Cognitive Reserve

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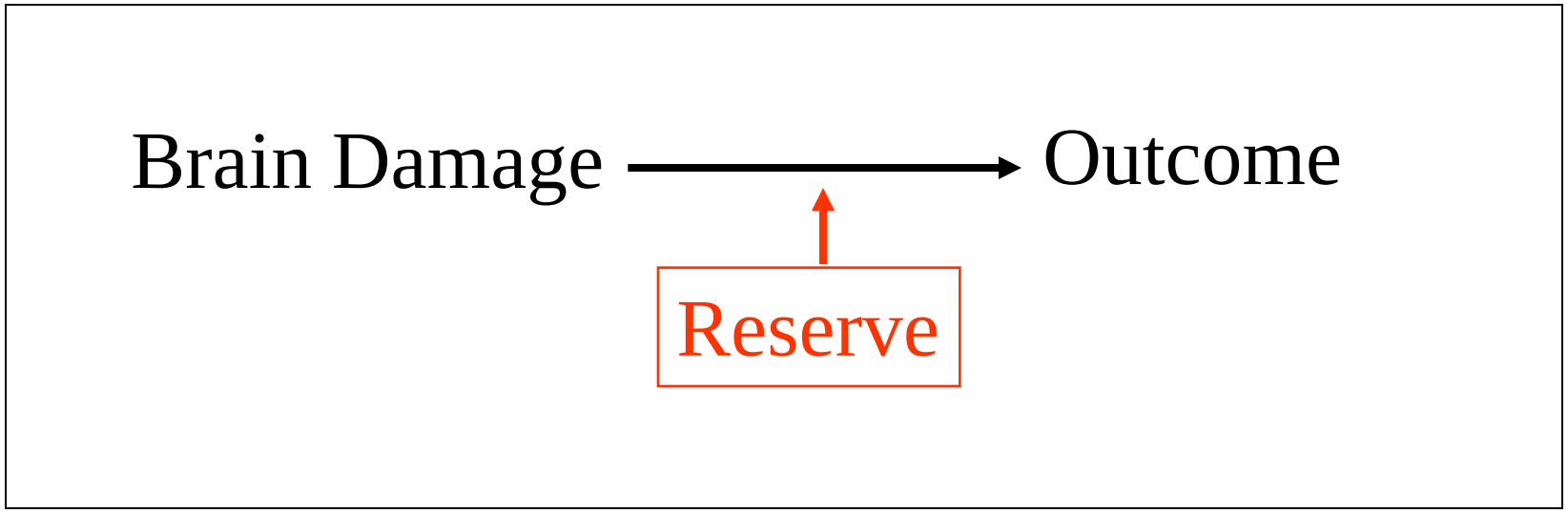
What is Cognitive Reserve?

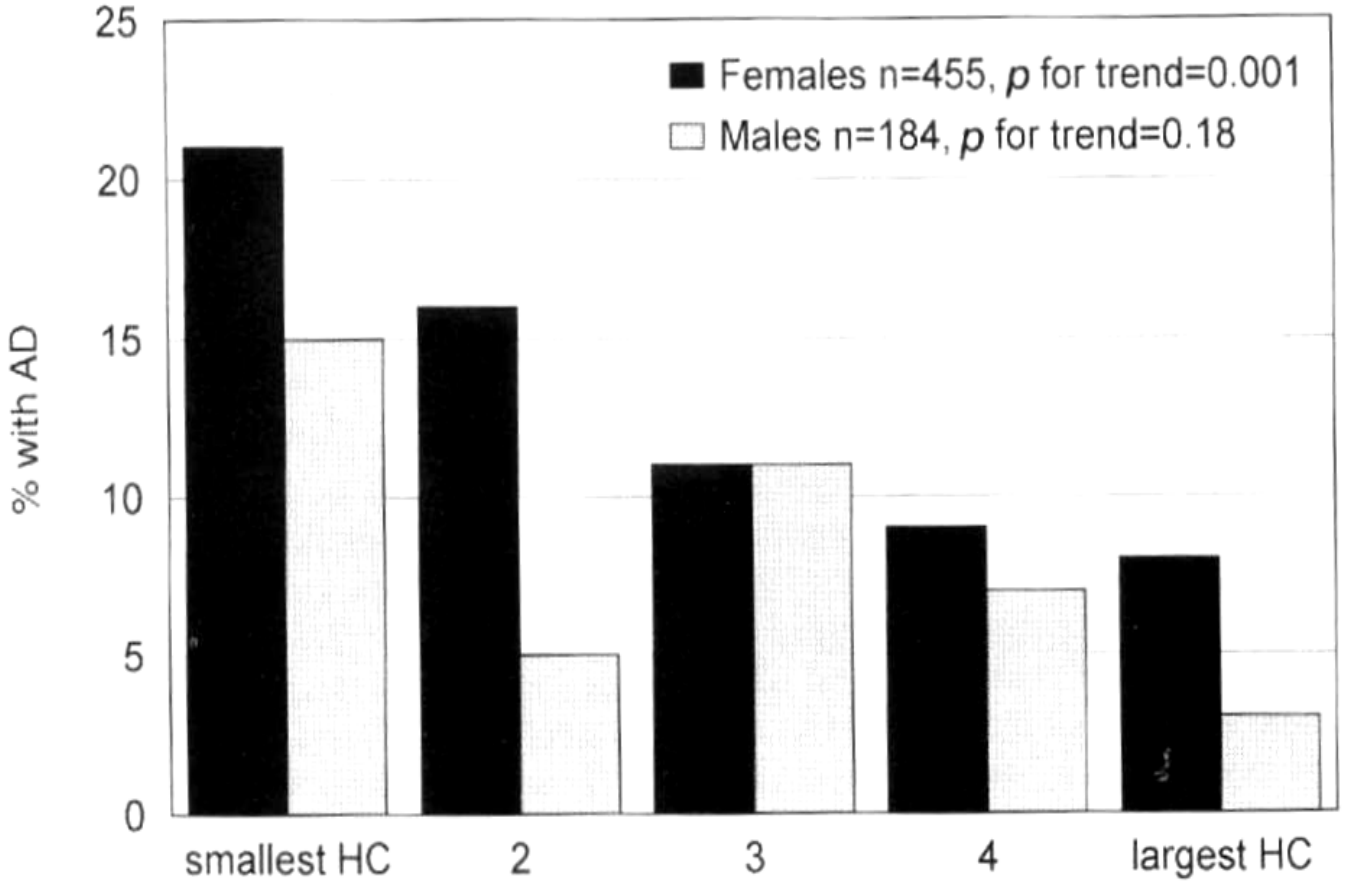


Cognitive reserve may explain the disjunction between the degree of brain damage and the clinical manifestation of that damage.

Mechanisms underlying reserve

- Brain reserve:
  - More neurons/synapses to lose
  - Anatomic changes on the basis of experience
- Cognitive Reserve:
  - Resilience/plasticity of cognitive networks in the face of disruption
- Brain Maintenance:
  - Direct effect of lifestyle/activities on aging/disease pathology

Brain Reserve: Association Between Head Circumference and Alzheimer's Disease



Schofield, et al, 1997

Brain Reserve is Not So Simple

The literature suggests that exercise and environmental stimulation can activate brain plasticity mechanisms and remodel neuronal circuitry in the brain.

They can increase:

- Vascularization (exercise)
- Neurogenesis in the dentate
- Brain volume/Cortical thickness
- Neuronal survival and resistance to brain insult
- Brain-derived neurotrophic factor (BDNF) -- benefits brain plasticity processes

Feature Review

Memory aging and brain maintenance

Lars Nyberg[1,2,3,7], Martin Lövdén[4,5,6], Katrine Riklund[1,3], Ulman Lindenberger[5] and Lars Bäckman[4]

- Relative lack of brain pathology is the biggest contributor to heterogeneity of cognitive aging
- Various lifestyle factors contribute to resisting the advent of pathology
- Issues:
  - Neuroprotective but not compensatory
  - Unlike reserve, does not account for maintained performance GIVEN pathology or brain damage

Trends in Cognitive Sciences May 2012, Vol. 16, No. 5

Can lifetime cognitive engagement impact amyloid development?

