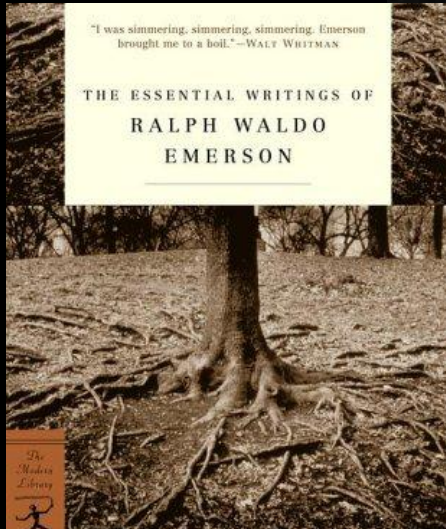


The Role of Cognitive Reserve in the clinical presentation of Alzheimer's Disease

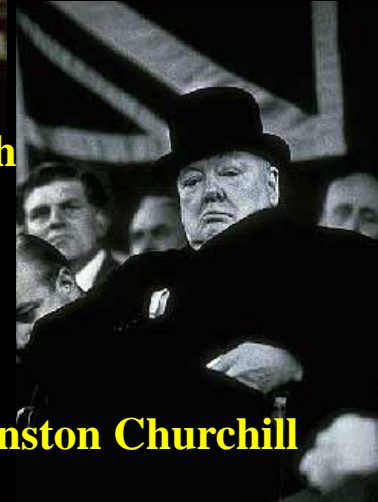
Dorene M. Rentz, PsyD

**Division of Cognitive and Behavioral Neurology, Brigham and Women's Hospital
Co-Director of the Center for Alzheimer Research and Treatment
Department of Neurology, Massachusetts General Hospital
Director of Neuropsychology, Massachusetts Alzheimer Disease Research Center
Associate Professor of Neurology, Harvard Medical School**

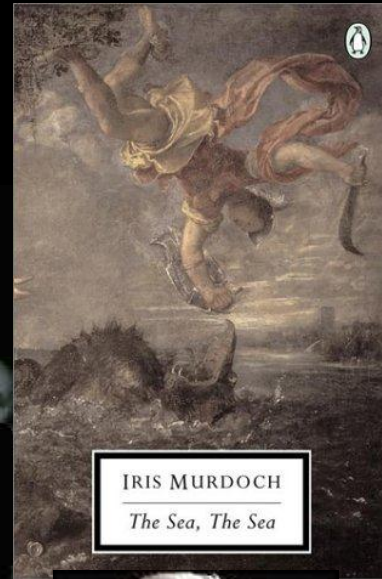
Famous People with Alzheimer's Disease



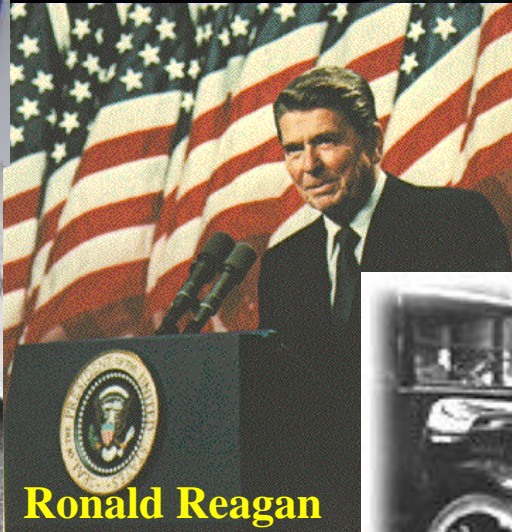
Burgess Meredith



Winston Churchill



IRIS MURDOCH
The Sea, The Sea



Ronald Reagan

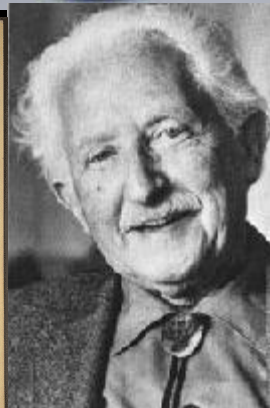


Charlton Heston



Fanfare for the
Common Man

Aaron Copland



Erik Erikson



Henry Ford

Reserve Model

Reserve is a hypothetical concept that refers to the variability observed between brain pathology and the expression of clinical symptoms.

This means that some people tolerate disease burden better than others.

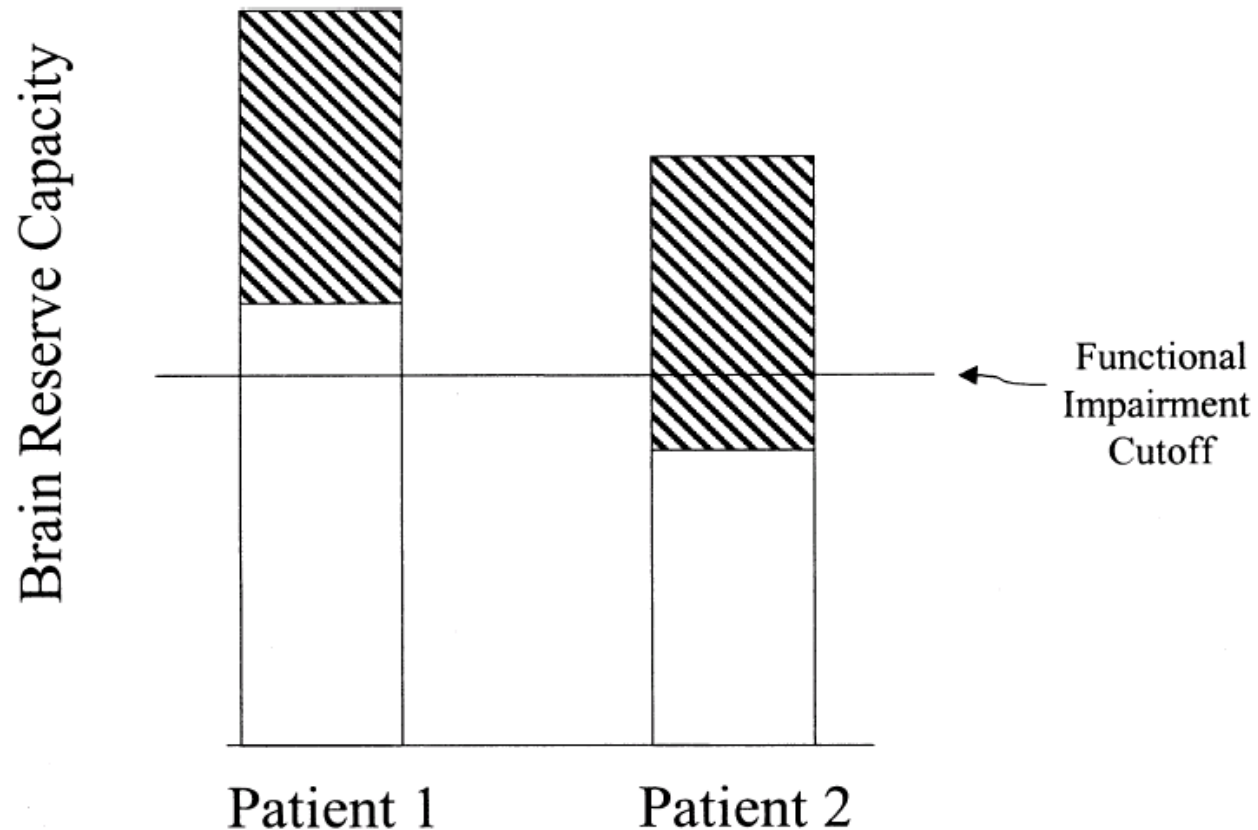
Mechanisms of Reserve

Theories of why some people can tolerate disease burden better than others:

