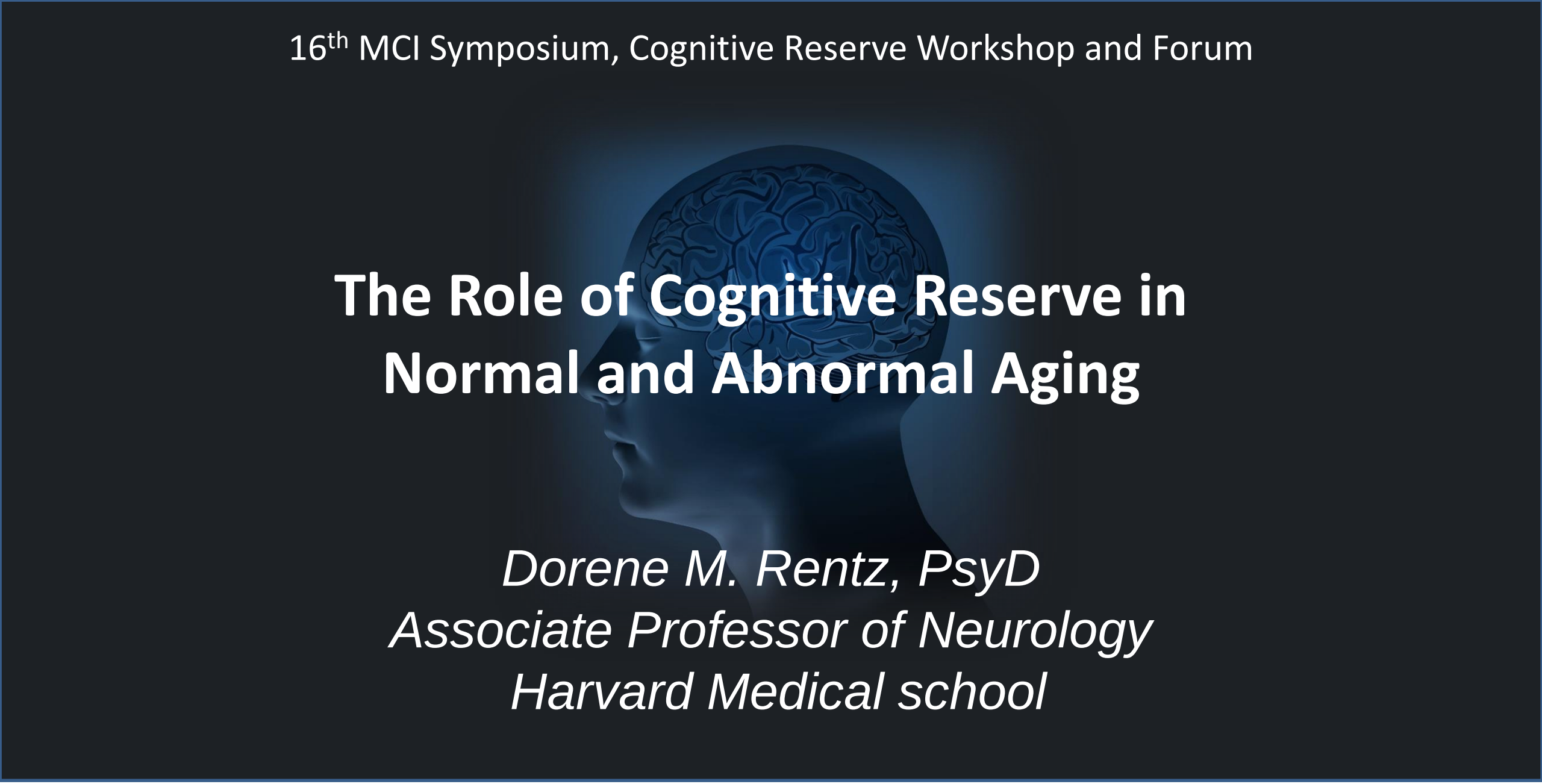
16th MCI Symposium, Cognitive Reserve Workshop and Forum



The Role of Cognitive Reserve in Normal and Abnormal Aging

Dorene M. Rentz, PsyD
Associate Professor of Neurology
Harvard Medical school

January 20-21, 2018 ● Miami Beach, Florida

DISCLOSURES

- Consulting / Scientific Advisory Boards
  - Eli Lilly Pharmaceutical Company
  - Neurotrack
  - Biogen Idec
  - Janssen Pharmaceuticals

These disclosures are not relevant to the work presented today

More and more people are living vibrant lives into old age

Who lives to 100+ ?

