



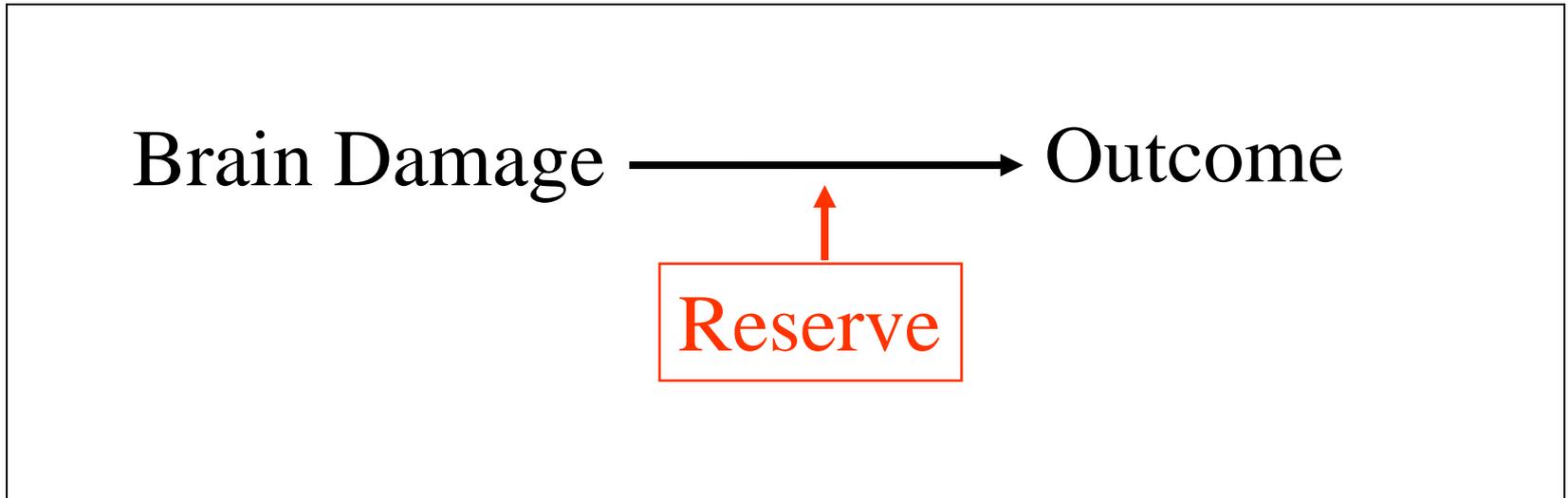
Cognitive Reserve: From Theory To Intervention

Yaakov Stern

Columbia University

www.cogneurosci.org

What is Reserve?