- Genetically **larger brains** (i.e., some individuals have increased synaptic or neuronal capacity)

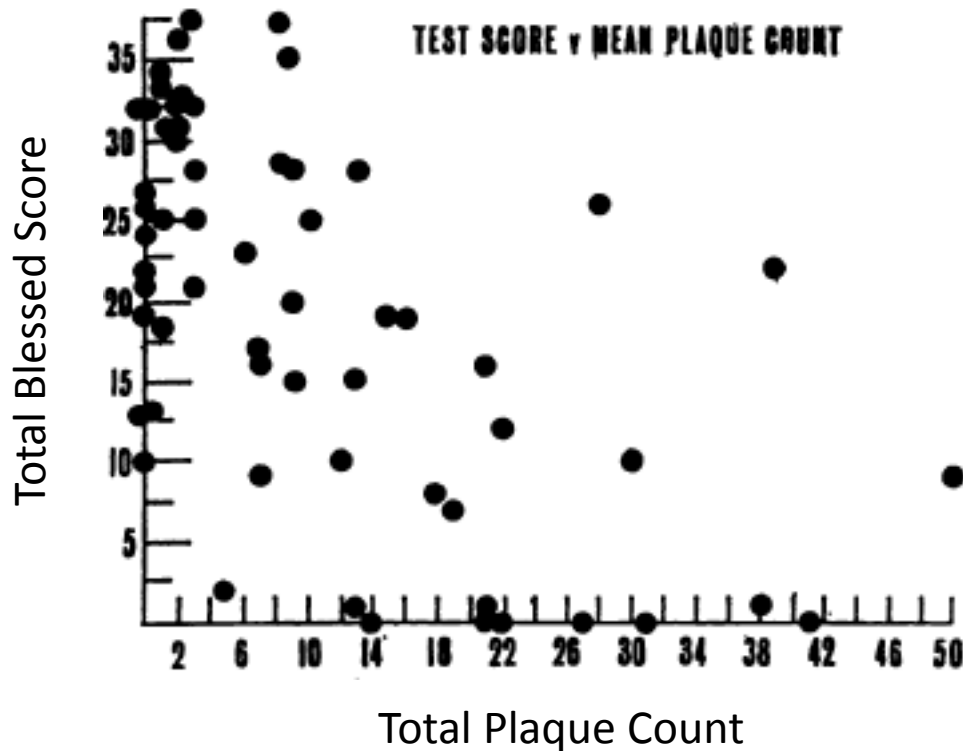
Brain Reserve

Stern, Y. *J Int Neuropsych Soc*, 2002; 8, 448-460



The Association Between Quantitative Measures of Dementia and of Senile Change in the Cerebral Grey Matter of Elderly Subjects

By G. BLESSED, B. E. TOMLINSON and MARTIN ROTH

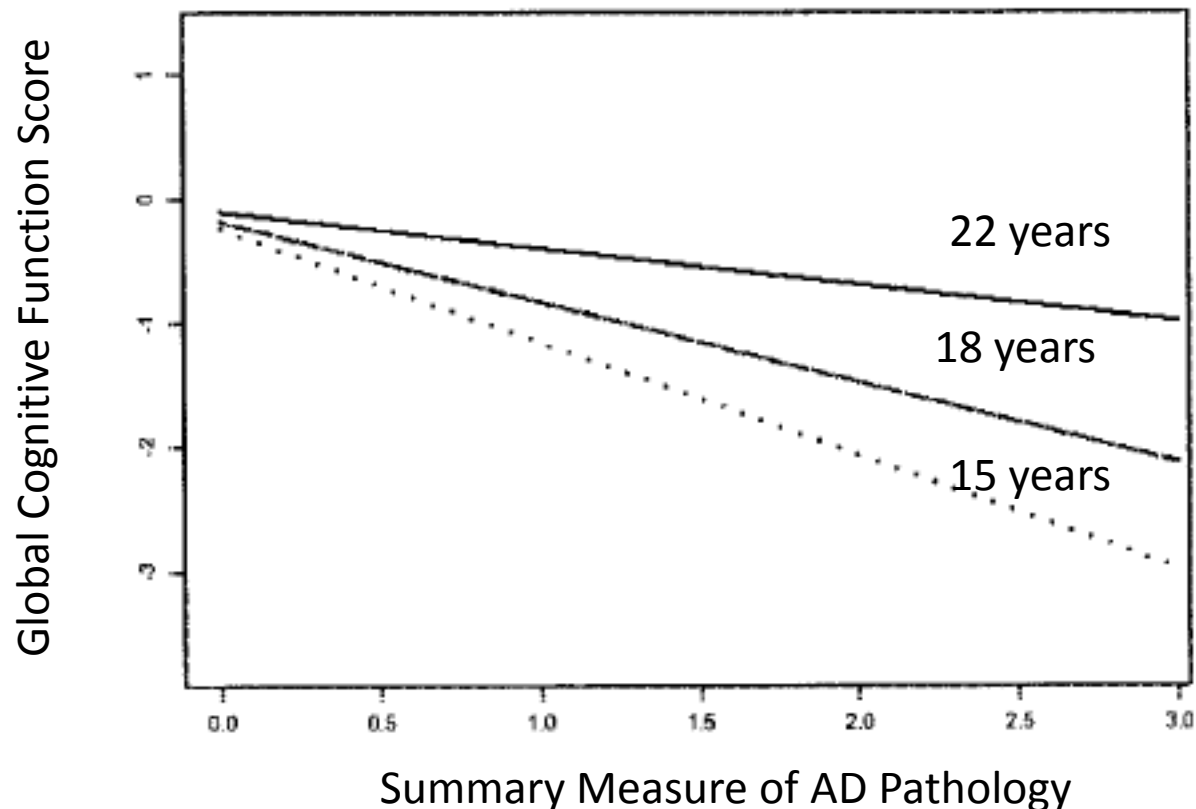


“It would appear that a certain amount of the change estimated by plaque count may be accommodated within the reserve capacity of the cerebrum without causing manifest intellectual impairment” (page 807).

Education modifies the relation of AD pathology to level of cognitive function in older persons

D.A. Bennett, MD; R.S. Wilson, PhD; J.A. Schneider, MD; D.A. Evans, MD; C.F. Mendes de Leon, PhD; S.E. Arnold, MD; L.L. Barnes, PhD; and J.L. Bienias, ScD

Neurology; 2003; 60: 1909-1915





Neuropathology of older persons without cognitive impairment from two community-based studies

D.A. Bennett, MD; J.A. Schneider, MD; Z. Arvanitakis, MD; J.F. Kelly, MD; N.T. Aggarwal, MD; R.C. Shah, MD; and R.S. Wilson, PhD

Neurology 2006; 66: 1837-1844

Table 4 Linear regression models examining level of cognition as a function of NIA-Reagan pathologic diagnosis

	NIA-Reagan pathologic AD		p Value	
	No	Yes	Model 1	Model 2
Episodic memory	0.44 (0.45)	0.18 (0.46)	0.01	0.004
Semantic memory	0.11 (0.47)	−0.05 (0.50)	0.16	0.17
Working memory	0.18 (0.71)	0.00 (0.58)	0.12	0.12
Perceptual speed	−0.15 (0.92)	−0.27 (0.77)	0.62	0.86
Visuospatial ability	0.03 (0.62)	0.12 (0.59)	0.26	0.85

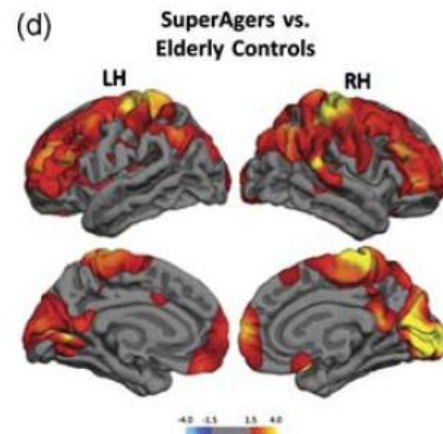
Model 1 controls for age, sex, and education. Model 2 controls for age, sex, education, cerebral infarctions, and Lewy bodies. Values are mean (SD).