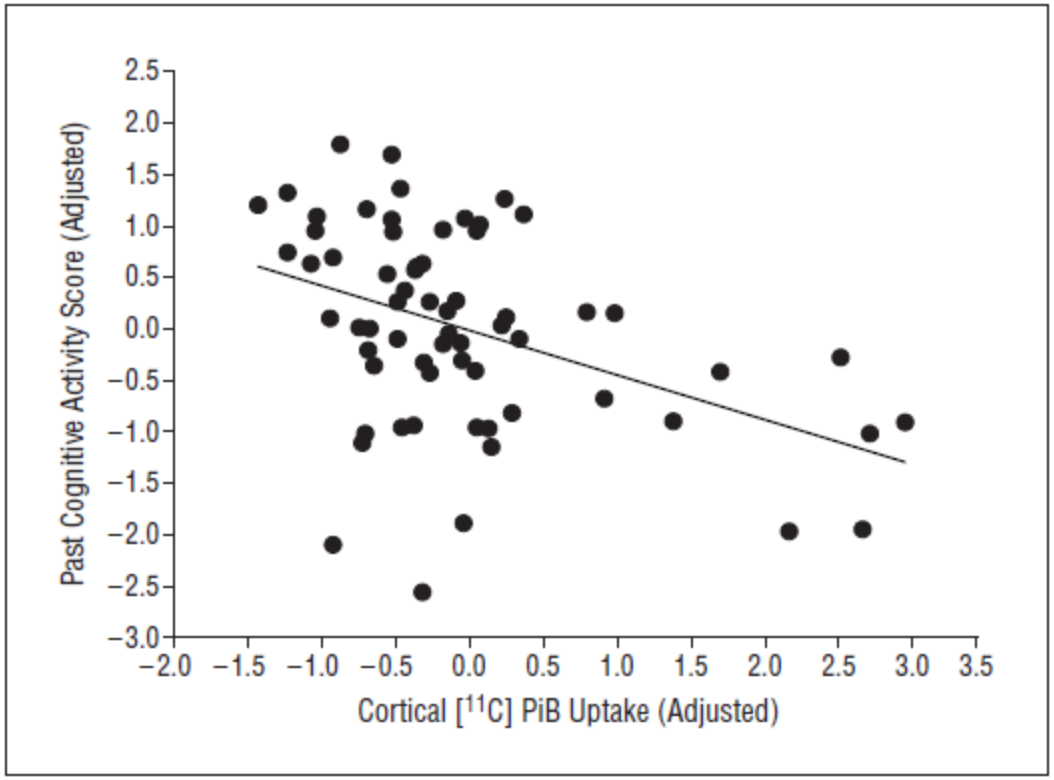
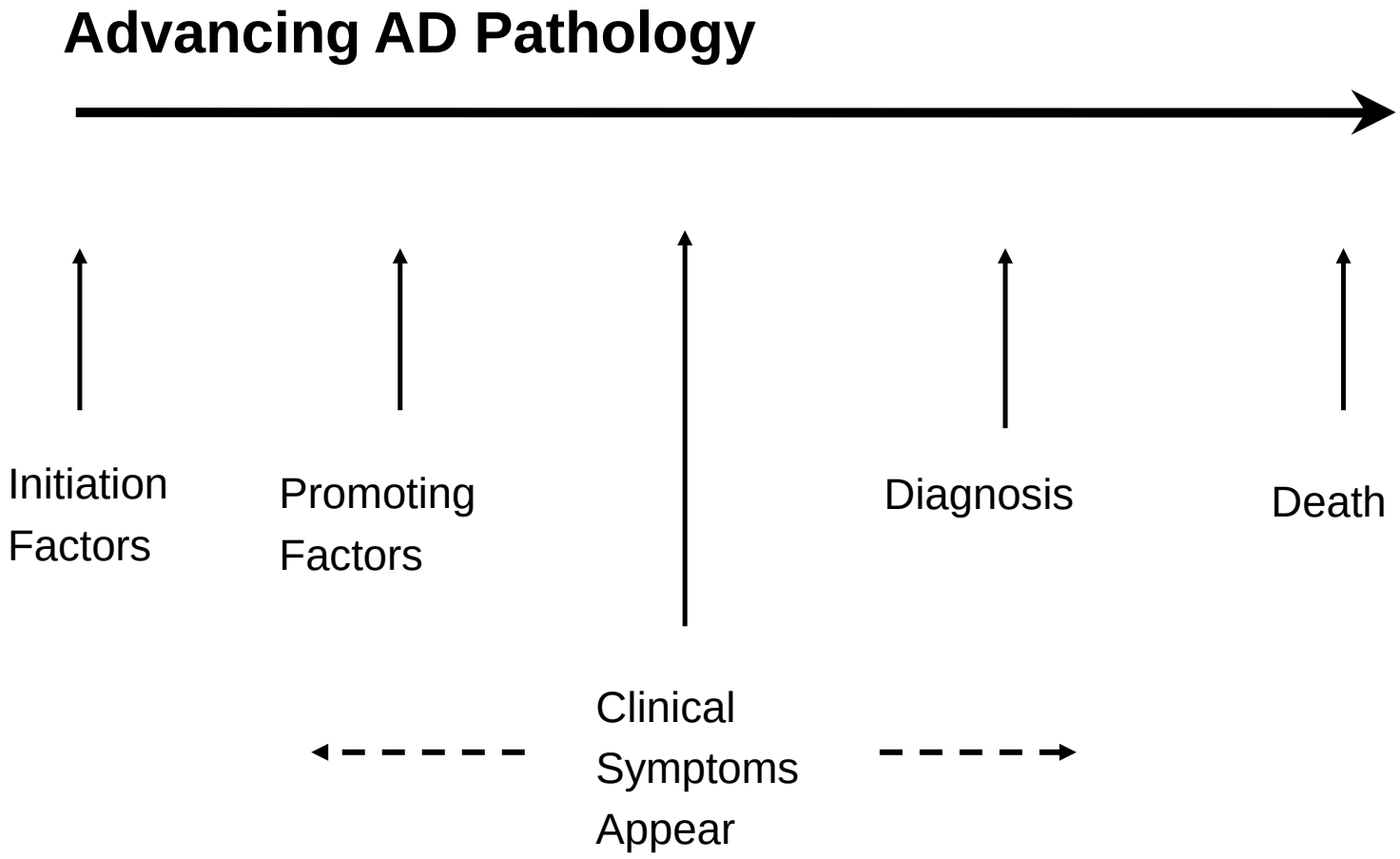


Figure 1. Individuals with greater cognitive engagement show reduced amyloid burden. Carbon 11–labeled Pittsburgh Compound B ([^{11}C]PiB) in cognitively normal older participants (x-axis) is inversely associated with past cognitive activity (y-axis) (linear regression, $\beta = -1.73 \pm 0.47$; $P < .001$). Both variables are residual values after correcting for age, sex, and years of education.

Landau et al, *Arch Neurol. Published online January 23, 2012*


Advancing AD Pathology
Initiation Factors
Promoting Factors
Clinical Symptoms Appear
Diagnosis
Death

Incident Dementia in The Washington Heights Study

Group	N	Incident Cases	Relative Risk	95% CI
Low Education	264	69	2.02	1.3-3.1
High Education	318	37	1	
Low Occupation	327	71	2.25	1.3-3.8
High Occupation	201	17	1	

Stern et al, JAMA 1994

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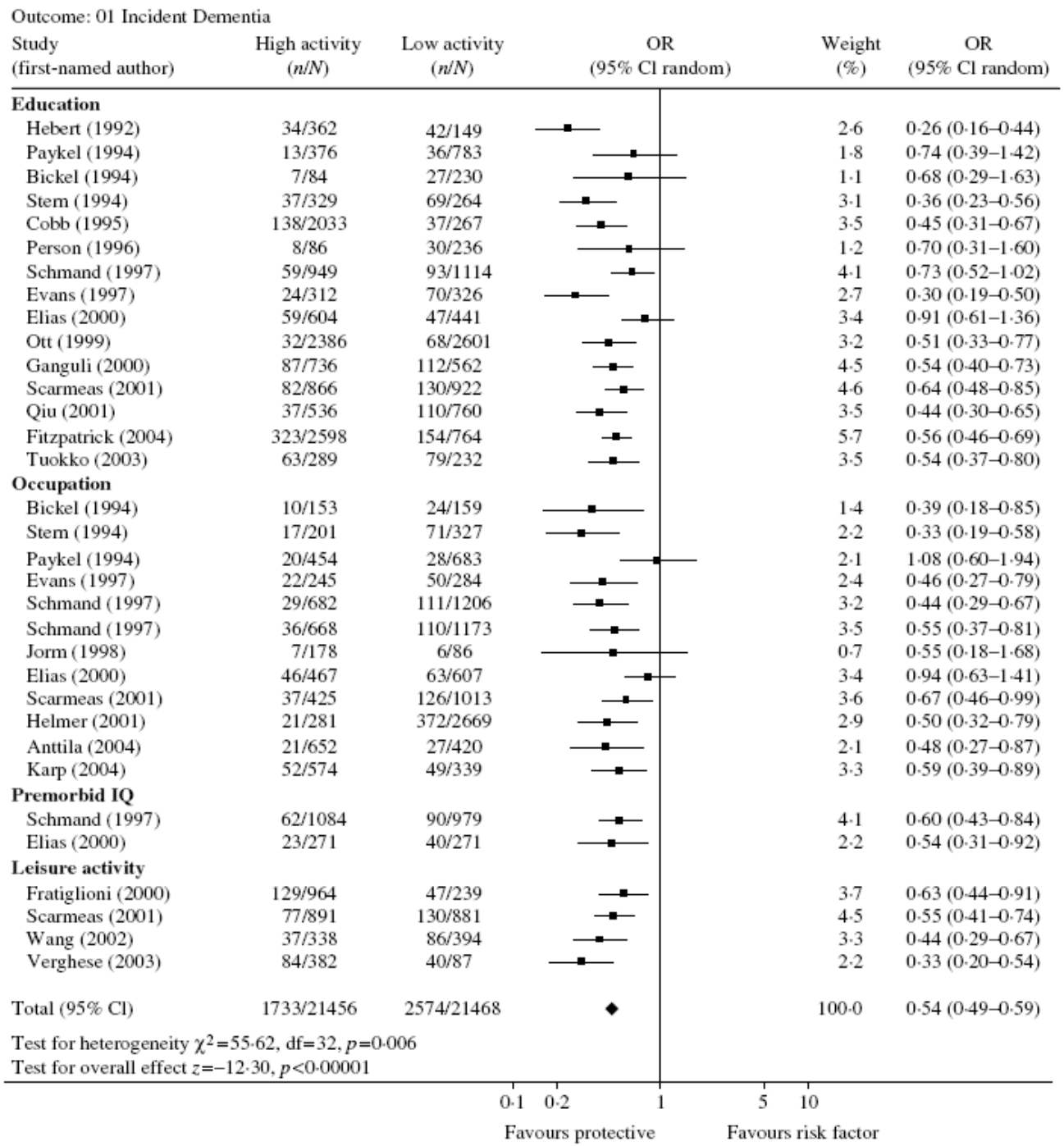
Incidence of Dementia As A Function of Past Leisure Activities