People who…

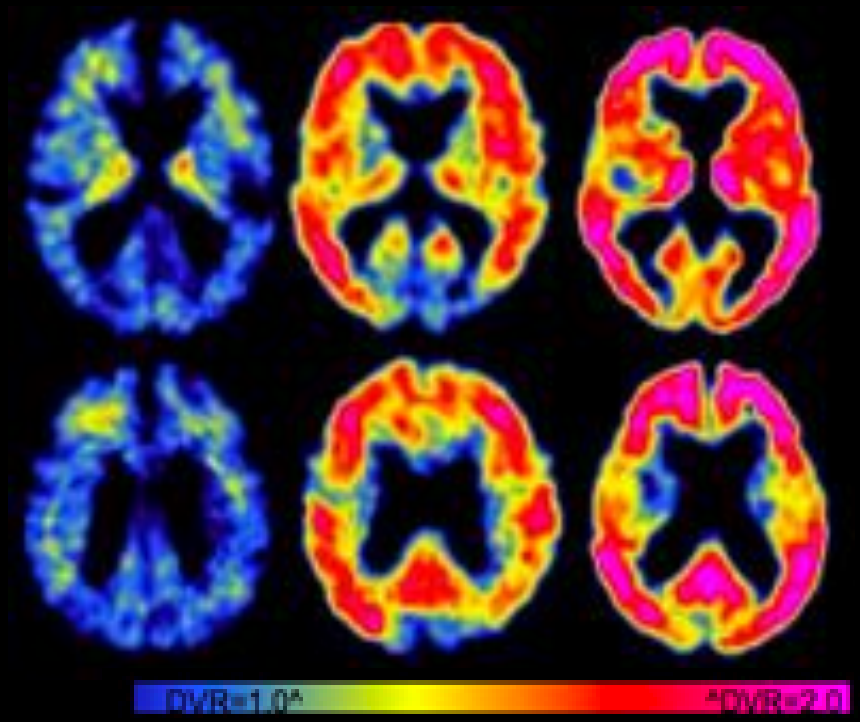
Claudia Kawas, MD

The 90+ Study

- Drank moderate amounts of alcohol or coffee
- Were overweight in their 70s
- Stopped smoking
- Ate plant-based diets
- Kept up constant low-level exercise
- Had family & social support

Keith Johnson, MD

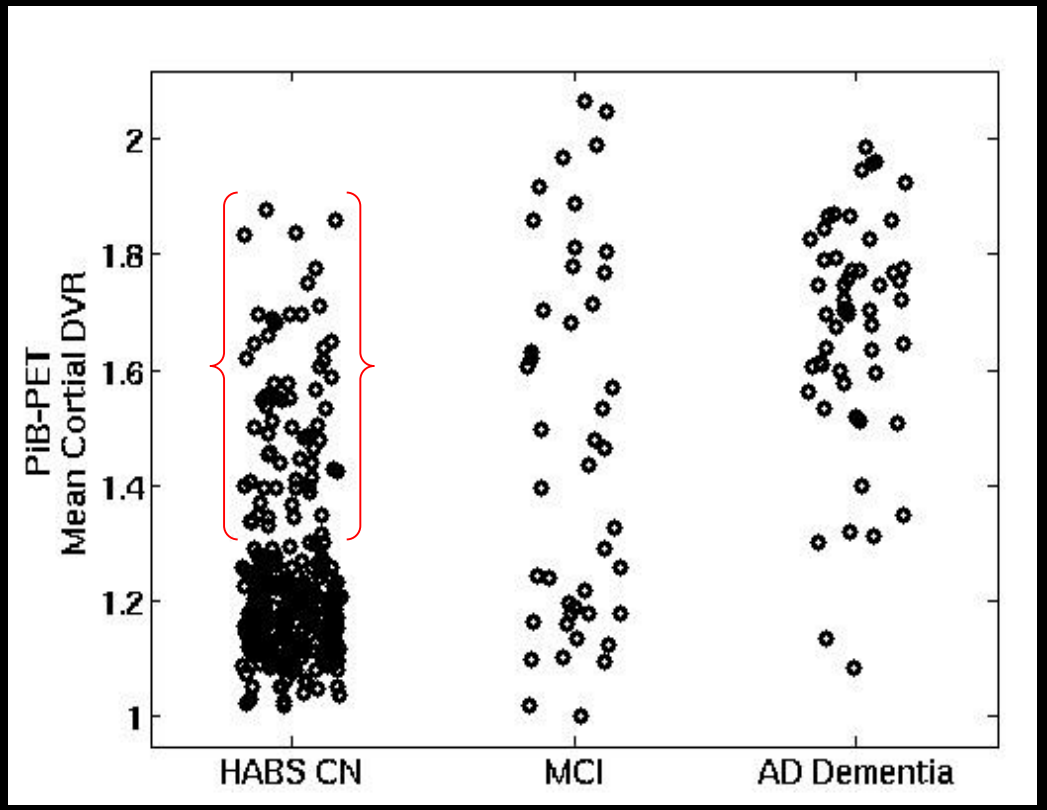
PET Amyloid Imaging in Clinically Normal Older Individuals



