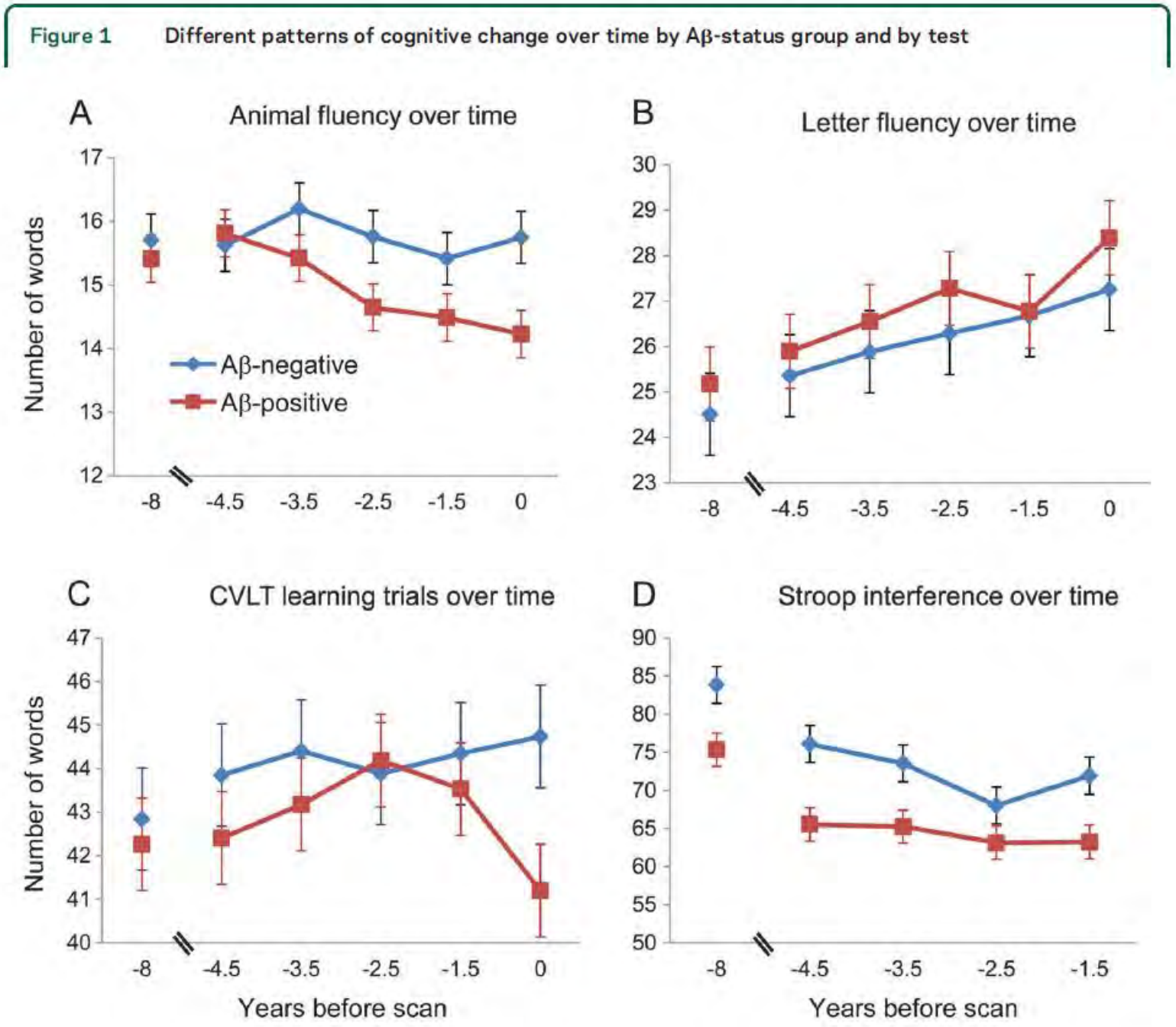
Age 90-99 (median 94.1)
N=13





Longitudinal trajectories of neuropsychological tests in Aβ- and Aβ+ non-demented participants