AD pathology is found in the brains of older persons without dementia and is related to subtle changes in episodic memory. Weakest association with perceptual speed.

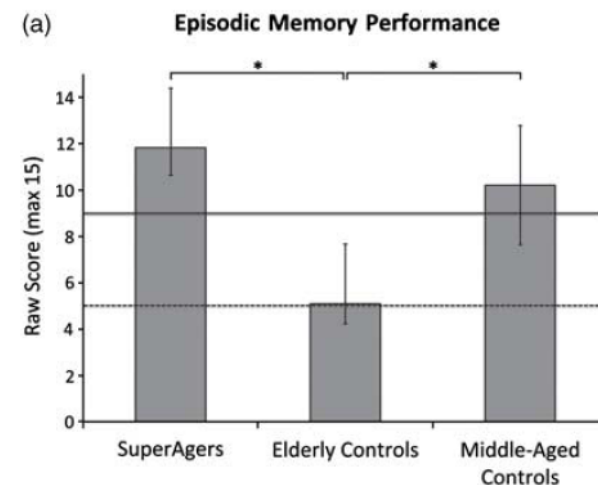
BRIEF COMMUNICATION

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 Rogalski¹



Red and yellow represent significantly thinner cortex in elderly controls compared to SuperAgers



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

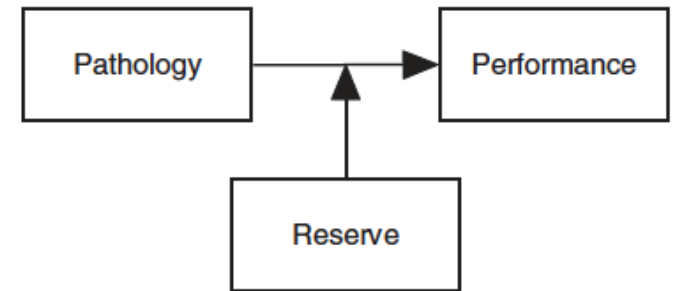
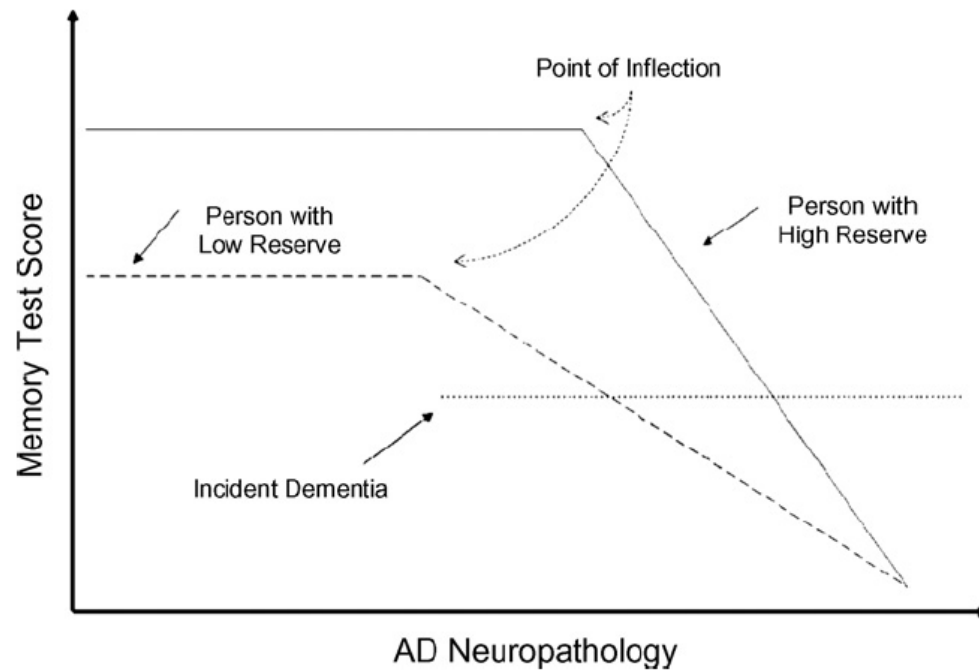
Mechanisms of Reserve

- Lifetime exposures or life course factors creating **more efficient brains**

(i.e., some individuals are able to more easily engage alternate brain networks or utilize different cognitive strategies to solve a problem)

- Educational advantage
- Reading ability
- Occupational and other lifetime activities

Cognitive Reserve



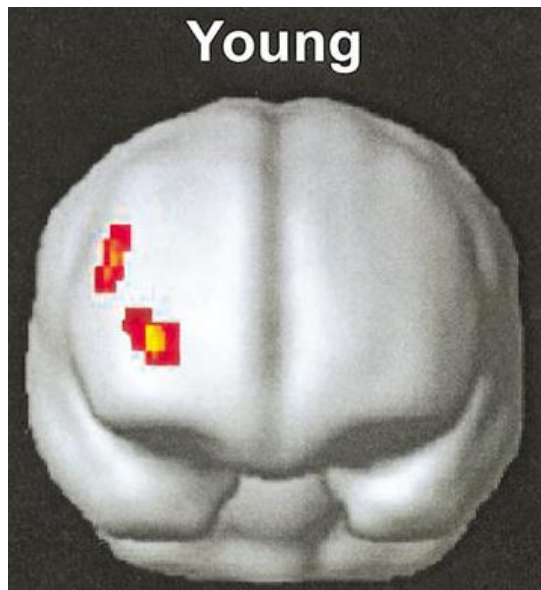
Reserve mediates the difference between pathology and performance

Stern, 2009, Neuropsychologia; 47: 2015-2028

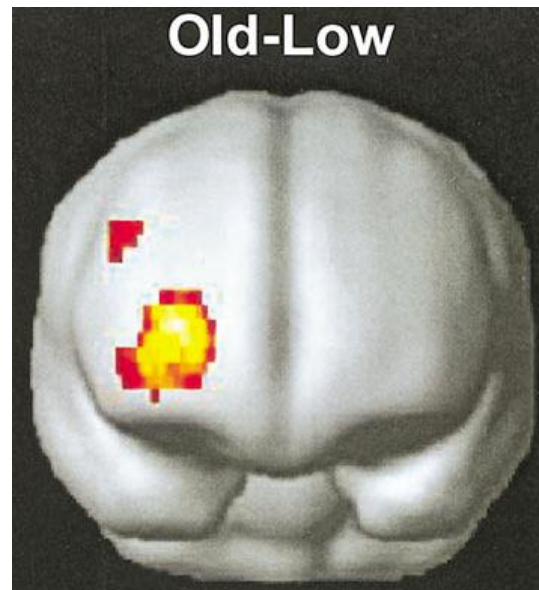
Aging Gracefully: Compensatory Brain Activity In High Performing Older Adults

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

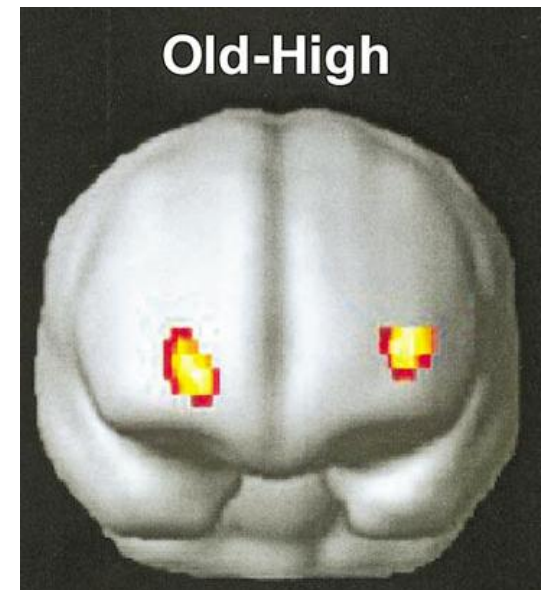
Old-High Adults were matched on a composite memory score with Young Adults. PFC activity during source memory was right lateralized in Young and Old-Low participants but bilateral in Old-High participants. Old-Low recruited similar network as Young, but used it inefficiently.