CN Aβ–

CN Aβ+

AD Aβ+



Harvard Aging Brain Sudy

Sperling, Mormino, Johnson *Neuron* 2014

Theories of Reserve

Two Proposed Models of Reserve

1. Brain Reserve – Neuroplasticity

Reserve Hypothesis

Neuroplasticity and cognitive reserve

- **Positive neuroplasticity** refers to the physiological ability of the brain to form and strengthen dendritic connections, produce beneficial morphological changes and increase cognitive reserve.

Whalley, L. Ageing Research Reviews, 2004

Is Neuroplasticity Helpful?

Journal of the International Neuropsychological Society (2012), **18**, 1081–1085.

doi:10.1017/S1355617712000847

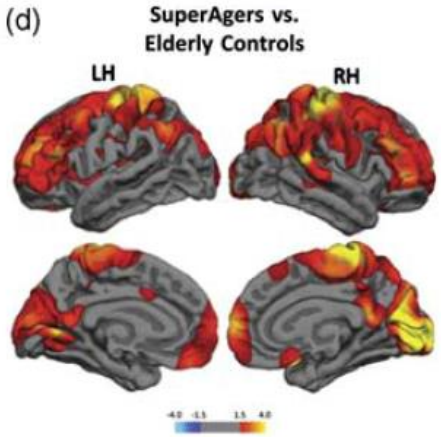
BRIEF COMMUNICATION

Superior Memory and Higher Cortical Volumes in Unusually Successful Cognitive Aging

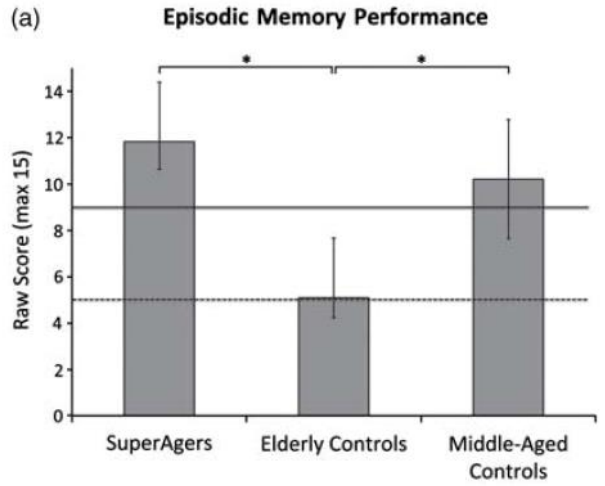
Theresa M. Harrison,[1] Sandra Weintraub,[1,2] M.-Marsel Mesulam,[1,3] AND Emily Rogalski[1]

[1]Cognitive Neurology and Alzheimer's Disease Center, Northwestern University (NU) Feinberg School of Medicine, Chicago, Illinois
[2]Department of Psychiatry and Behavioral Sciences, NU Feinberg School of Medicine, Chicago, Illinois
[3]Department of Neurology, NU Feinberg School of Medicine, Chicago, Illinois

(RECEIVED April 17, 2012; FINAL REVISION May 18, 2012; ACCEPTED May 2



Red and yellow represent
Significantly thinner cortex
In elderly controls
compared
SuperAgers