Alzheimers Dement. 2013 March ; 9(2): 199–203



Neurology; 2013;80:1378–1384

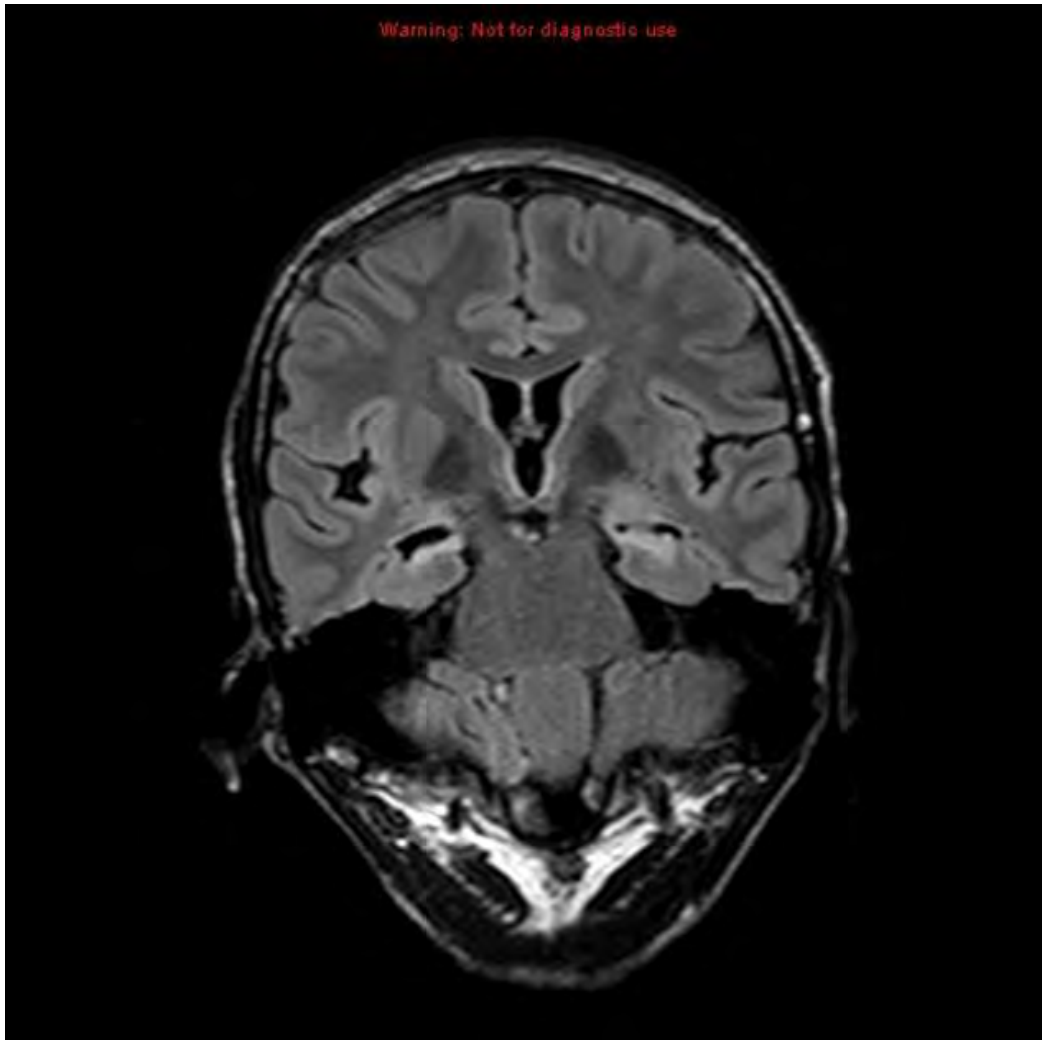
Mean cognitive performance by Aβ-status groups (6SE) estimated from mixed models at discrete timepoints, showing patterns of change over time

(A) steeper decline in semantic verbal fluency in the Aβ+ compared to Aβ- group;

(B) practice effects over time on phonemic verbal fluency in both groups;

(C) practice effects on verbal learning in both groups until approximately 2.5 years before neuroimaging, then decline in the Aβ+ but continued practice effect in the Aβ- group;

(D) similar rates of decline in inhibitory control in both groups, with consistently lower performance in the Aβ+ group.