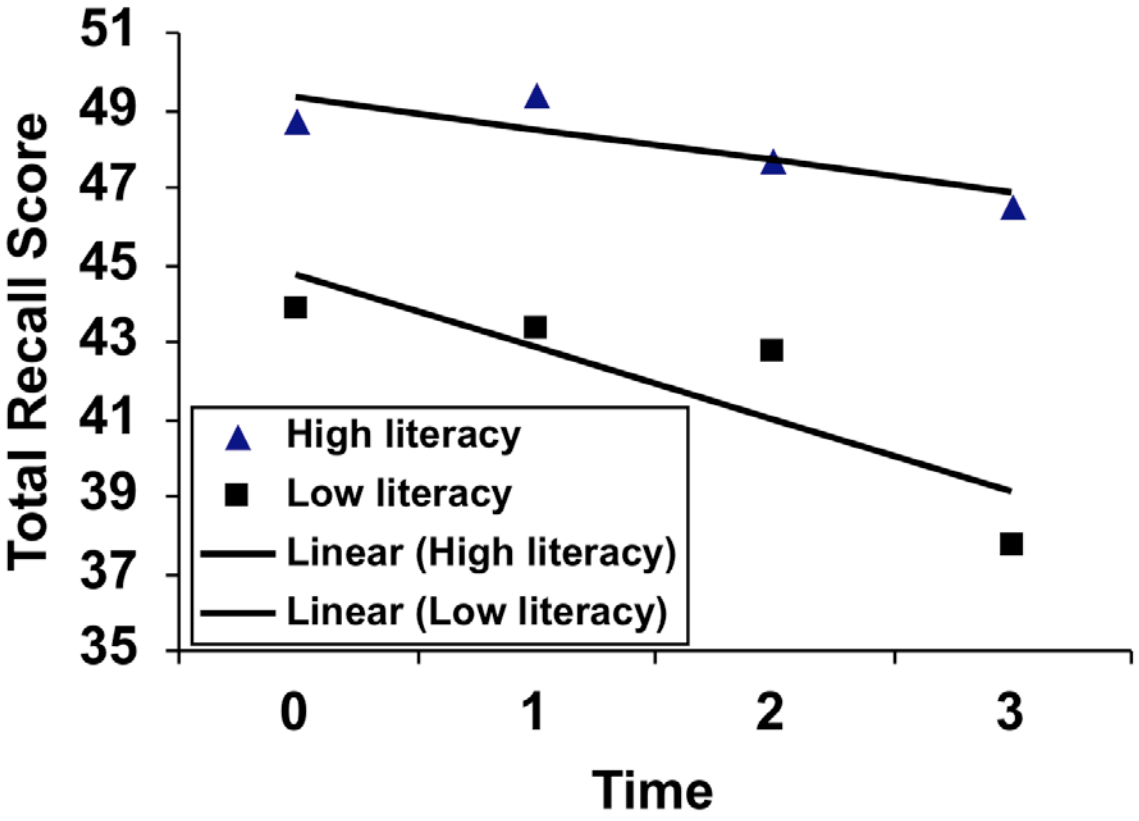
- Relative risk of incident dementia in high vs. low leisure
  - RR= 0.59 (0.44-0.79)
- Same analysis, controlling for education and occupation
  - RR= 0.62 (0.46-0.83)

Scarmeas et al, Neurology 2001



Valenzuela & Sachdev, Psychological Medicine, 2005

Literacy and memory decline in non-demented elders



Manly et al, JCEN 2003

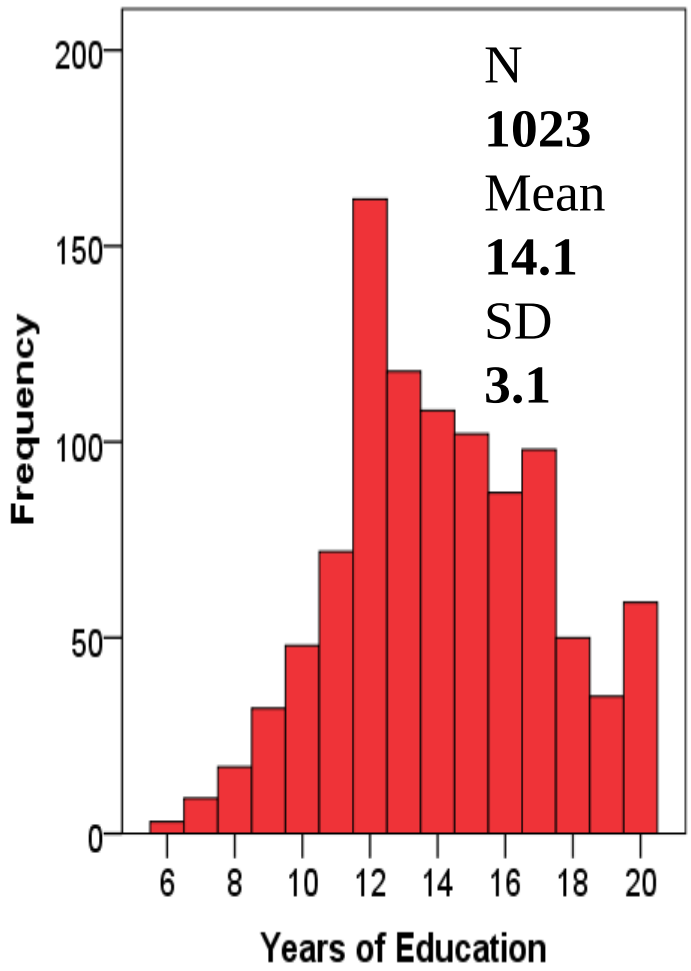
Journal of the International Neuropsychological Society (2011), **17**, 1039–1046.

doi:10.1017/S1355617711001044

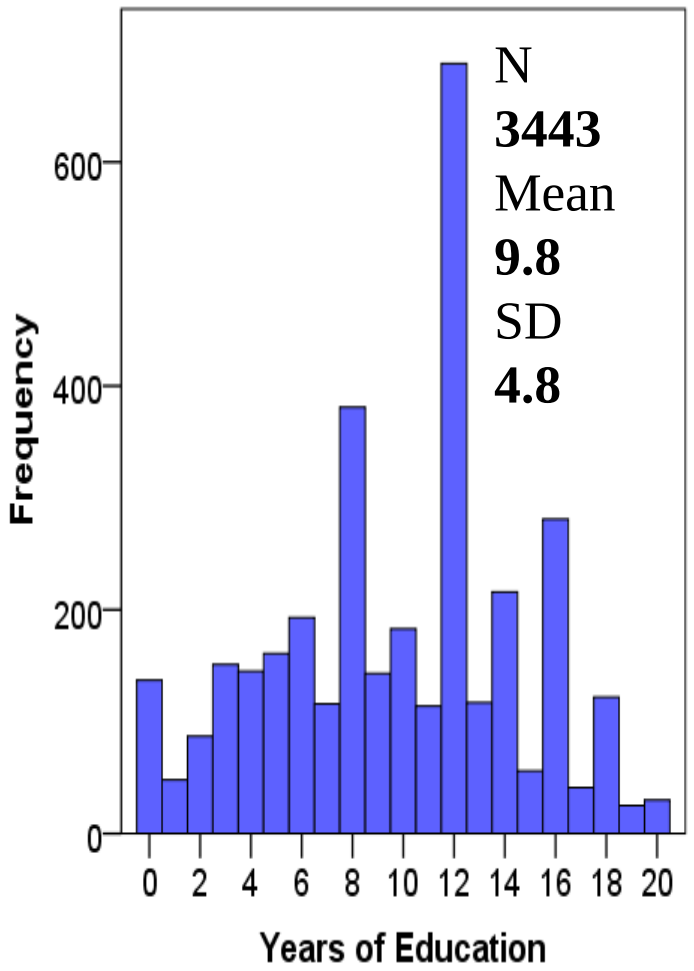
Education Does Not Slow Cognitive Decline with Aging:
12-Year Evidence fro