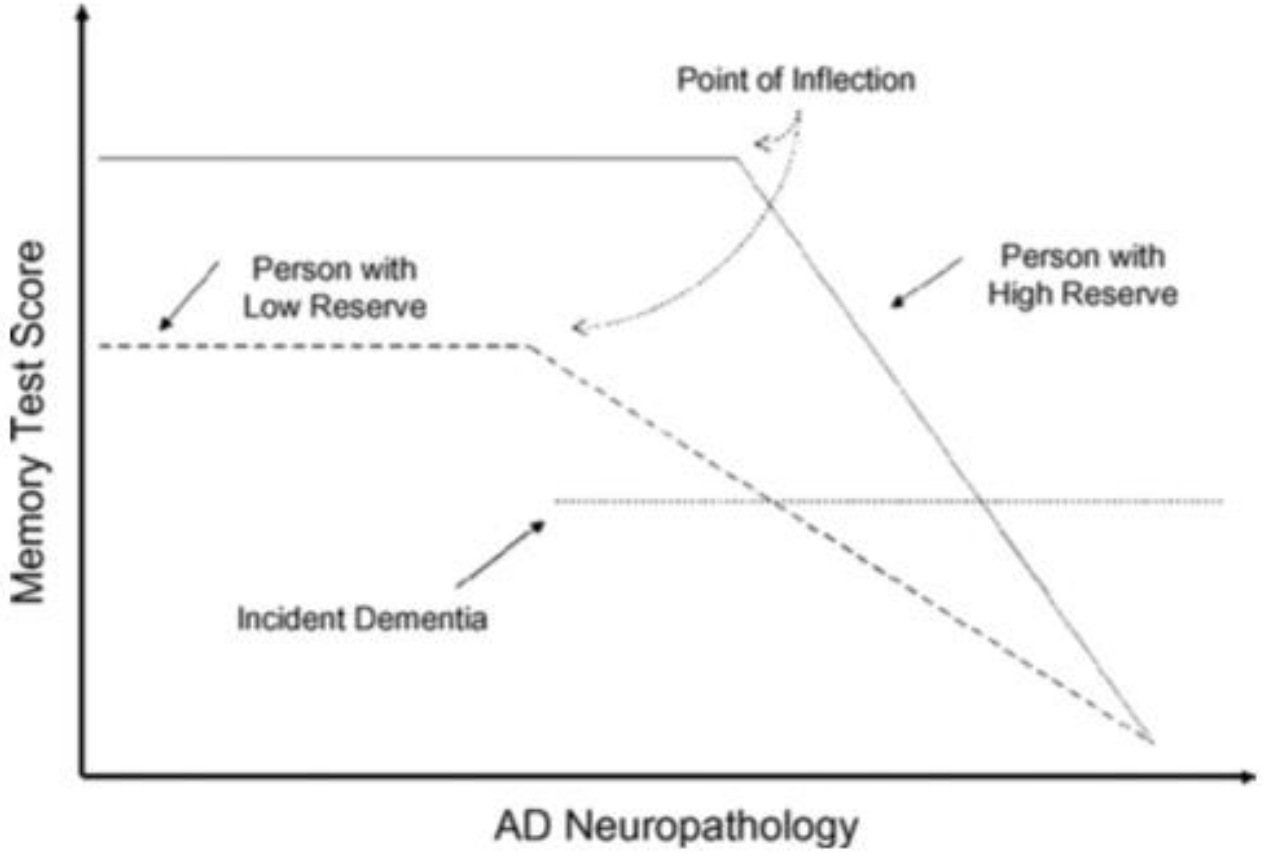
SuperAgers perform similar to middle-aged controls on a memory test

Theories of Reserve

Two Models of Reserve

2. Cognitive Reserve- Compensation

How Cognitive Reserve May Mediate Between AD Pathology and Clinical Expression

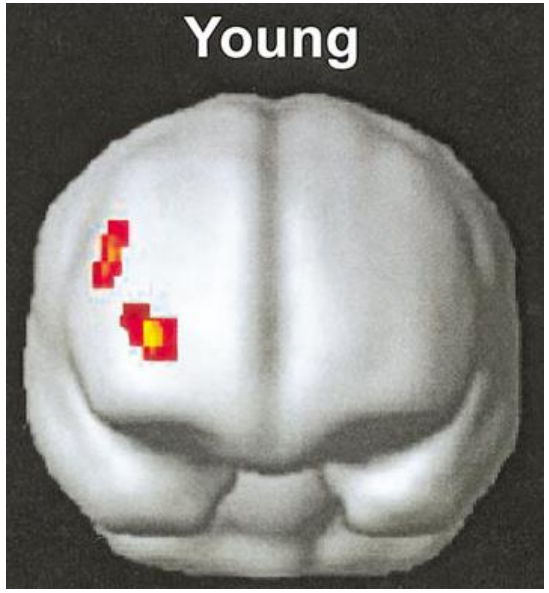


Stern Y, *Neuropsychologia.* 2009:47; 2015-2028

Aging Gracefully: Compensatory Brain Activity In High Performing Older Adults

Roberto Cabeza, et al, NeuroImage 2002, 17:1394-1402

Old-High Adults were matched on a composite memory score with Young Adults.
PFC activity during source memory was right lateralized in Young and Old-Low participants but bilateral in Old-High participants. Old-Low recruited similar network as Young, but used it inefficiently.