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

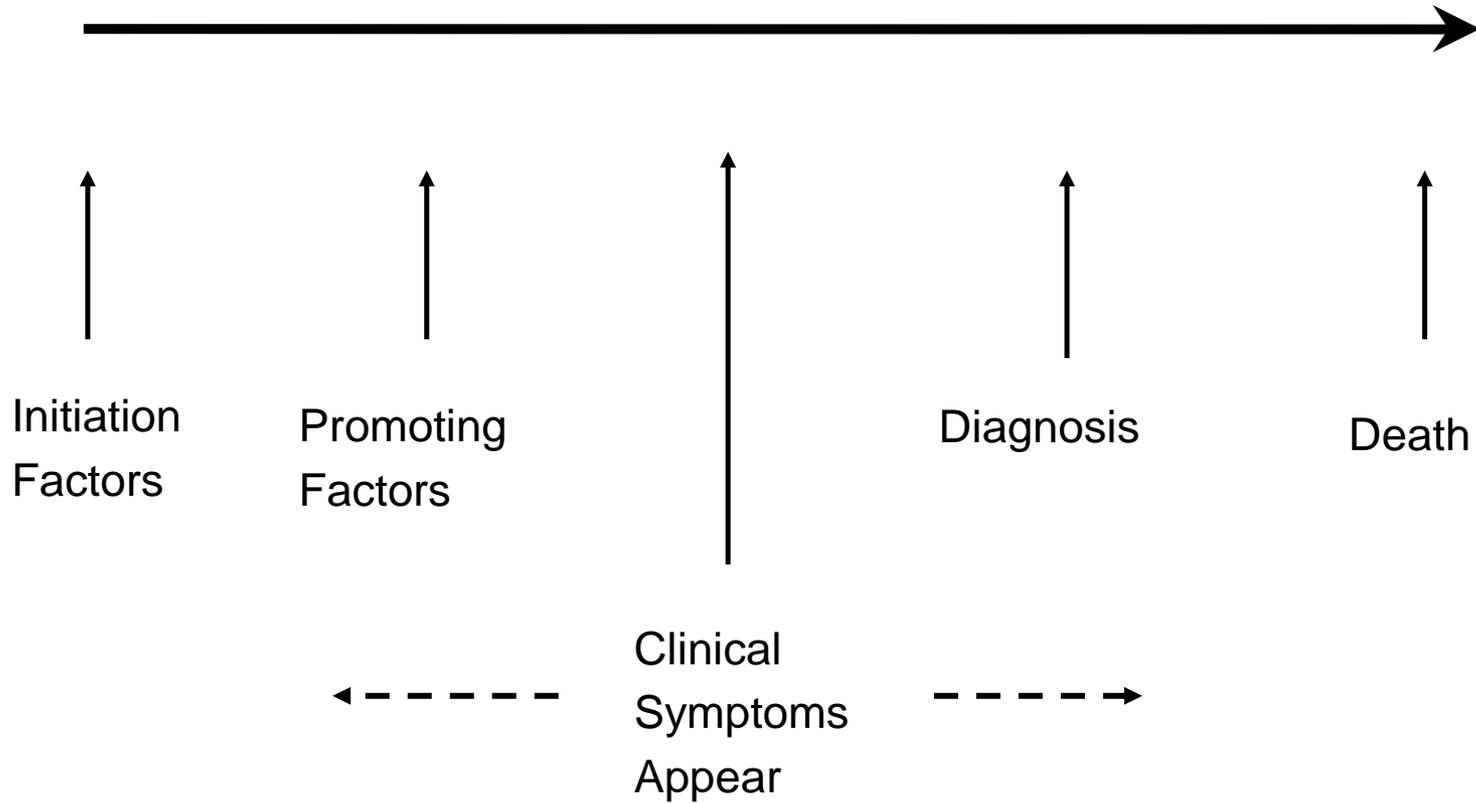
Brain Reserve is Not So Simple

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
- Neuronal survival and resistance to brain insult
- Brain-derived neurotrophic factor (BDNF) -- benefits brain plasticity processes
- Serotonin, dopamine, IGF-1