N=12



N=8

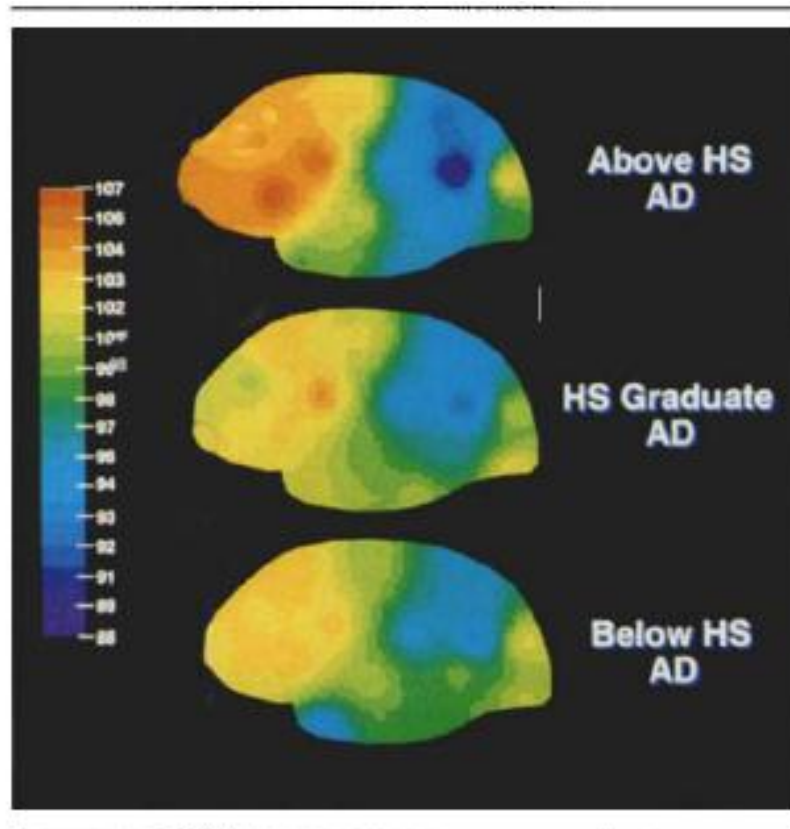


N=8

Inverse Relationship Between Education and Parietotemporal Perfusion Deficit in Alzheimer's Disease

Yaakov Stern, PhD, Gene E. Alexander, PhD, Isak Prohovnik, PhD, and Richard Mayeux, MD

Neurology; 1992; 32: 371- 375



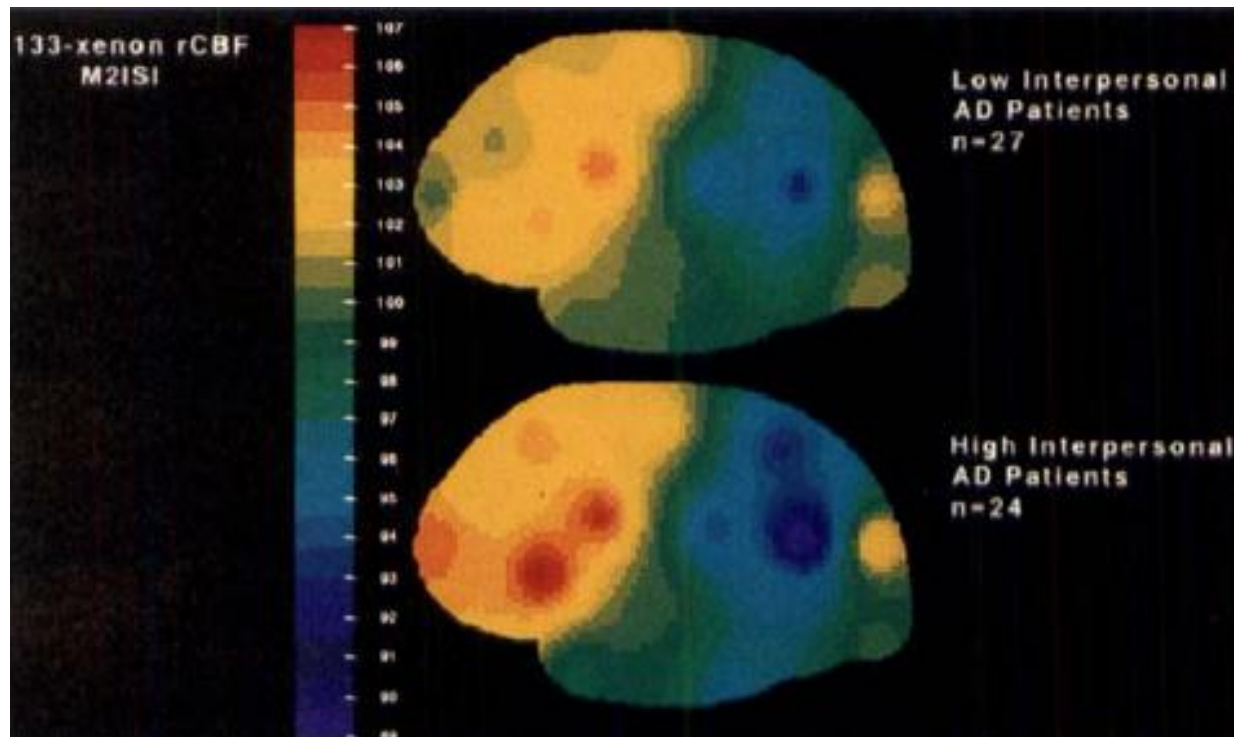
After matching subjects for age and disease severity; subjects with higher education had greater hypometabolism indicating that AD was more advanced in this group

Relationship between lifetime occupation and parietal flow:

Implications for a reserve against Alzheimer's disease pathology

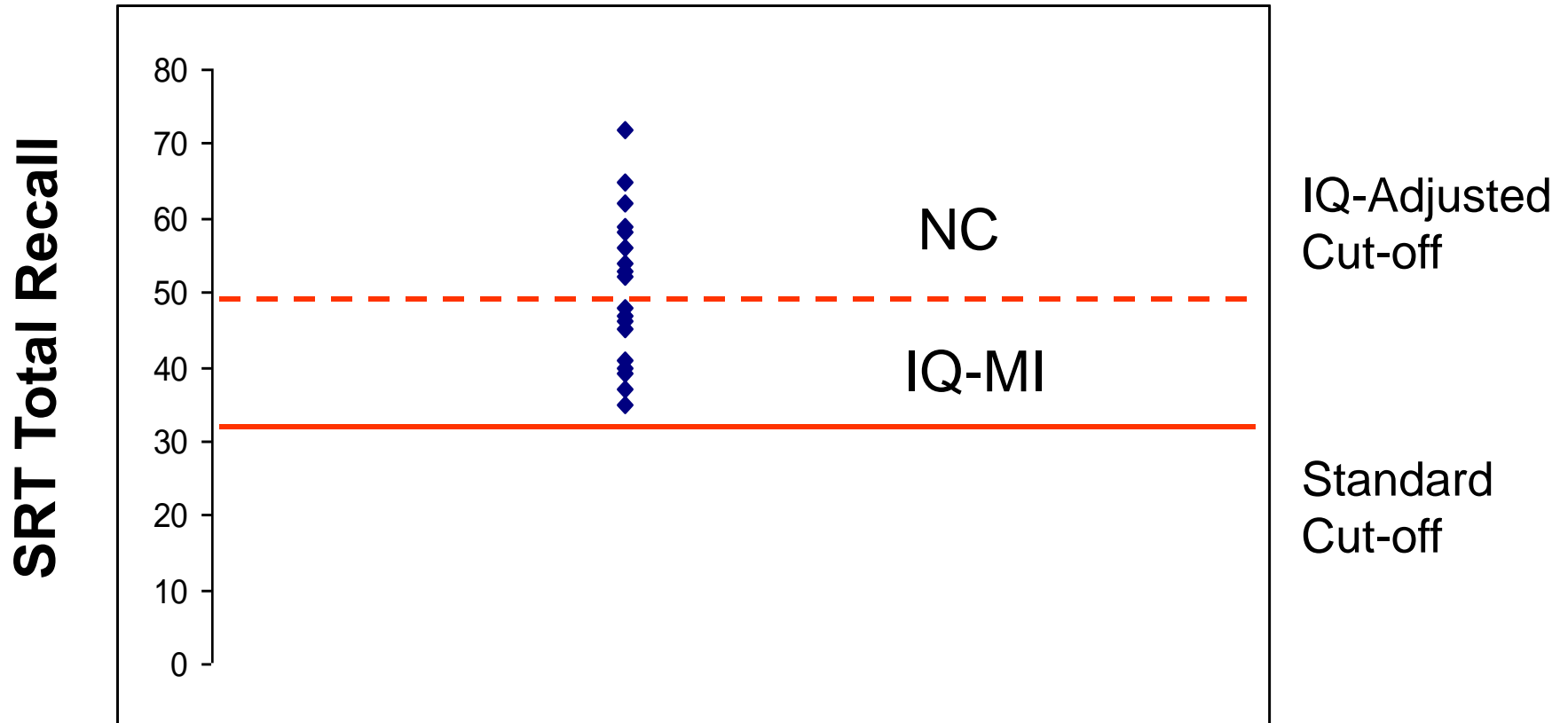
Y. Stern, PhD; G.E. Alexander, PhD; I. Prohovnik, PhD; L. Stricks, MS;
B. Link, PhD; M.C. Lennon, PhD; and R. Mayeux, MD

Neurology; 1995; 45: 55-60

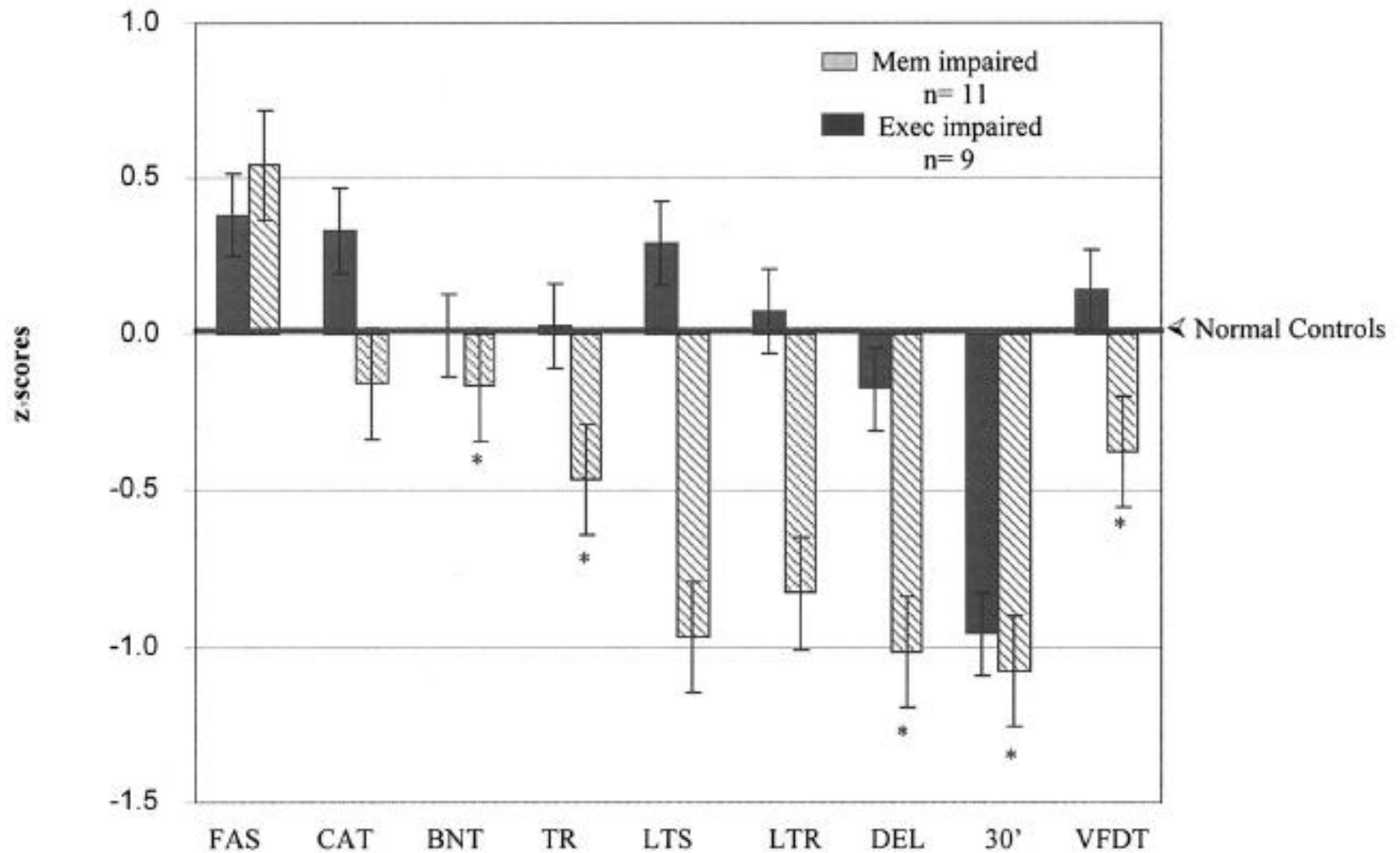


After controlling for age, education and dementia severity, greater hypoperfusion in parietal regions for subjects whose occupations were associated with higher interpersonal skills and fewer physical demands.