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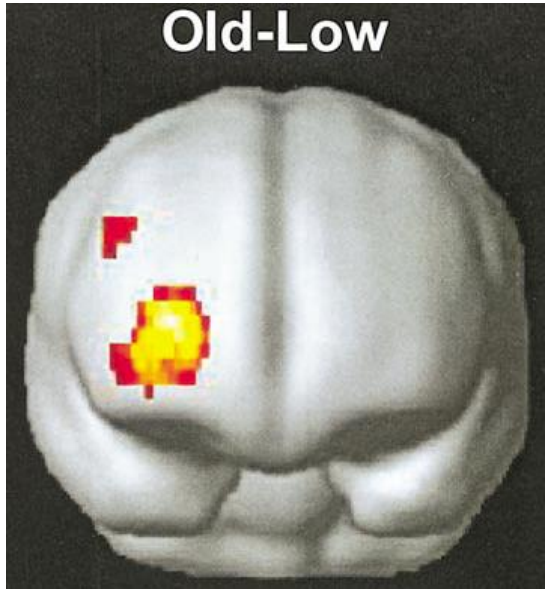

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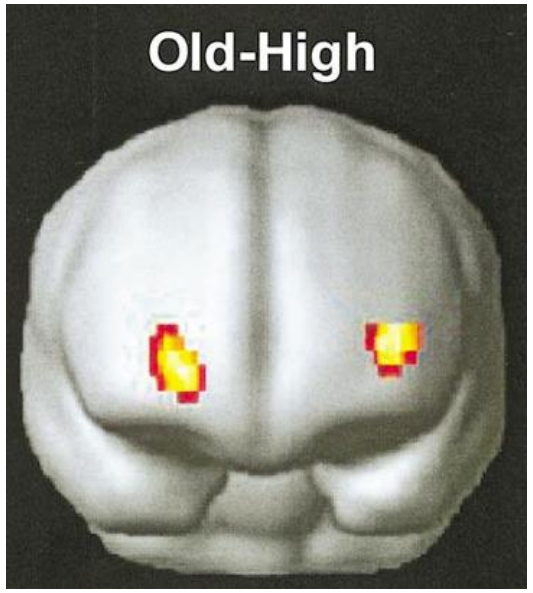
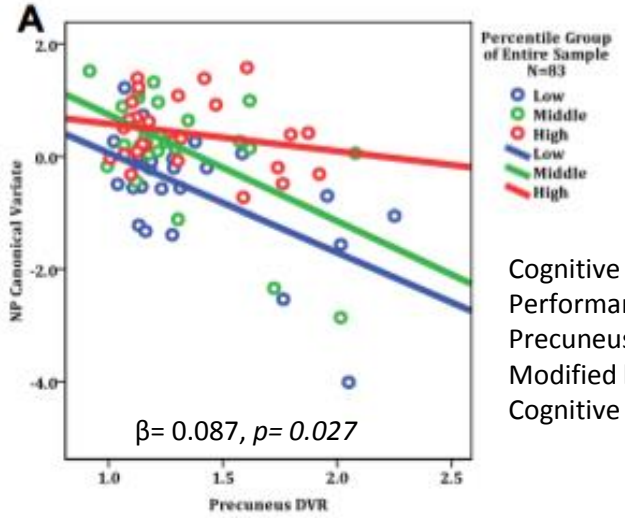


N=8

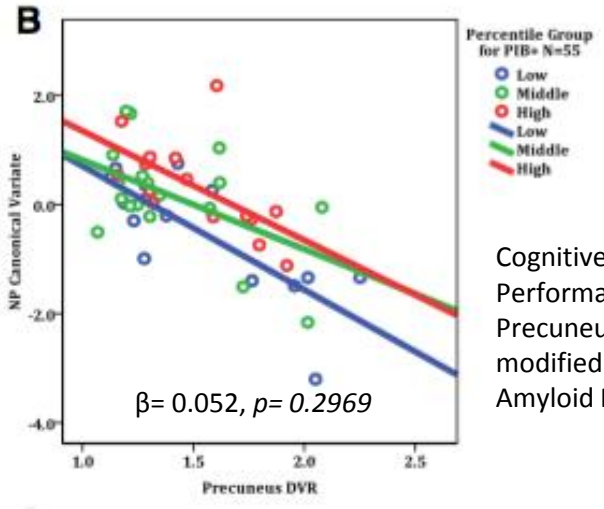
Cognition, Reserve, and Amyloid Deposition in Normal Aging