Advancing AD Pathology

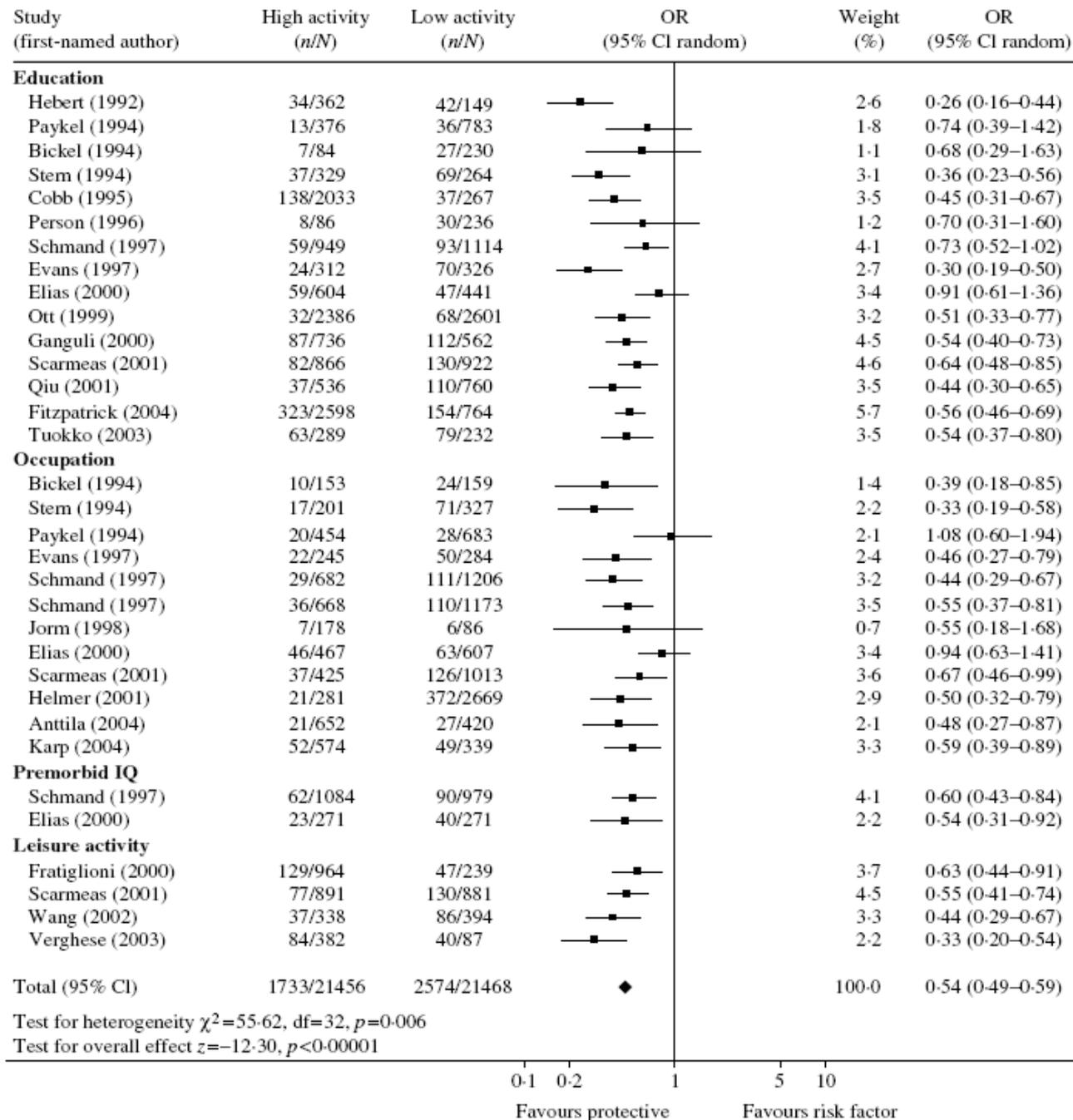


Incident Dementia in The Washington Heights Study

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	

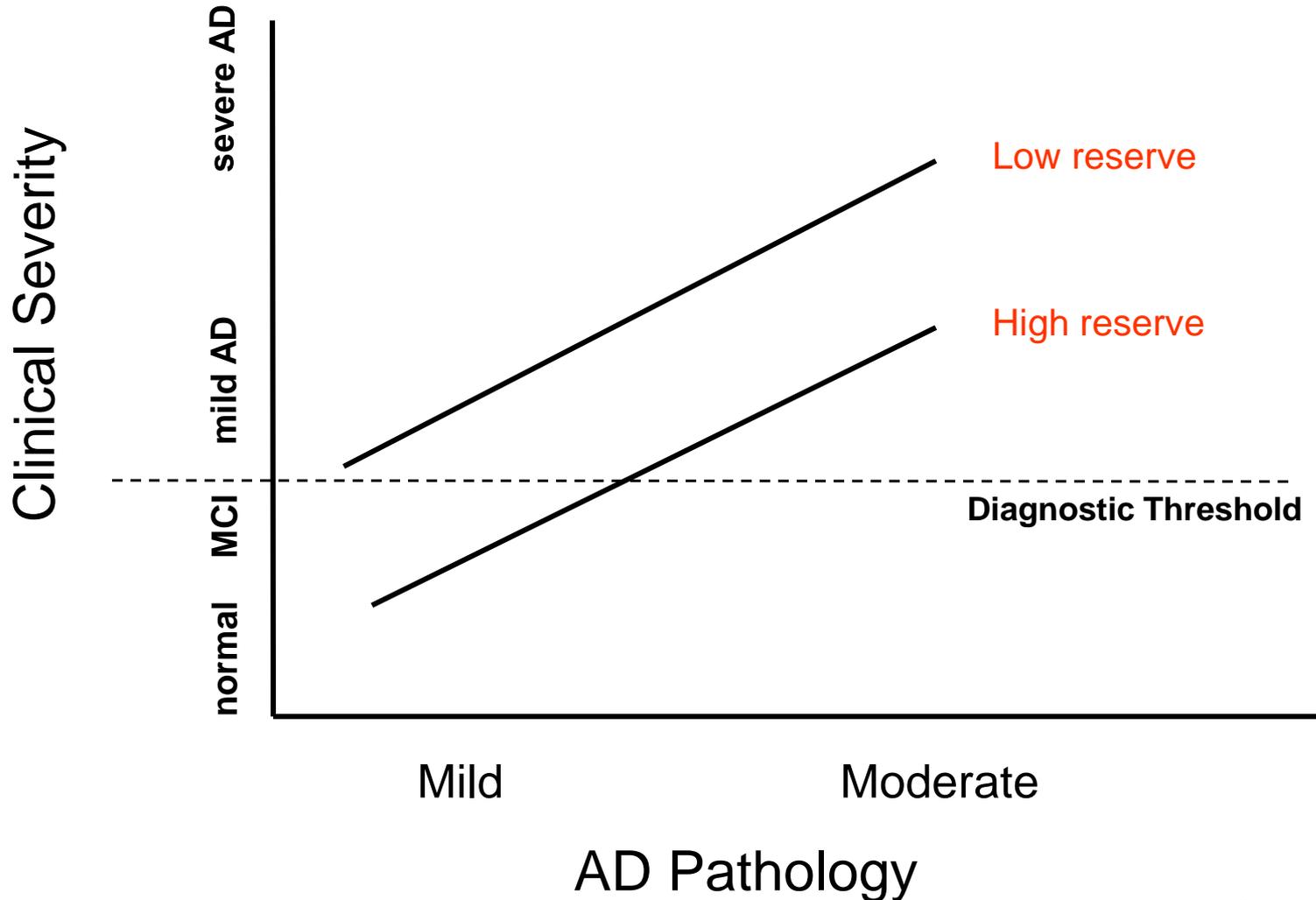