Laura B. Zahodne,[1] M. Maria Glymour
Stuart W.S. MacDonald,[3] AND Jennifer

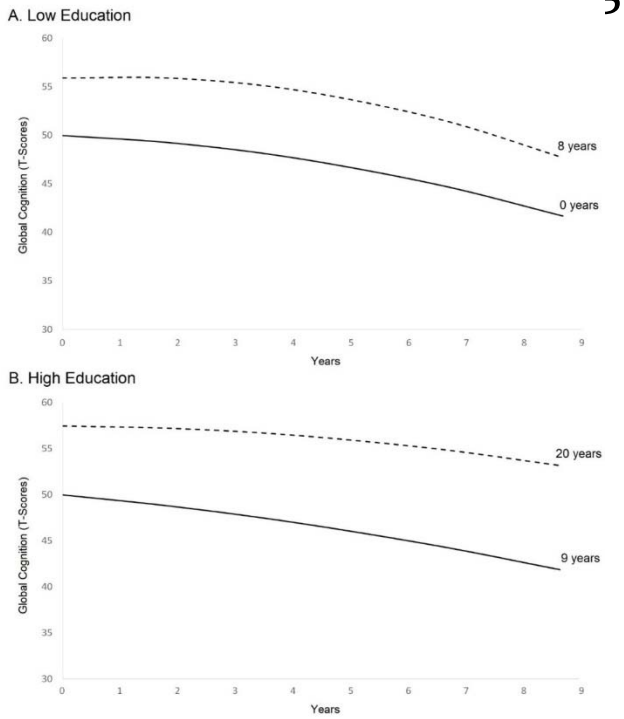
VLS

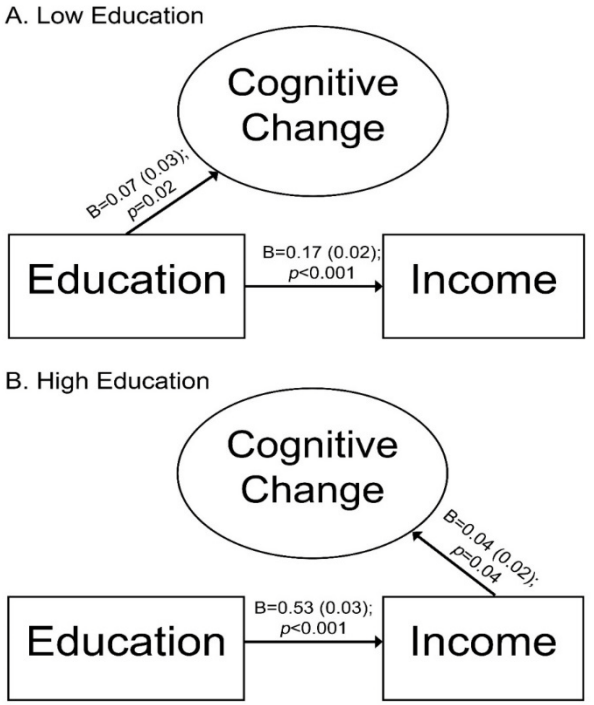


WHICAP



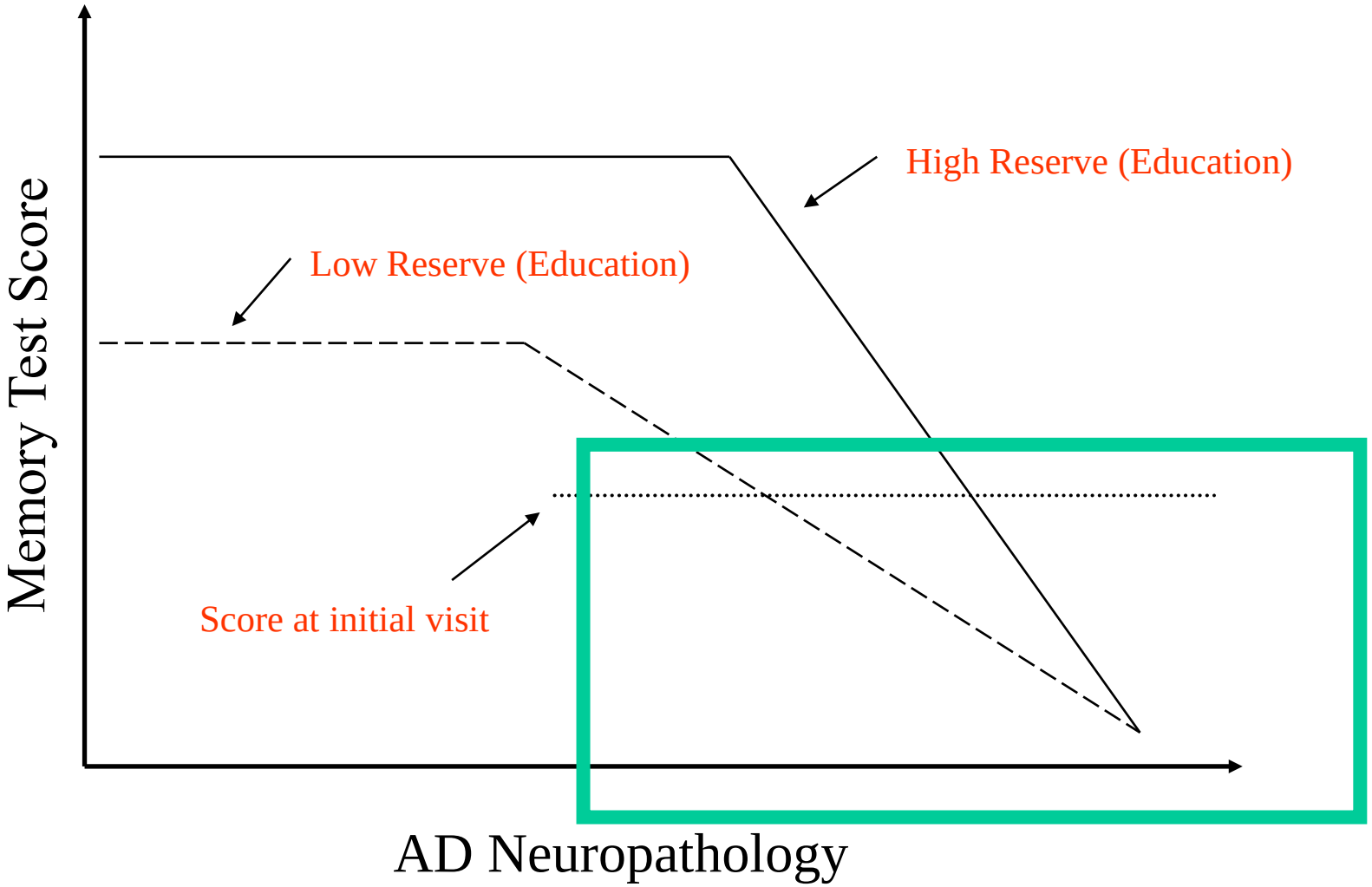
Association of Education With Cognitive Decline in the Washington Heights Study