Dorene M. Rentz, PsyD,[1,2] Joseph J. Locascio, PhD,[2,3] John A. Becker, PhD,[4] Erin K. Moran, BA,[4] Elisha Eng, BA,[1] Randy L. Buckner, PhD,[4,5,6,7,8] Reisa A. Sperling, MD,[1,2] and Keith A. Johnson, MD[1,2,4]

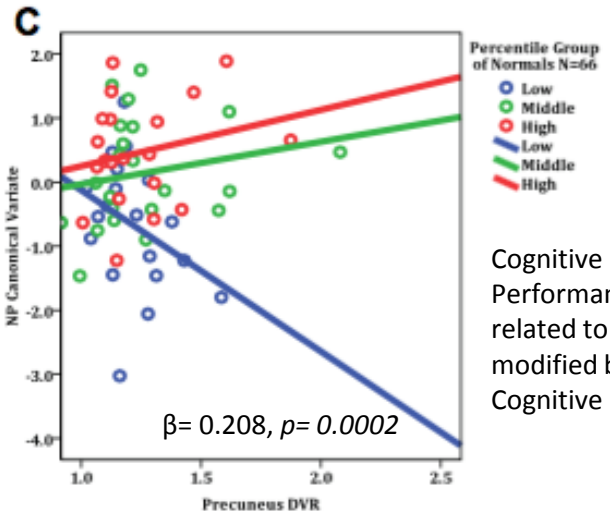
DM Rentz, et al. *Ann Neurol* 2010; 67:353-364.



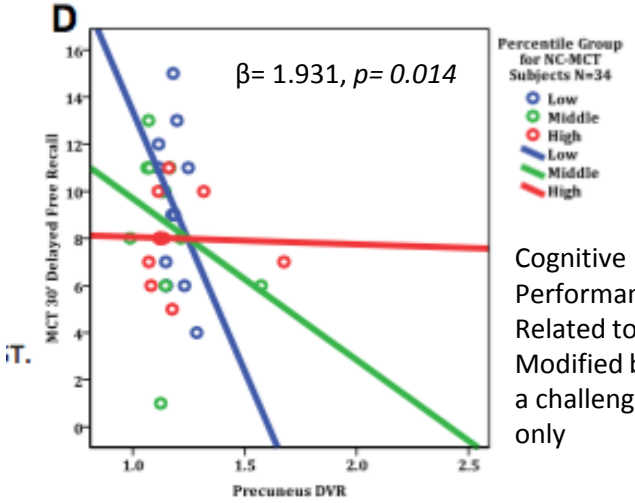
Cognitive Performance vs. Precuneus Aβ Is Modified by Cognitive Reserve



Cognitive Performance vs. Precuneus Aβ is not modified by CR in Amyloid Positive

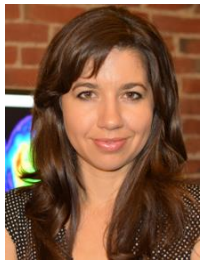


Cognitive Performance is not related to Aβ but Is modified by Cognitive Reserve



Cognitive Performance is Related to Aβ and Modified by CR on a challenging test only

Brain Imaging and Behavior (2017) 11:383–390
DOI 10.1007/s11682-016-9640-4



SI: RESILIENCE/RESERVE IN AD

Cognitive resilience in clinical and preclinical Alzheimer's disease: the Association of Amyloid and Tau Burden on cognitive performance