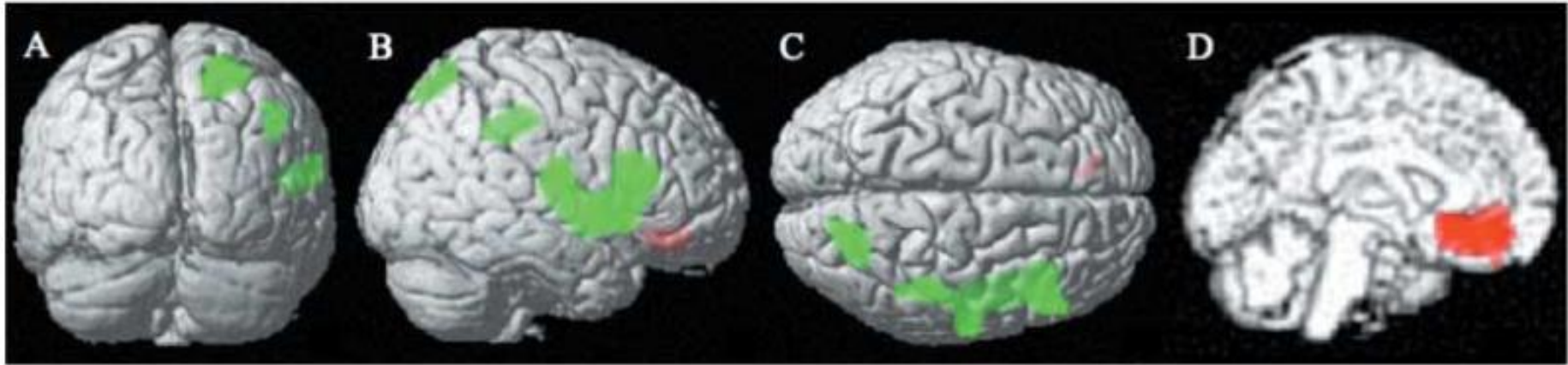
Robert R. Faust, Andrew E. Budson, Leonard F. M. Scinto, Reisa A. Sperling, and Kirk R. Daffner
Brigham and Women's Hospital and Harvard Medical School



Clinically Significant Longitudinal Decline in IQ-Memory Impaired



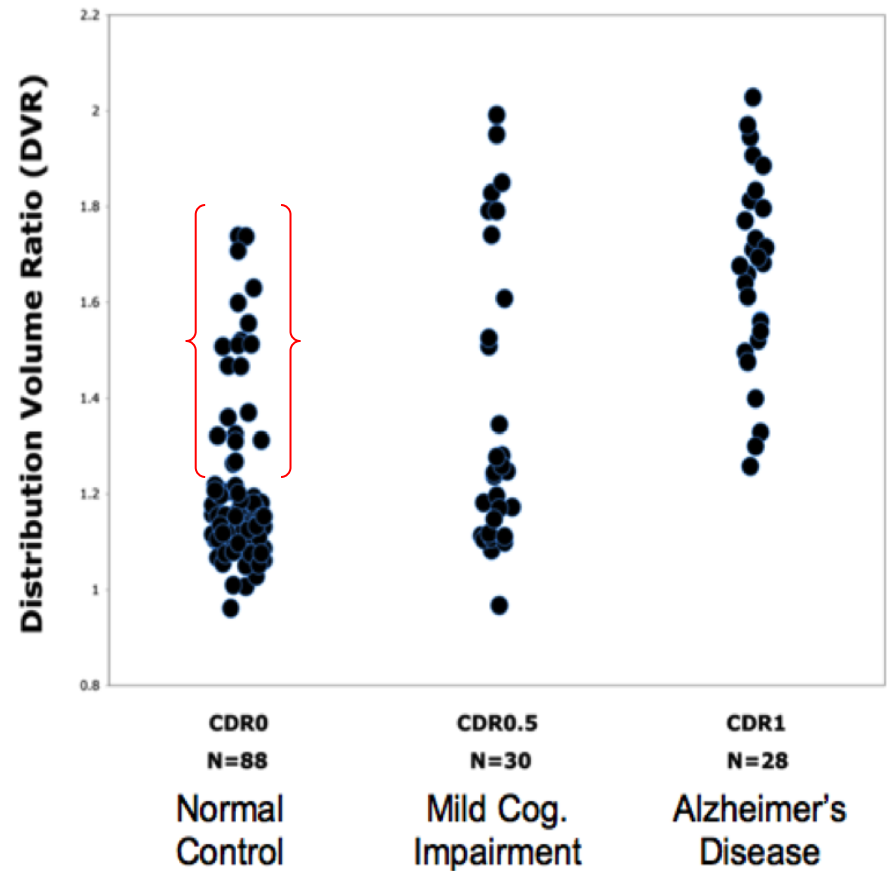
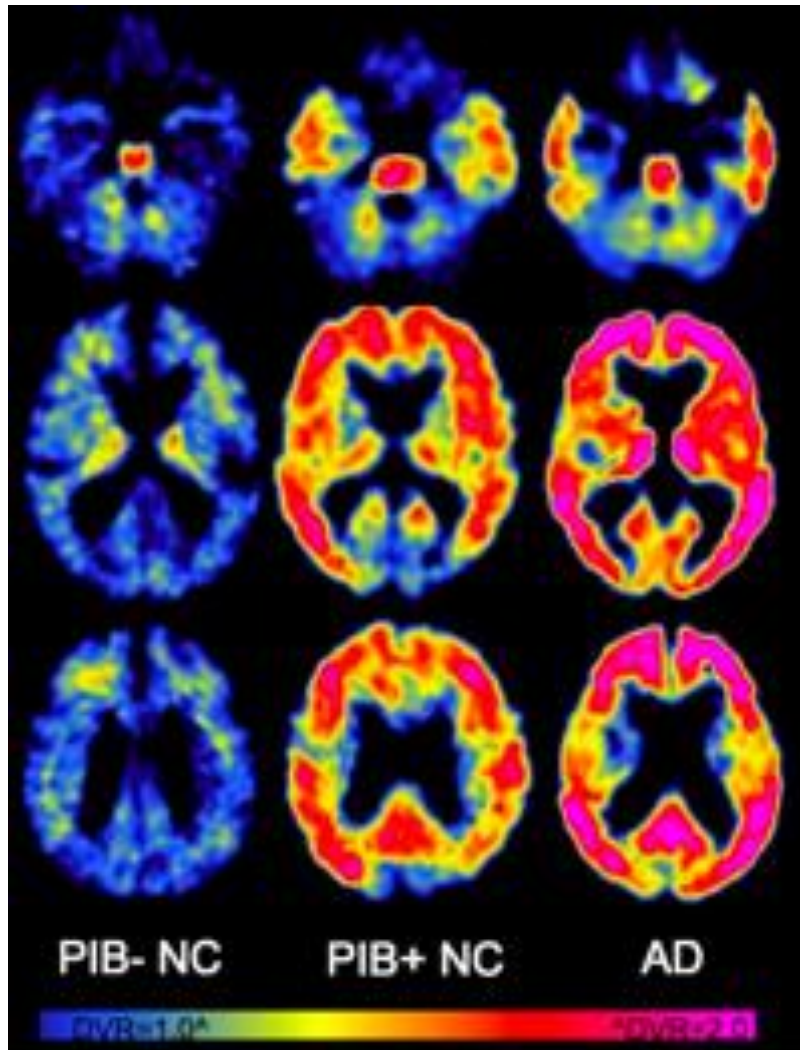
SPECT Perfusion Deficits in IQ-adjusted Memory Impairment



Rentz et al, *JINS*; 2007; 13: 821-831

Perfusion *decreases* in IQ-MI compared to IQ-MN in parietal/precuneus, temporal and opercular frontal are shown in posterior (A), right lateral (B), and superior (C) surface projections. Perfusion *increase* in IQ-MI compared to IQ-MN is shown in the left medial frontal and rostral anterior cingulate regions (D).