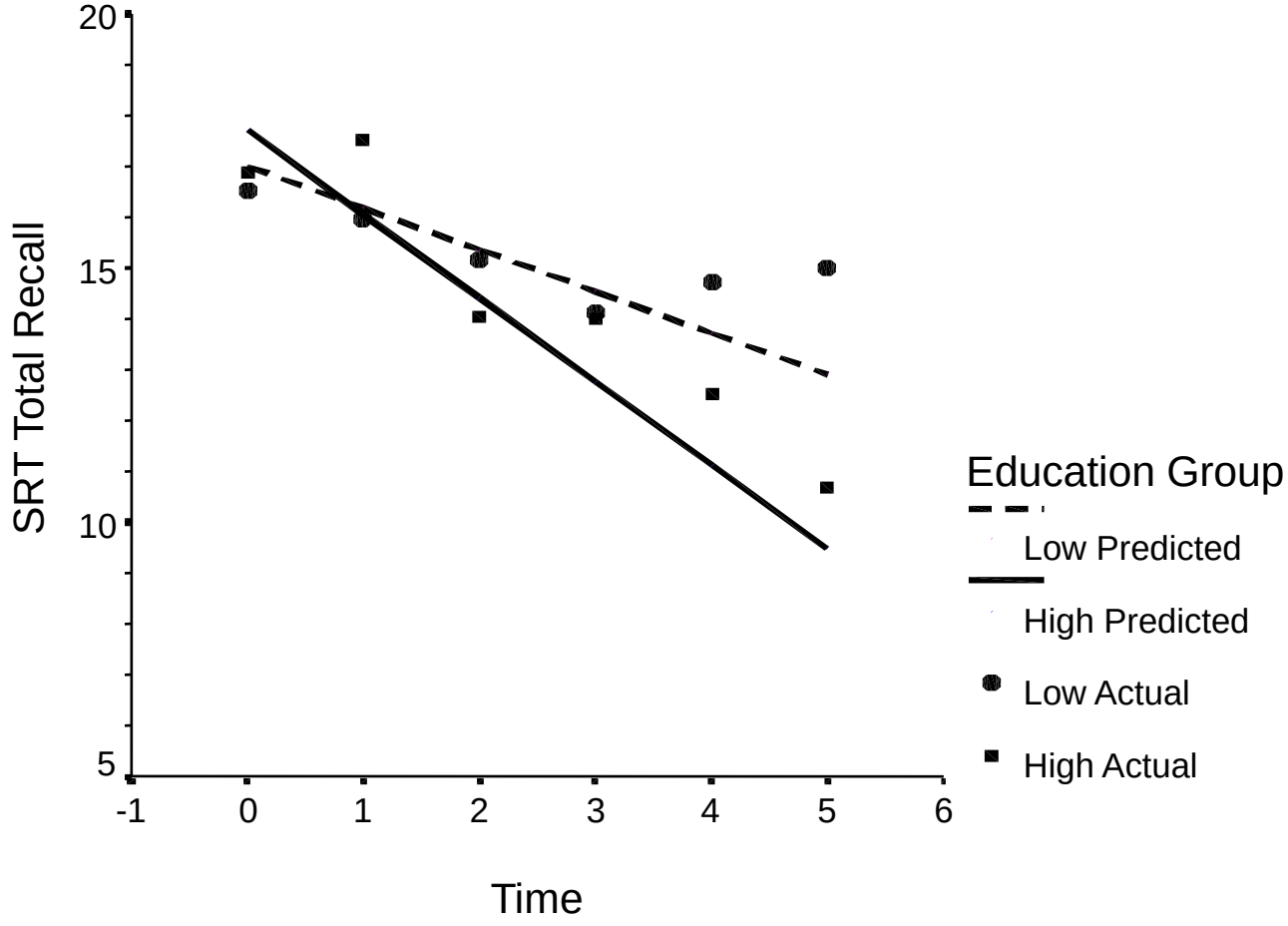


Model-estimated cognitive trajectories for 76-year-old, White, non-Hispanic Males born 1900-1909, recruited in 1992, with low (0-8 years) or high (9-20 years) education

Zahodne et al, Neuropsychology 2014

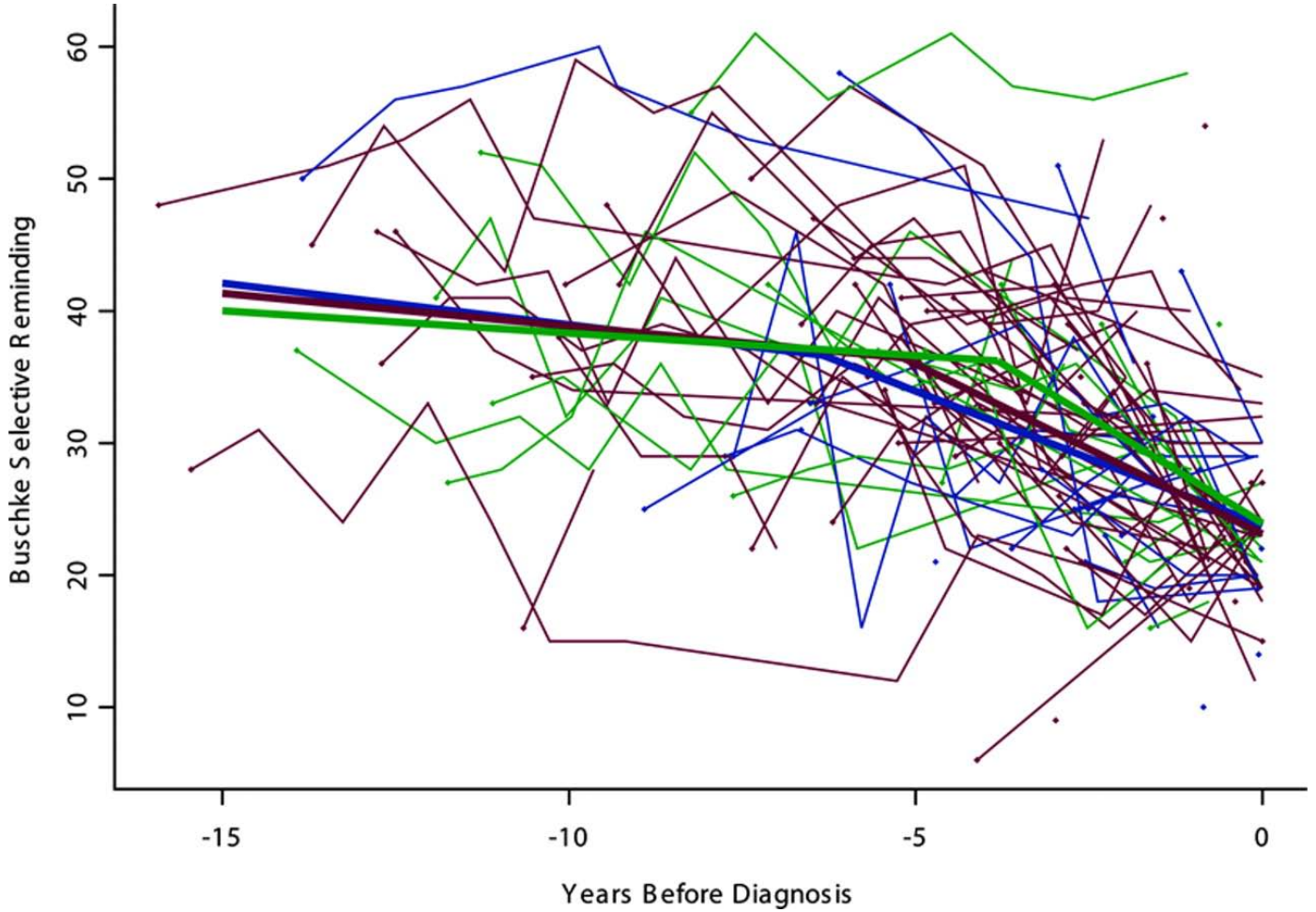

Memory Test Score
High Reserve (Education)
Low Reserve (Education)
Score at initial visit
AD Neuropathology

More rapid memory decline in AD patients with higher educational attainment



Stern et al Neurology 1999;53:1942-1957

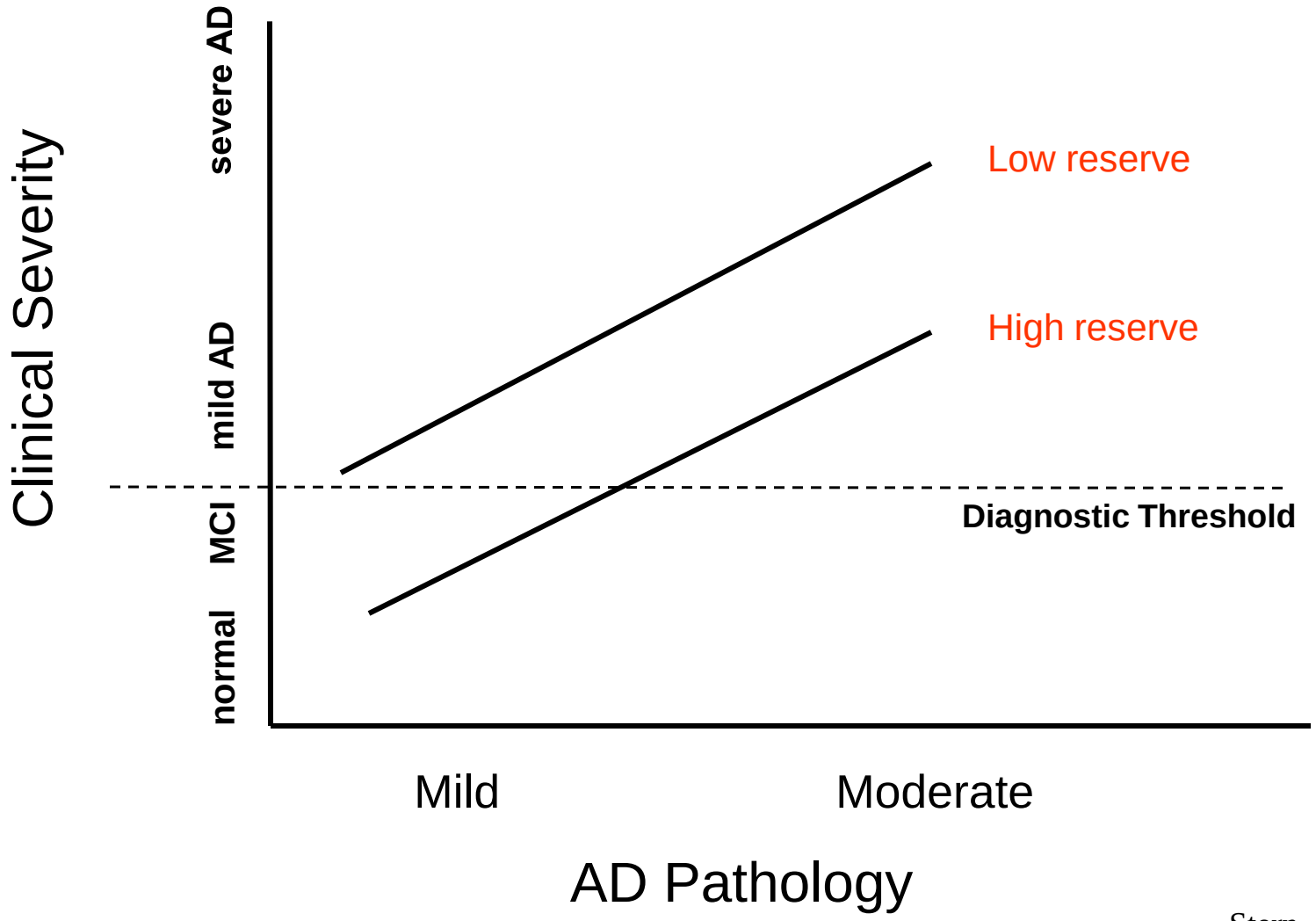
Bronx Aging Study



Blue indicates less than 7 years education (32 Ss), red indicates 8 to 11 years (64 Ss), and green indicates 12 or more years education (21 Ss).