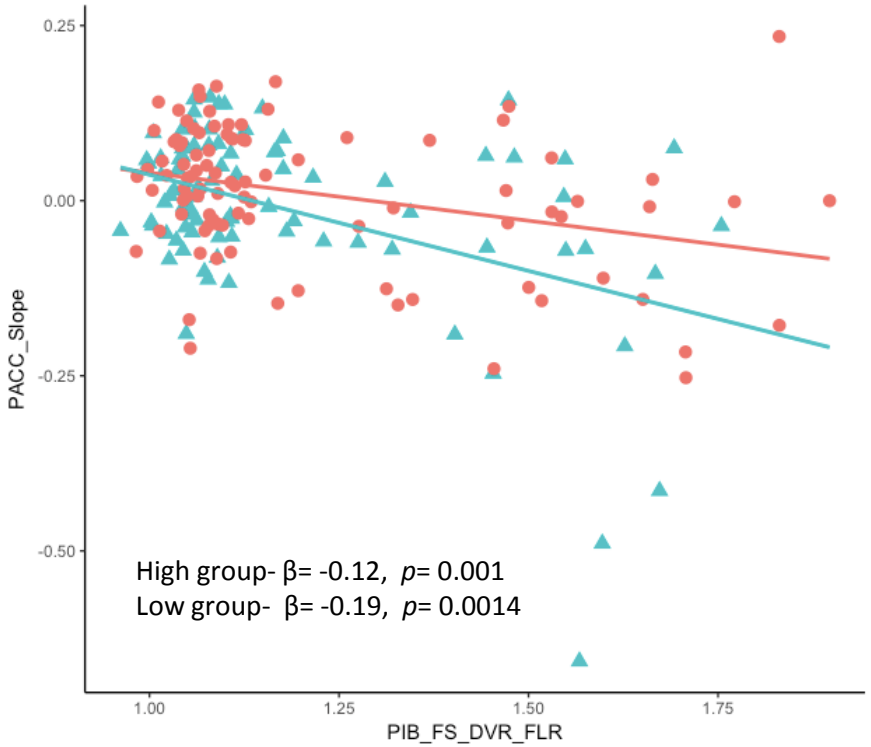
Dorene M. Rentz[1,2] · Elizabeth C. Mormino[1] · Kathryn V. Papp[1,2] · Rebecca A. Betensky[3] · Reisa A. Sperling[1,2,4] · Keith A. Johnson[1,2,4,5]

	CN Mean (SD) or count (n)	*MCI/AD* Mean (SD) or count (n)	*Mean Difference*	*p*
n	133	17/6		
Age	76.17 (6.23)	69.41 (9.97)	6.76	0.001
Sex (M/F)	59/74	19/4		0.001
Education (years)	15.91 (2.96)	16.29 (3.38)	0.38	0.597
Inferior Temporal T807	1.20 (0.09)	1.61 (0.44)	0.40	0.001
PiB	1.21 (0.21)	1.50 (0.26)	0.28	0.001
MMSE	29.18 (1.02)	26.61(3.06)	2.57	0.001
AMNART	121.59 (8.75)	121.22 (8.01)	0.37	0.850
Global CDR (1/0.5/0)	0.03 (0.13)	0.41 (0.05)	0.38	0.001

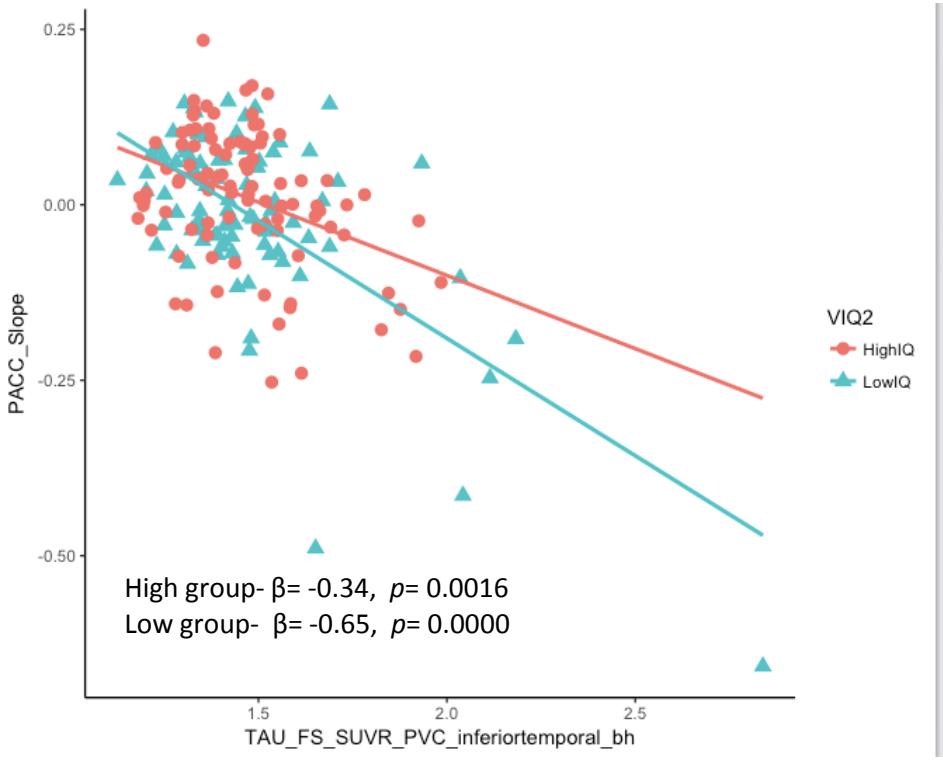
MMSE Mini Mental Status Exam, *CDR* Clinical Dementia Rating, *MCI* Mild Cognitive Impairment, *AD* Alzheimer's disease, *AMNART*- American National Adult Reading Test