Stern et al, JAMA 1994

Outcome: 01 Incident Dementia

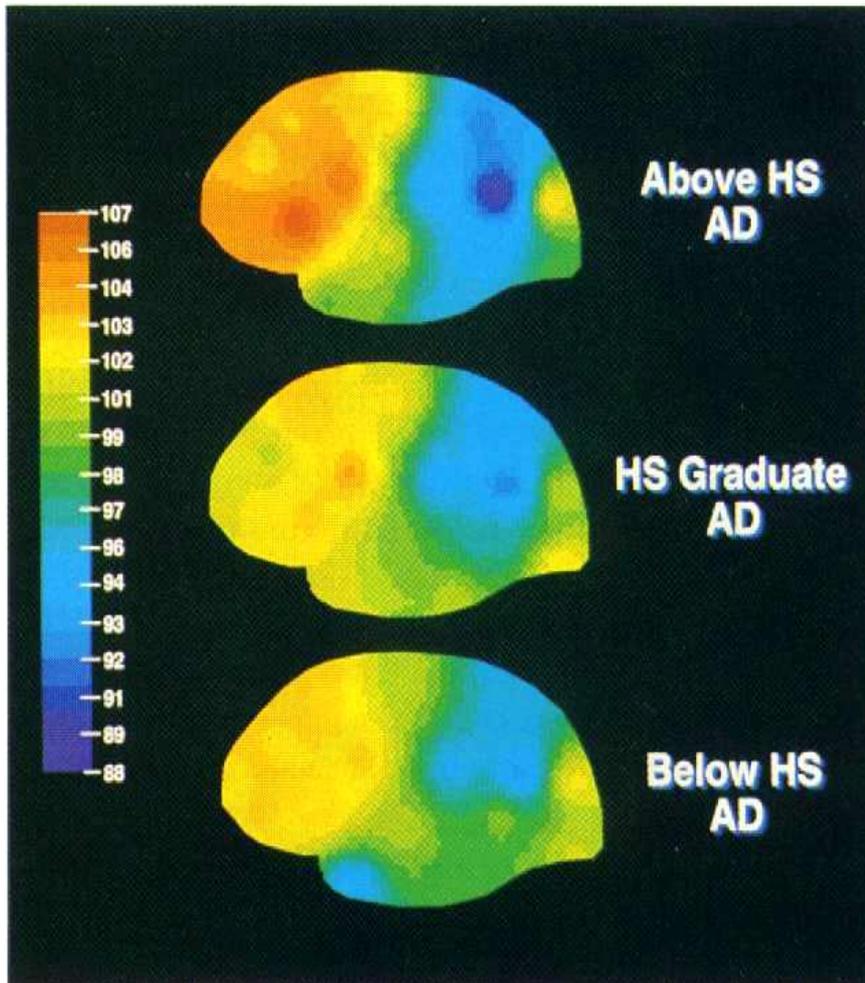


Valenzuela &
Sachdev,
Psychological
Medicine, 2005

Reserve, AD Pathology, and Clinical Diagnosis