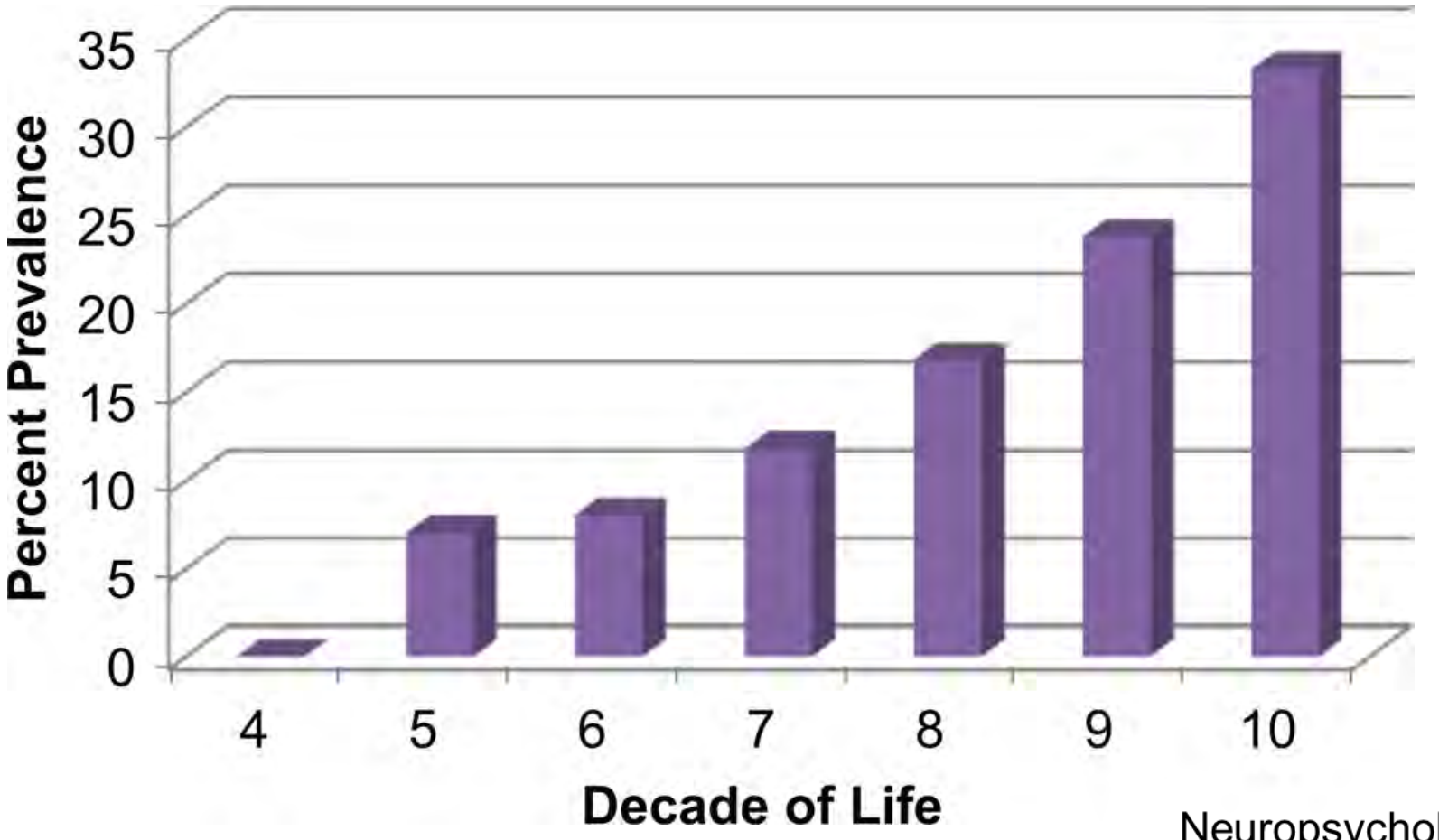


Prevalence of HS:

No other pathology	2-4%
Vascular/degen path	12-20%

Bilateral hippocampal sclerosis

Current Neurology and Neuroscience Reports 2008, 8: 363 – 370



Prevalence of MRI infarction by decade of life among subjects of the Framingham Heart Study