CR modifies Aβ & Tau burden on PACC over time

PIB*VIQ*Time β= 0.007 *p*= 0.09



T807*VIQ*Time β= 0.24 *p*= 0.010



Unpublished data

Reserve Hypothesis

- **Negative neuroplasticity** refers the same physiological ability of the brain to atrophy and weaken dendritic connections, produce detrimental morphological changes and decrease cognitive reserve.

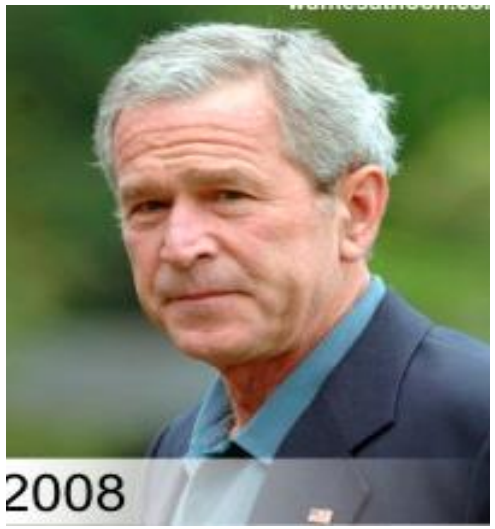
Whalley, L. Ageing Research Reviews, 2004

Reserve Hypothesis

Factors that promote **negative neuroplasticity** and decreases in cognitive reserve:

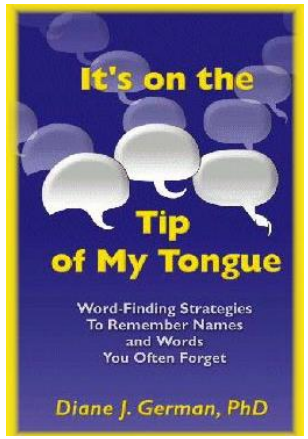
- Poor health
- Poor sleep hygiene
- Poor nutrition
- Substance abuse
- Depression
- Anxiety/ stress

Don’t become President of the US!!



What Can I Do to Delay the Onset of Dementia

Cognitive Changes with Age: What's normal????



Who's that movie star?

What's that word?

Where did I park the car?

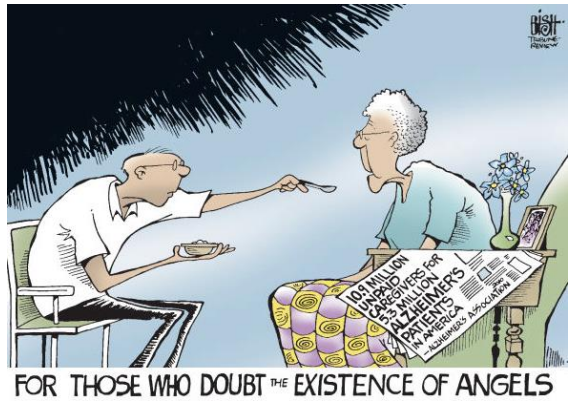
What did I come in here for?

What was I going to do?

When to Worry?

- **Memory loss**- not just forgetfulness
- **Problems with language**- not just word finding
- **Getting lost** or disoriented in familiar places
- **Misplacing things**- not just your glasses or keys
- **Loss of initiative**- for previously enjoyed activities

What Can I Do?



- **Volunteer** for a research study
- Become an **Advocate**
  - Generate action from elected officials
  - Elevate Alzheimer's from a disease to a cause
- **Support** a Walker or Rider to End Alzheimer's Disease
- **Help a caregiver**

HARVARD MEDICAL SCHOOL

Thank you to our Funding Sources:

NIA/ NIH
Alzheimer's Association

MASSACHUSETTS GENERAL HOSPITAL

BRIGHAM AND WOMEN'S HOSPITAL