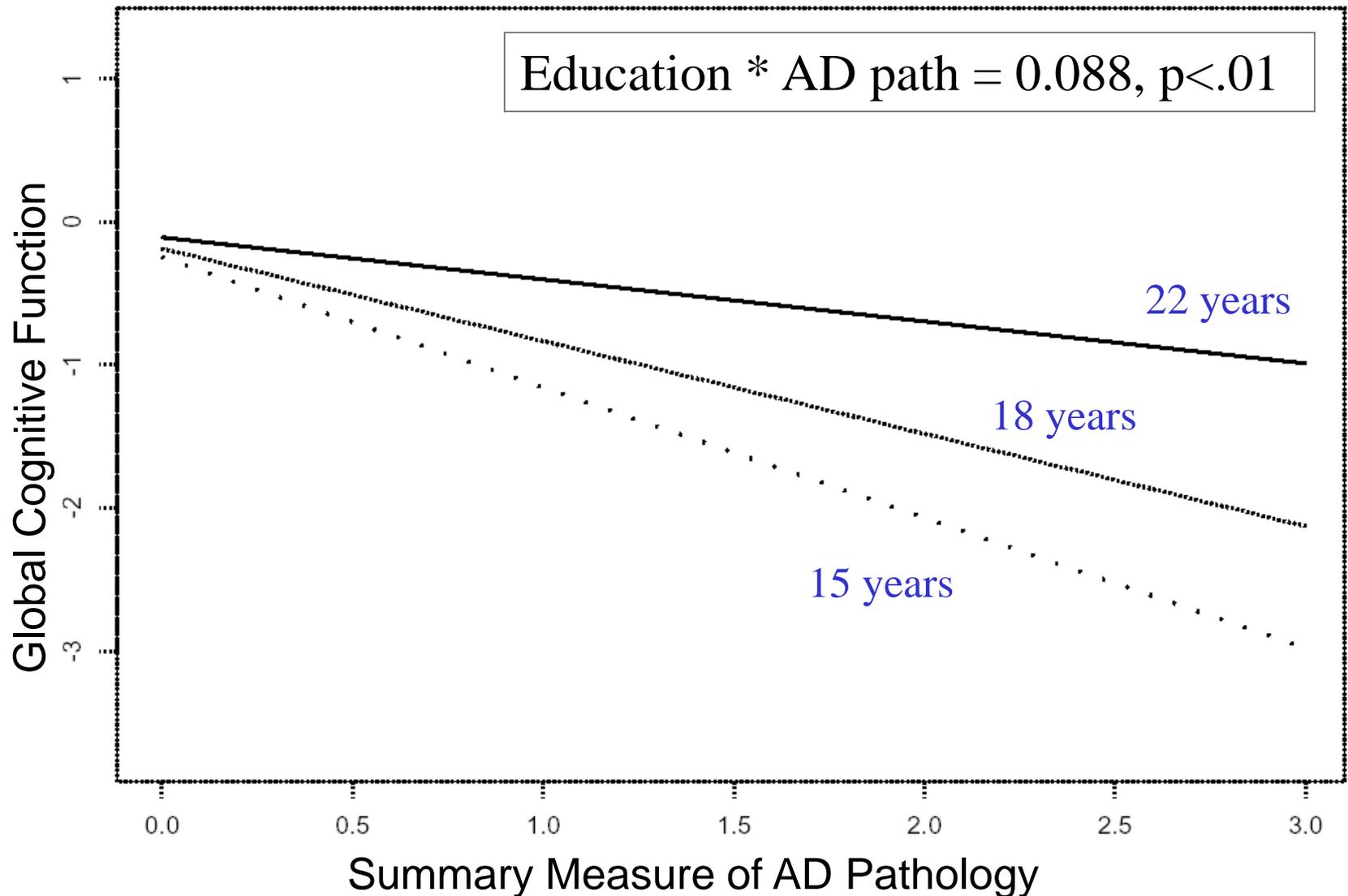


Education and rCBF



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

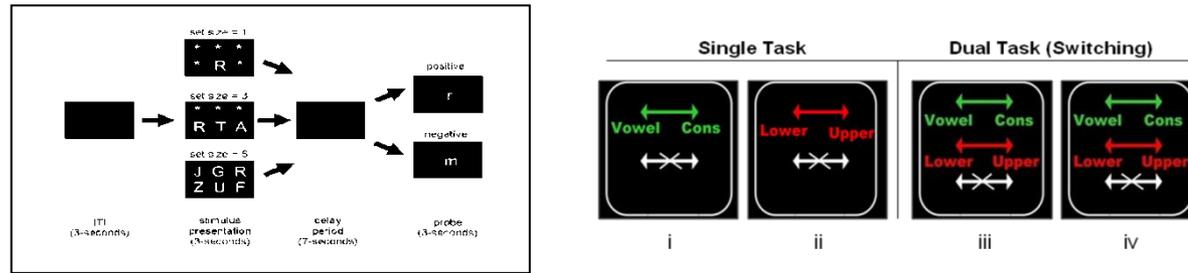
Interaction of AD Pathology and Education