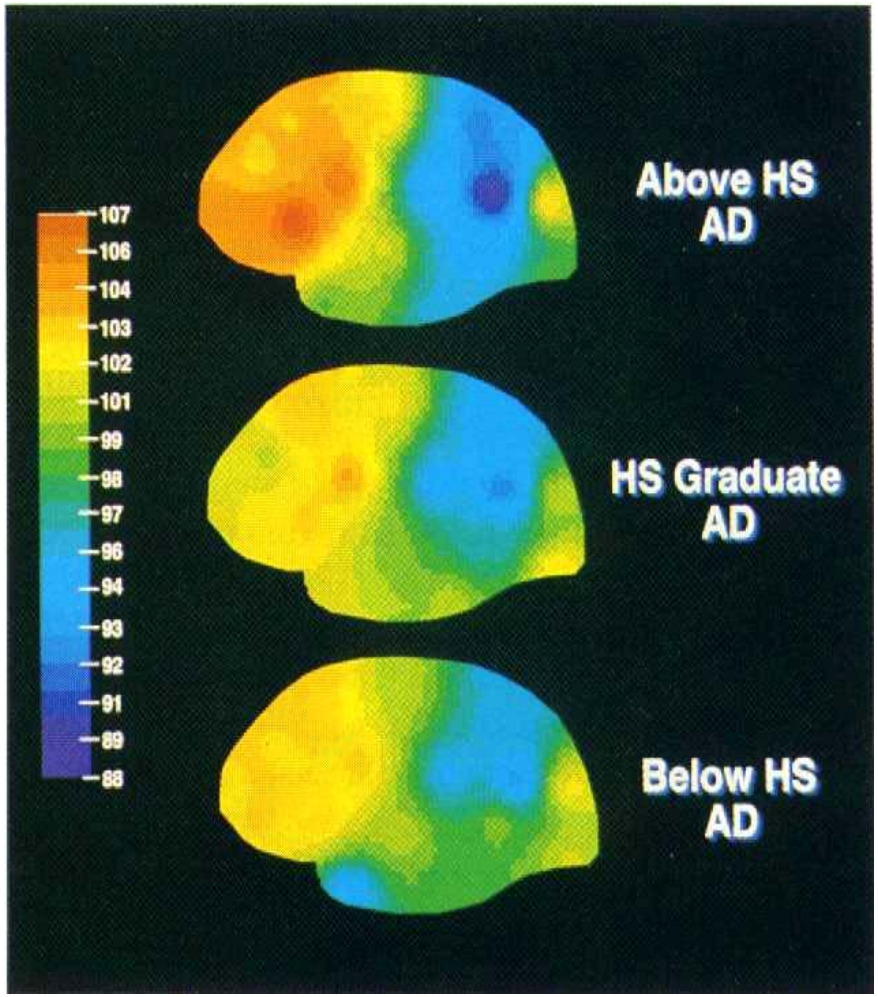
Hall, C. B. et al. Neurology 2007;69:1657-1664

Reserve, AD Pathology, and Clinical Diagnosis



Stern, JINS 2002

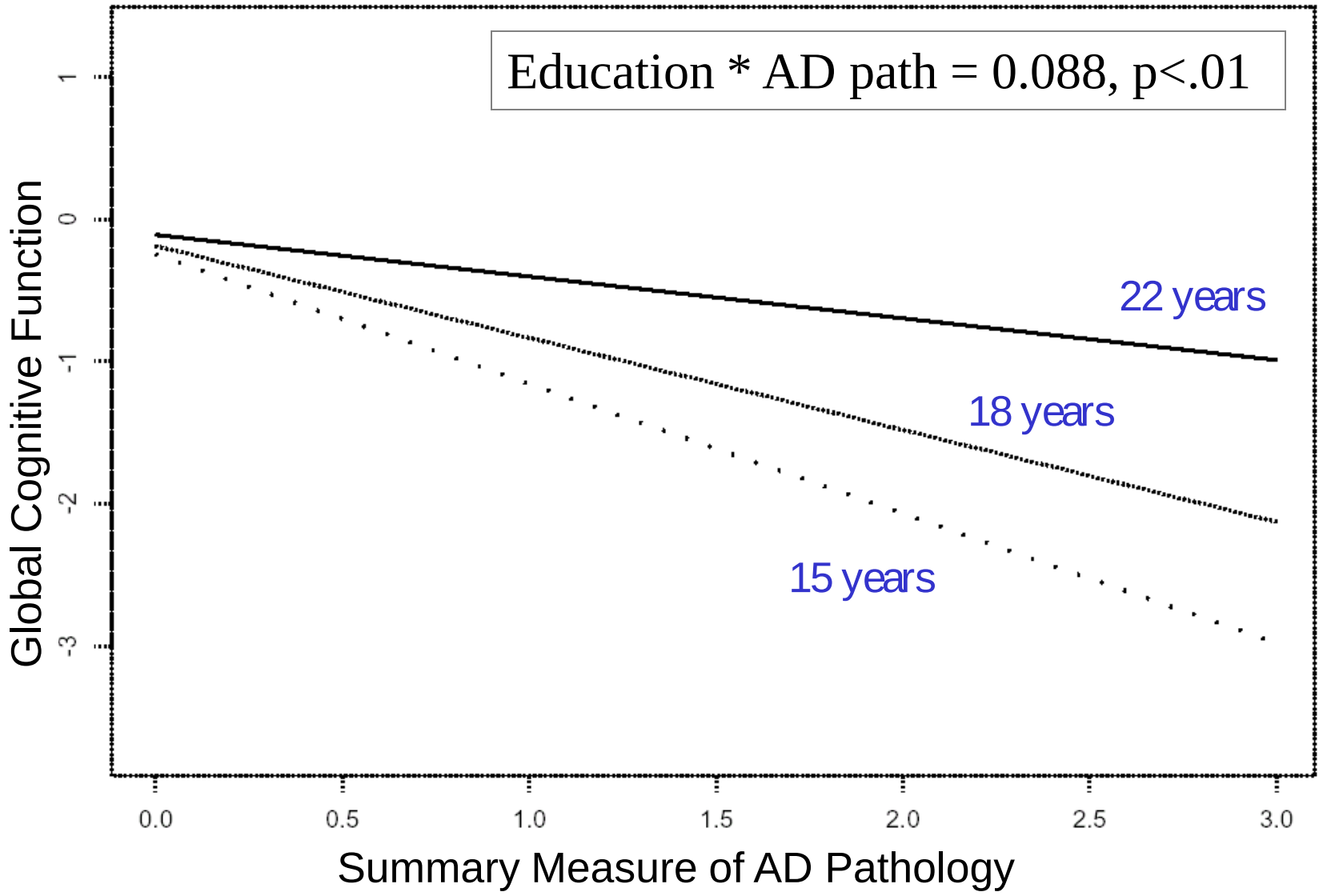
Education and rCBF



Controlling for clinical disease severity, there is an inverse relationship between education and a functional imaging proxy for AD pathology

Stern et al, Ann Neurol 1992

Interaction of AD Pathology and Education

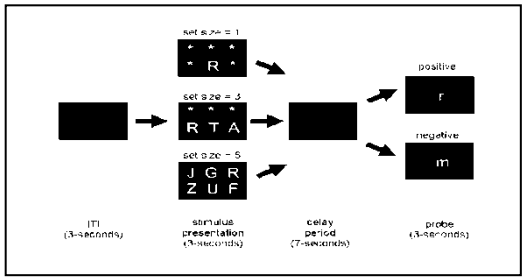


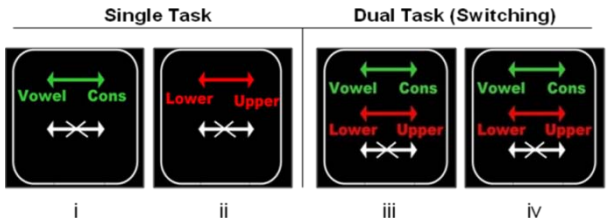
Bennett DA et al, Neurology 2003

Cognitive Reserve, Aging and AD

- Two individuals who appear the same clinically, whether demented of non-demented, can have widely divergent levels of underlying age-related neural changes or AD pathology.
- Thus, the clinical diagnosis of normal aging, MCI or AD may be accompanied by very minimal pathology or more than enough to meet pathological criteria for AD.
- Measuring CR therefore becomes an important component of diagnosing and characterizing aging and dementia.