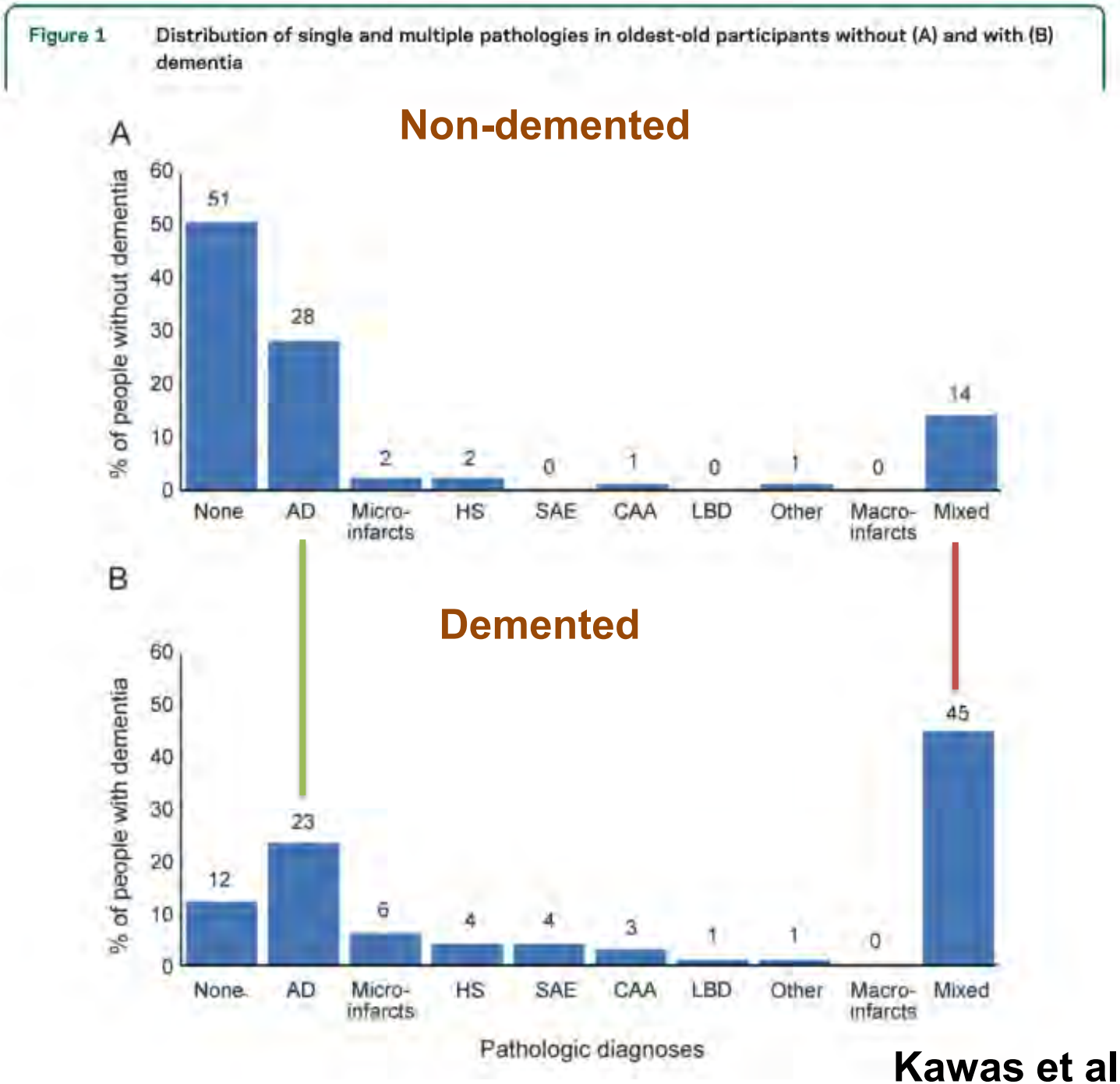
Neuropsychol Rev. 2014 Sep; 24(3): 271–289

Table 2. Age-Specific Prevalence of Cerebral Microbleeds (10-Year Strata)

Age Range	No. of Persons	Cerebral Microbleeds, N (%)	Multiple Cerebral Microbleeds, N (%)
45–50 yr	413	27 (6.5)	3 (0.7)
50–59 yr	1696	195 (11.5)	57 (3.4)
60–69 yr	1350	227 (16.8)	66 (4.9)
70–79 yr	377	109 (28.9)	56 (14.9)
>80 yr	143	51 (35.7)	32 (22.4)
Total	3979	609 (15.3)	214 (5.4)

The Rotterdam Scan Study

90+ Study



N=104
Age 90-107

Kawas et al., Neurology 2015

CONCLUSIONS

1. With ageing, there is a decline in volumes of brain volumes that continues into the 11th decade of life
2. The reduction is linear in some structures,. In other structures, there is stability followed by decline in later life.
3. There are critical ages for decline, esp for the hippocampus and the cerebral white matter.
4. These changes occur in both sexes, and big brain size and education do not appear to moderate the decline.
5. Cortical thinning continues to occur into the 11th decade, and the effect is strongest in the frontal and superior temporal regions.
6. The change in brain volumetrics has a strong genetic component.
7. WMHs increase through life, with an increasing trajectory later in life.
8. The difference between demented and non-demented individuals in brain volumetrics is much less in the old-old cf. the young-old. The structure-function relationships become weaker in very late life.
9. Brain network efficiency continues to decline with age. Healthy ageing is also associated with decreased specialization in brain function.
10. The older brain appears to compensate for the structural changes by recruiting additional regions/ networks.
11. Amyloid positivity increases steadily from the 3rd decade, with a marked rise after 60 years. E4 + individuals are more at risk and positivity is related to poorer cognitive function, even in the very old.
12. Amyloid positivity is common in non-demented elderly. The presence of 2 or 3 pathologies (Ab+, hippo vol, WMH) increases the odds of having dementia.
13. Other pathologies that increase with age are hippocampal sclerosis, infarcts, microbleeds etc.