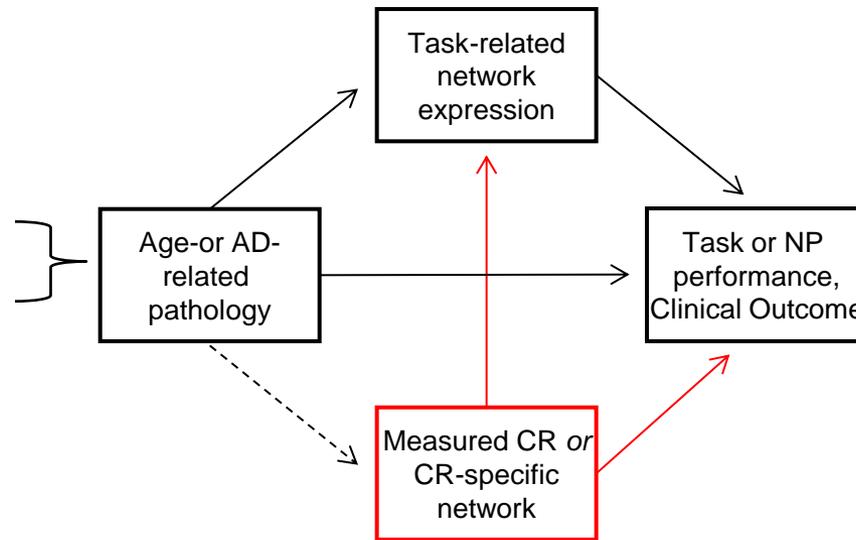
Cognitive Reserve, Aging and AD

- Two individuals who appear the same clinically, whether demented or 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.