Current Study of the Neural Implementation of Cognitive Reserve





Task-related network expression

Volume
Cortical Thickness
WMH Burden
WM Tract integrity
Resting CBF
Resting connectivity
Amyloid burden

Age-or AD-related pathology

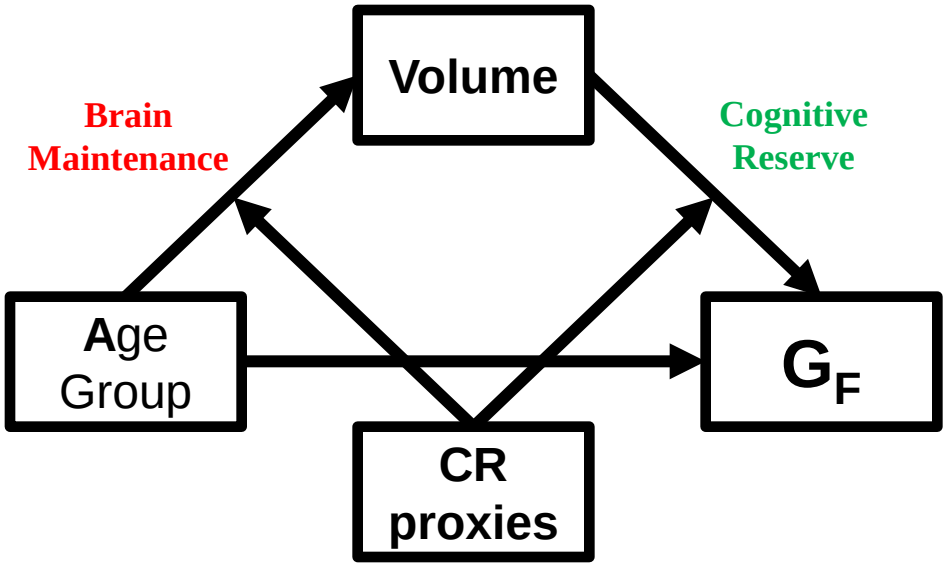
Task or NP performance, Clinical Outcome

Activation Task Performance
Cognitive Domains
Function / ADL
Cognitive decline over time/
Incident MCI/AD

Measured CR *or* CR-specific network

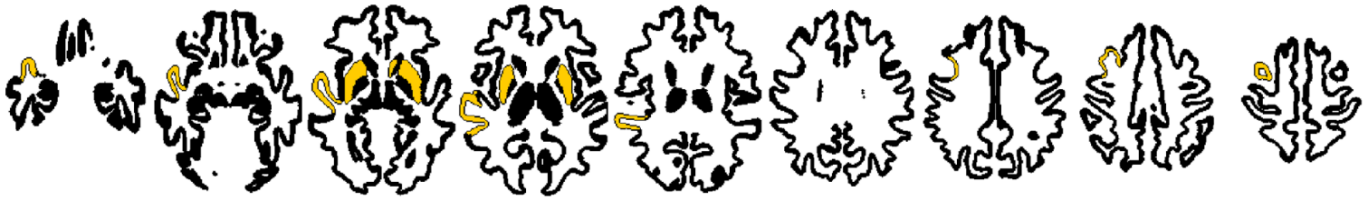
Measured IQ
Education/Literacy
Leisure Activity
CR Network

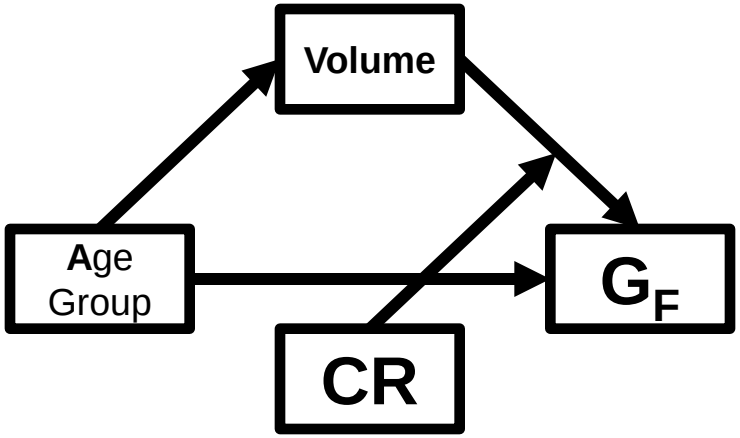
Current Directions: Moderated Mediation Analyses



Steffener et al, PLoS ONE 2014

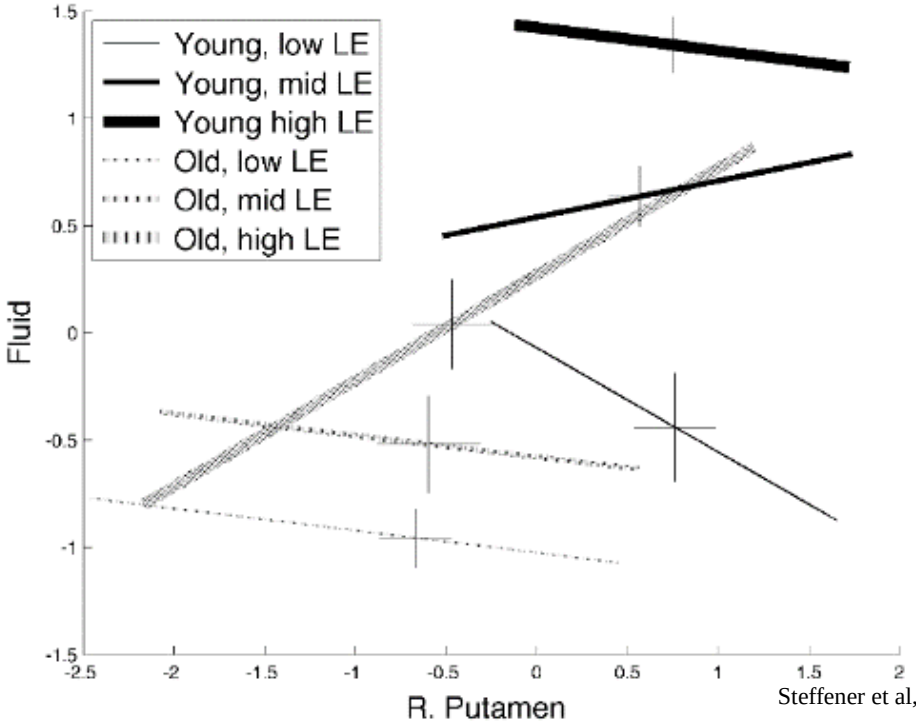
Areas with significant mediated moderation





Steffener et al, PLoS ONE 2014

Mediated Moderation Sample Result



Steffener et al, PLoS ONE 2014

Influence of Cognitive Reserve on Strategy Selection in Normal Aging

- 100 two-digit by two-digit multiplication problems were presented, e.g. 58 X 32
- Participants were asked to choose the strategy that would get them closest to the actual product: rounding both digits up or both down
- They solved the problem and stated their strategy