PiB-PET Amyloid Imaging



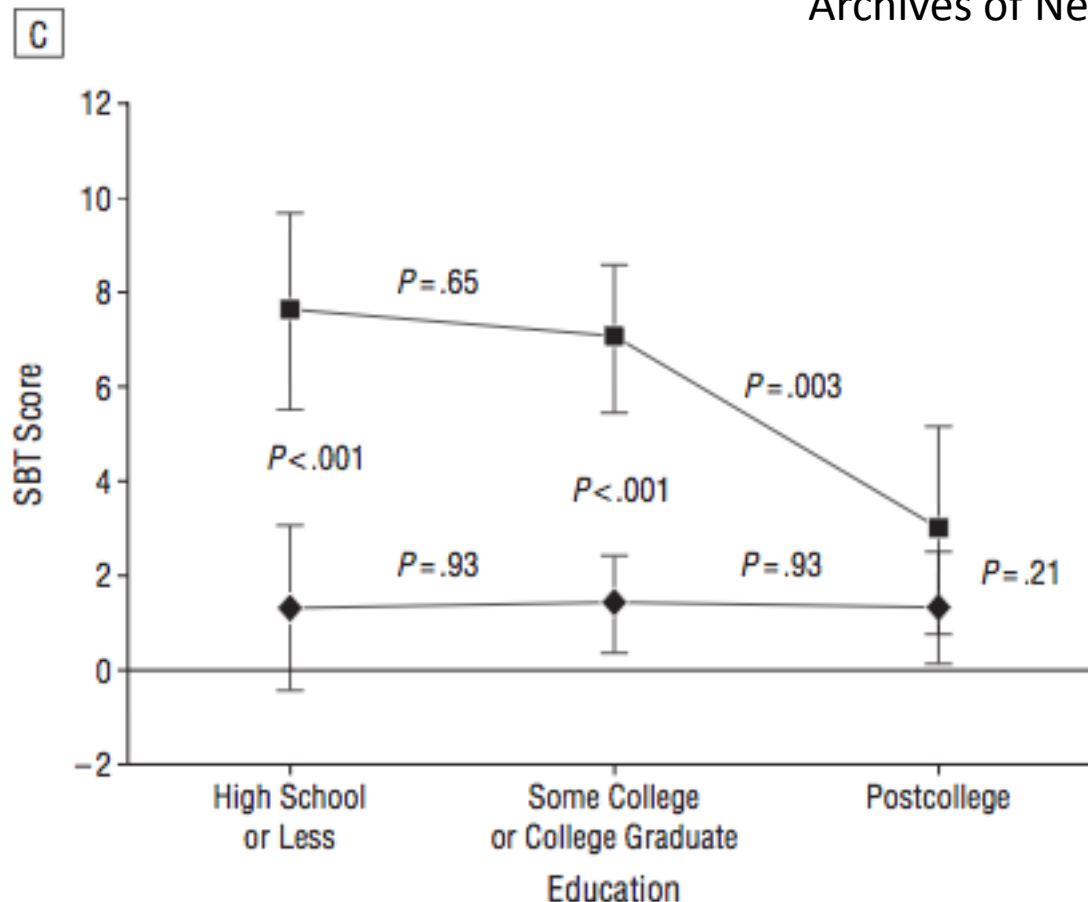
Sperling R, Johnson K *NeuroMolecular Medicine* 2010

Alzheimer Disease and Cognitive Reserve

Variation of Education Effect With Carbon 11–Labeled Pittsburgh Compound B Uptake

Catherine M. Roe, PhD; Mark A. Mintun, MD; Gina D'Angelo, PhD;
Chengjie Xiong, PhD; Elizabeth A. Grant, PhD; John C. Morris, MD

Archives of Neurology; 2008; 65: 1467-1471

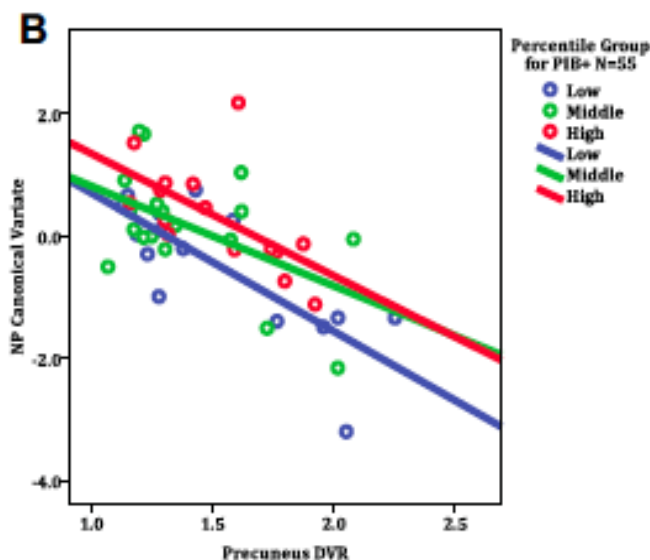
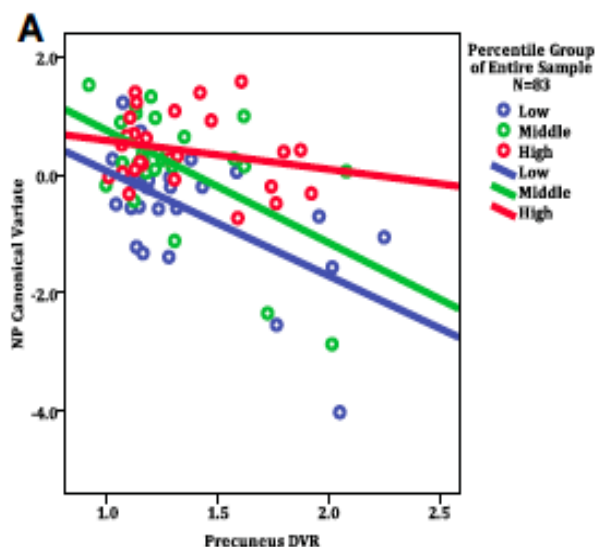


Education modifies relation of performance on the Short Blessed Test and amyloid deposition

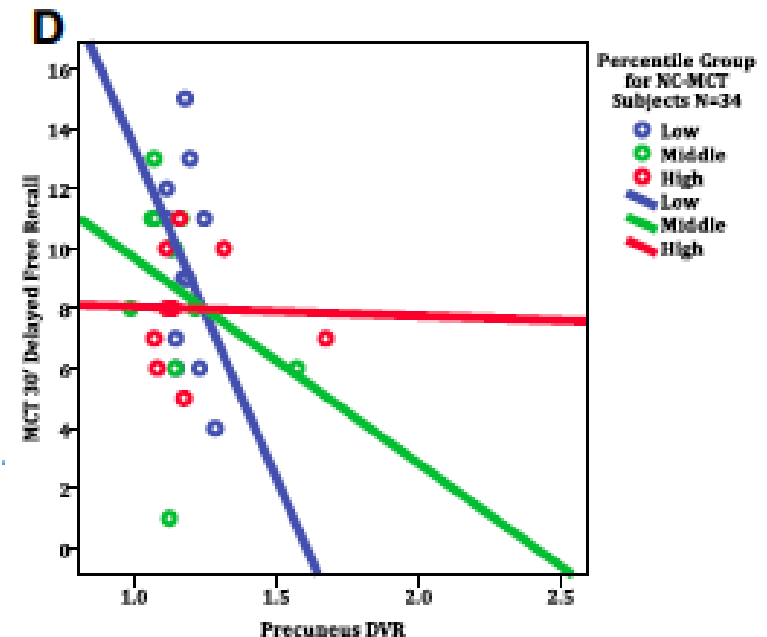
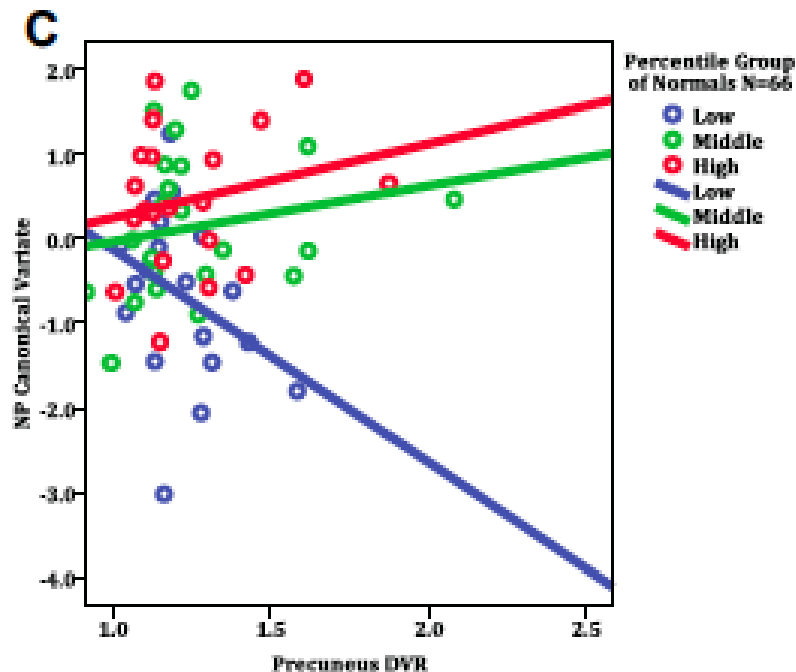
Cognition, Reserve, and Amyloid Deposition in Normal Aging