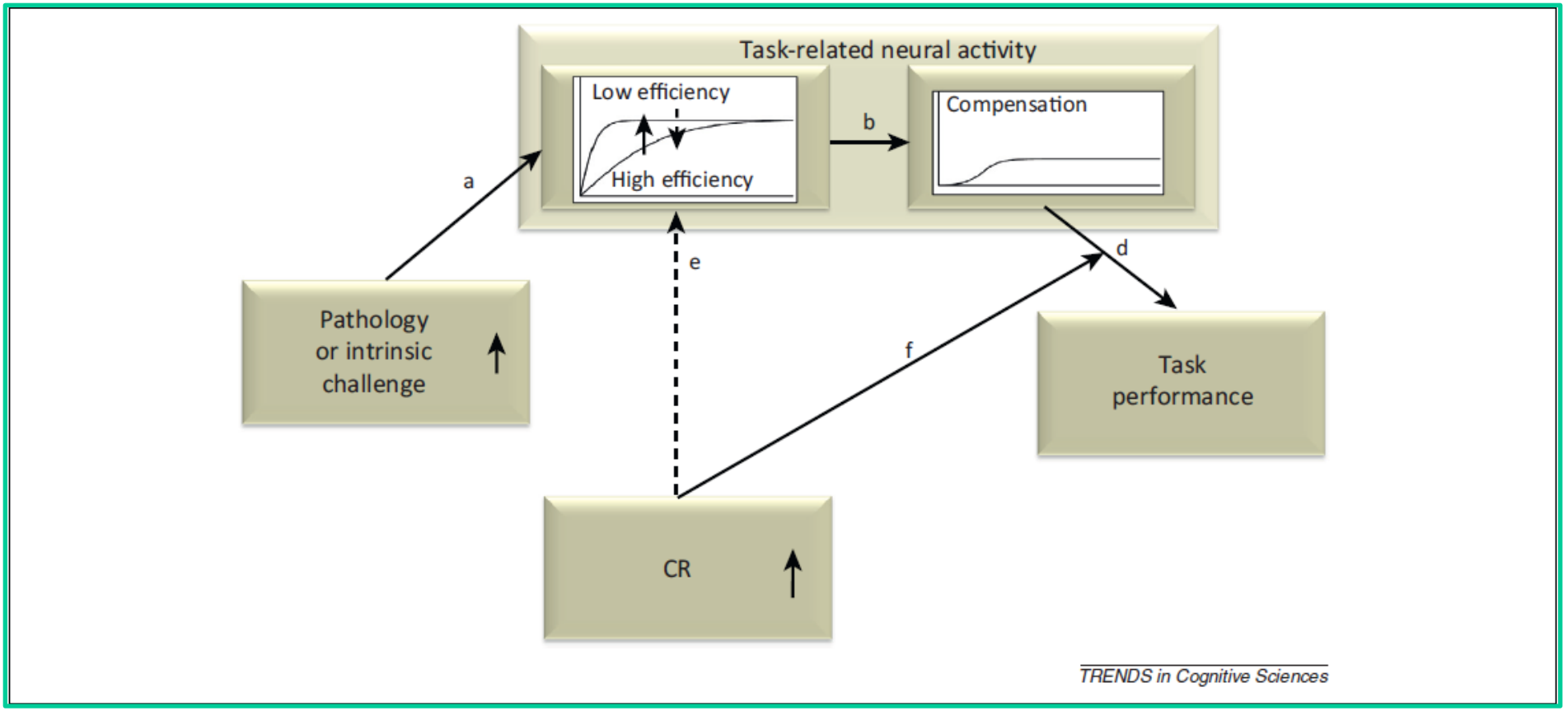
Barulli el al, JINS 2013

Influence of Cognitive Reserve on Strategy Selection in Normal Aging

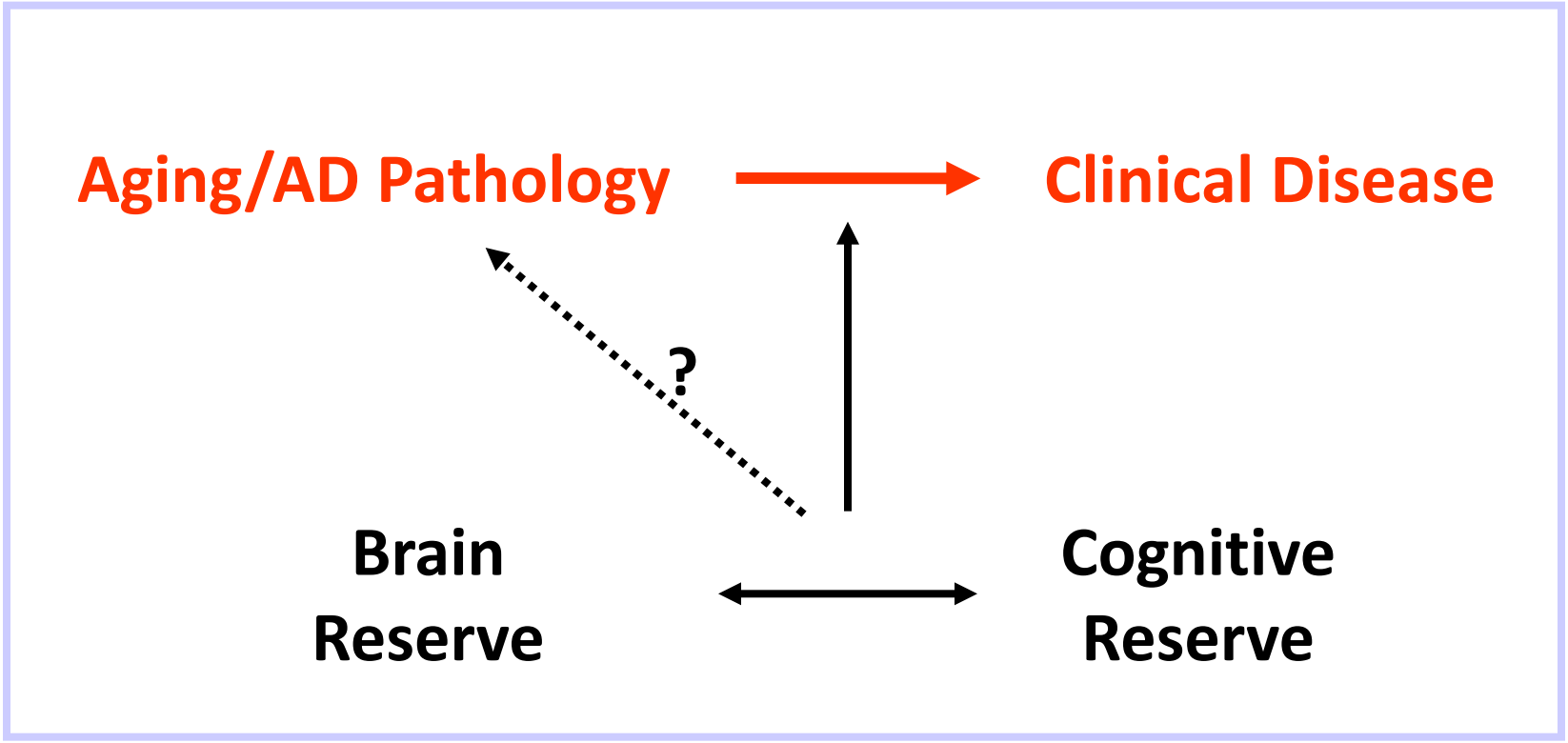
- Older participants were significantly worse at using the appropriate strategy than younger participants, and had longer reaction times
- Elders with higher verbal IQ chose the best strategy more often than those with lower verbal IQ; almost association with IQ was seen in the younger group
- This could suggest a relationship between CR and strategy selection

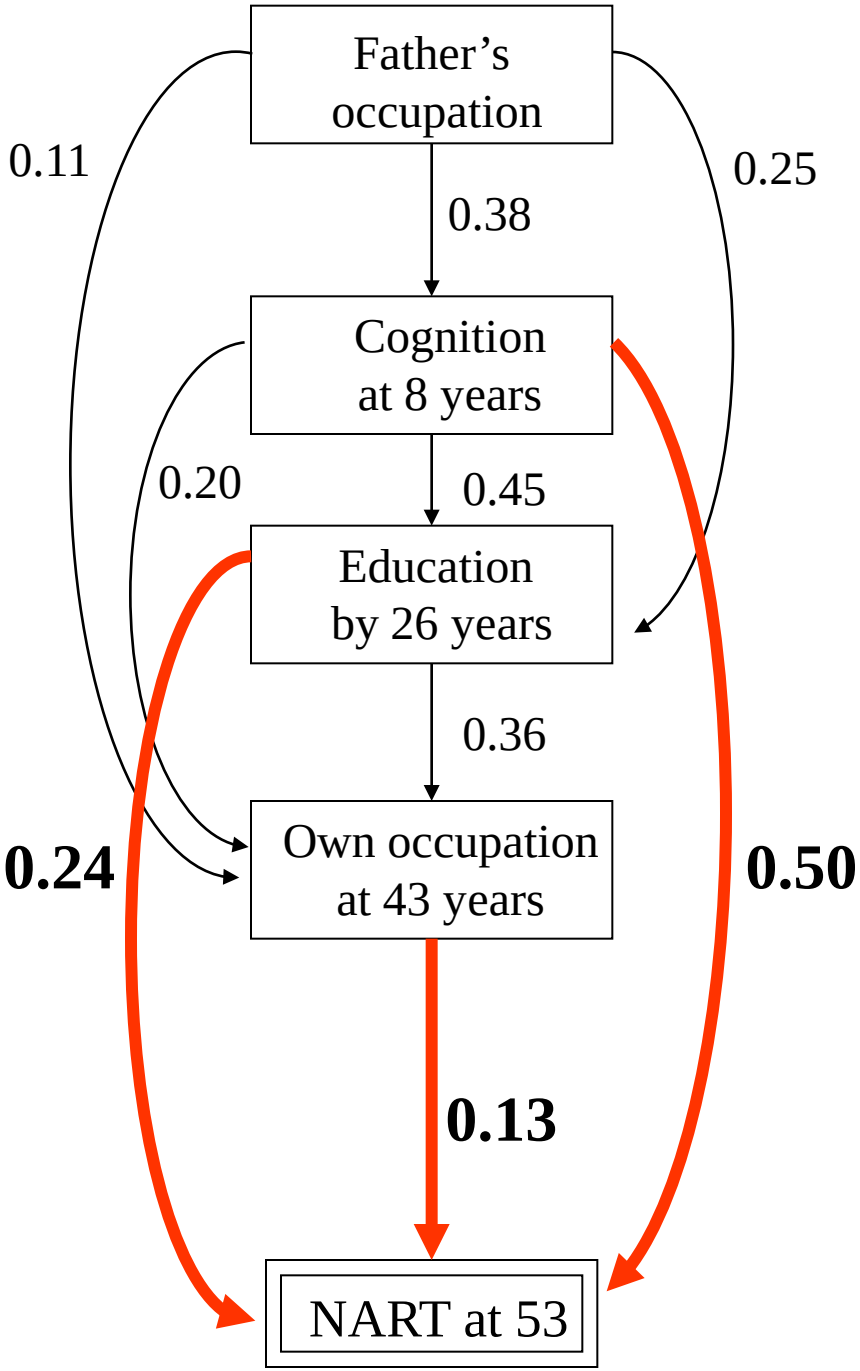
Barulli el al, JINS 2013

Neural Implementation of CR



How Would Reserve-based Interventions Work?





Richards, JCEN 2003

Conclusions

- Epidemiologic and imaging evidence support the concept of reserve
- Reserve is malleable: it is influenced by aspects of experience in every stage of life
- The concept of cognitive reserve is applicable to a wide range of conditions that impact on brain function at all ages
- Imaging studies can help clarify the neural implementation of reserve
- Influencing reserve can delay or reverse the effects of aging or brain pathology