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}

Annals of Neurology; 2010; 67; 353-364



Normals: Cognitive Performance was related to Cognitive Reserve but not Amyloid Deposition except when a Challenging Memory Test was used



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



Face-name associative memory performance is related to amyloid burden in normal elderly

Dorene M. Rentz^{a,b,*}, Rebecca E. Amariglio^a, J. Alex Becker^c, Meghan Frey^a, Lauren E. Olson^{a,b}, Katherine Frishe^a, Jeremy Carmasin^c, Jacqueline E. Maye^c, Keith A. Johnson^{a,b,c}, Reisa A. Sperling^{a,b}



Isabelle



Miriam



Editor



Nutritionist



Courtney



Jane



Dancer



Weaver

Figure 1

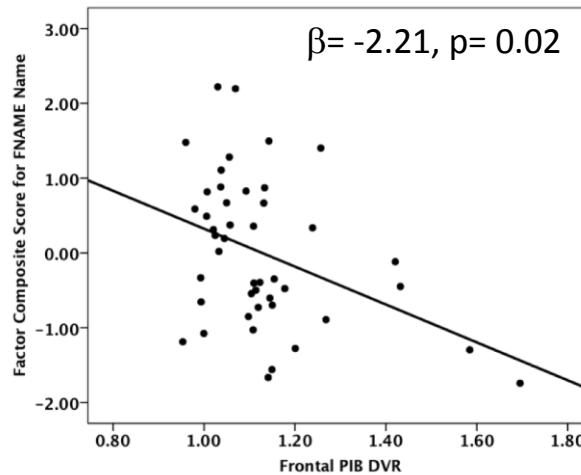
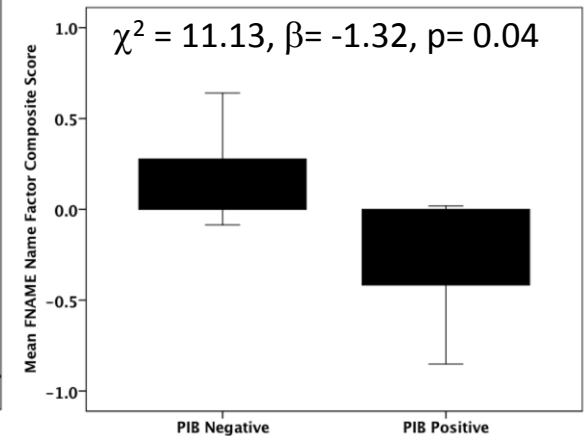


Figure 2





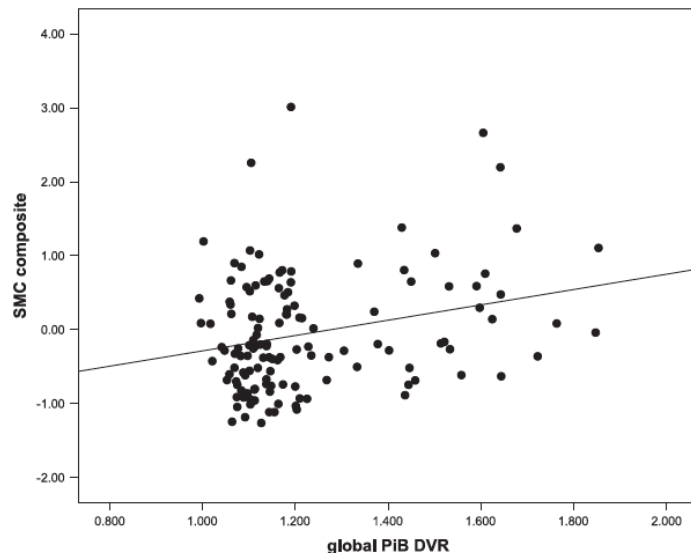
Contents lists available at SciVerse ScienceDirect

Neuropsychologia

journal homepage: www.elsevier.com/locate/neuropsychologia

Subjective cognitive complaints and amyloid burden in cognitively normal older individuals

Rebecca E. Amariglio^{a,b,*}, J. Alex Becker^c, Jeremy Carmasin^{c,1}, Lauren P. Wadsworth^b,
 Natacha Lorus^{a,b}, Caroline Sullivan^b, Jacqueline E. Maye^c, Christopher Gidicsin^c, Lesley C. Pepin^c,
 Reisa A. Sperling^{a,b}, Keith A. Johnson^{a,b,c}, Dorene M. Rentz^{a,b}



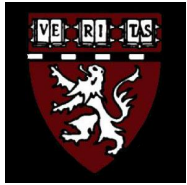
	β	p
SCC-Total	0.188	0.025
GDS	-0.383	0.70

Summary

- Cognitive Reserve is a theoretical concept to explain the observation that individuals can remain clinically normal in the context of increasing brain pathology.
- Cognitive reserve can influence diagnostic tests:
 - Cognition- subjects continue to perform normally
 - Subjects may be apt to have complaints
 - PET imaging reveals greater hypometabolism and increased amyloid deposition
 - MRI structural changes shows increased atrophy
 - Rate of decline is faster once a threshold has been crossed

Implications

- Individuals with higher cognitive reserve are apt to be misdiagnosed as normal and are at increased risk for not receiving treatments when available
- While function is maintained longer, the rate of decline is rather steep once the threshold is crossed suggesting that they require further follow-up during the course of the disease
- Subjective complaints may be a warning that early changes are occurring rather than implying the “worried well”.
- Alzheimer Prevention trials will need to take into account the modifying effects of cognitive reserve when selecting subjects for enrollment



Acknowledgements



Investigators/ Faculty

- Reisa A. Sperling, MD
- Keith A. Johnson, MD
- Rebecca Amariglio, PhD
- Kathryn Papp, PhD
- Yakeel Quiroz-Gaviria, PhD
- Gad Marshall, MD
- Jasmeer Chhatwal, MD PhD
- Aaron Schultz, PhD
- John Alex Becker, PhD
- Brendon Boot, MD

- Tamy-Fee Menendez, BA
- Seihley Jaimes, BA
- Alison Pietras, BA
- Martha Vander Vliet RN
- Margaret Chute, BA

Funding:

NIH and Alzheimer's Association

***ALL THE SUBJECTS WHO MAKE
OUR RESEARCH POSSIBLE***

Research Assistants

THANK YOU!