Scheme for Studying Neural Implementation of Cognitive Reserve



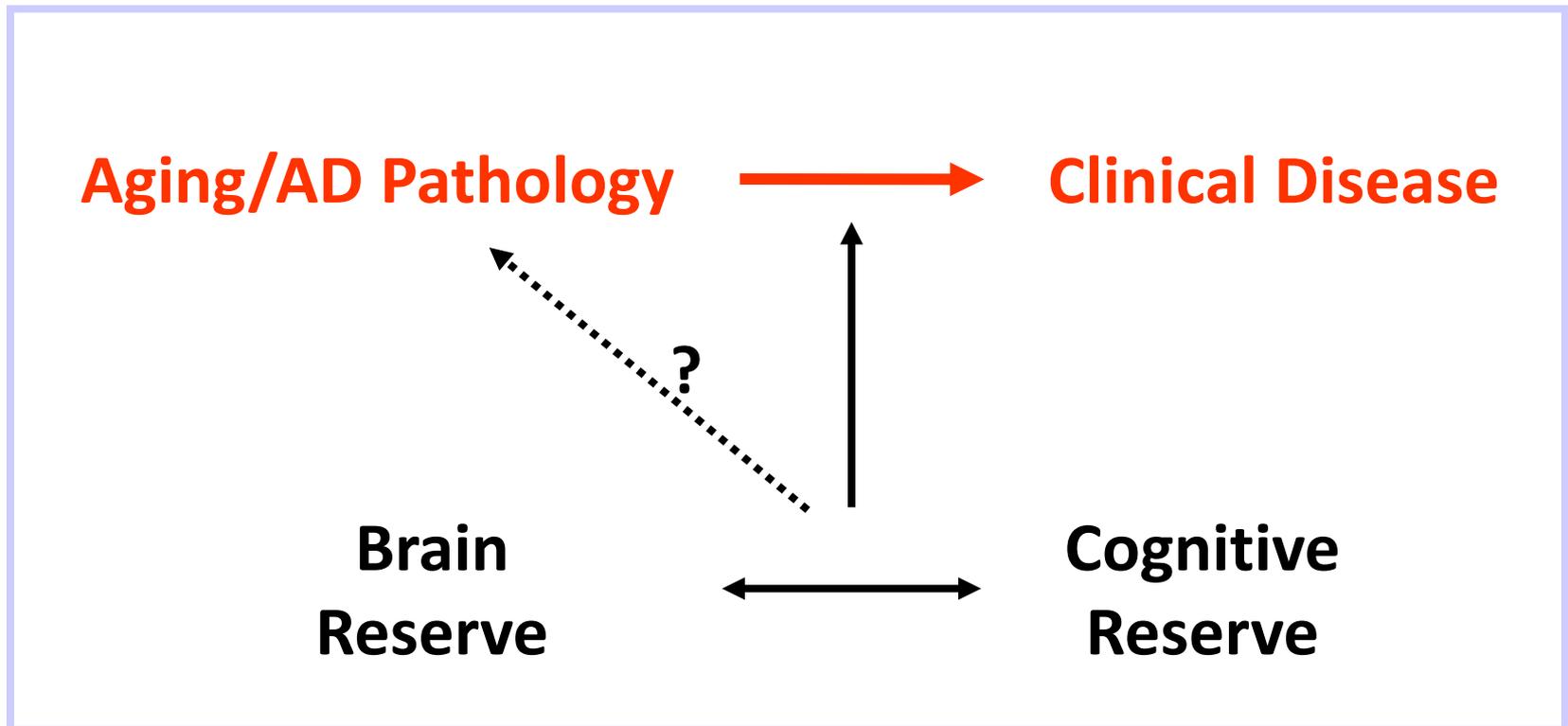
Volume
Cortical Thickness
WMH Burden
WM Tract integrity
Resting CBF
Resting connectivity
Amyloid burden

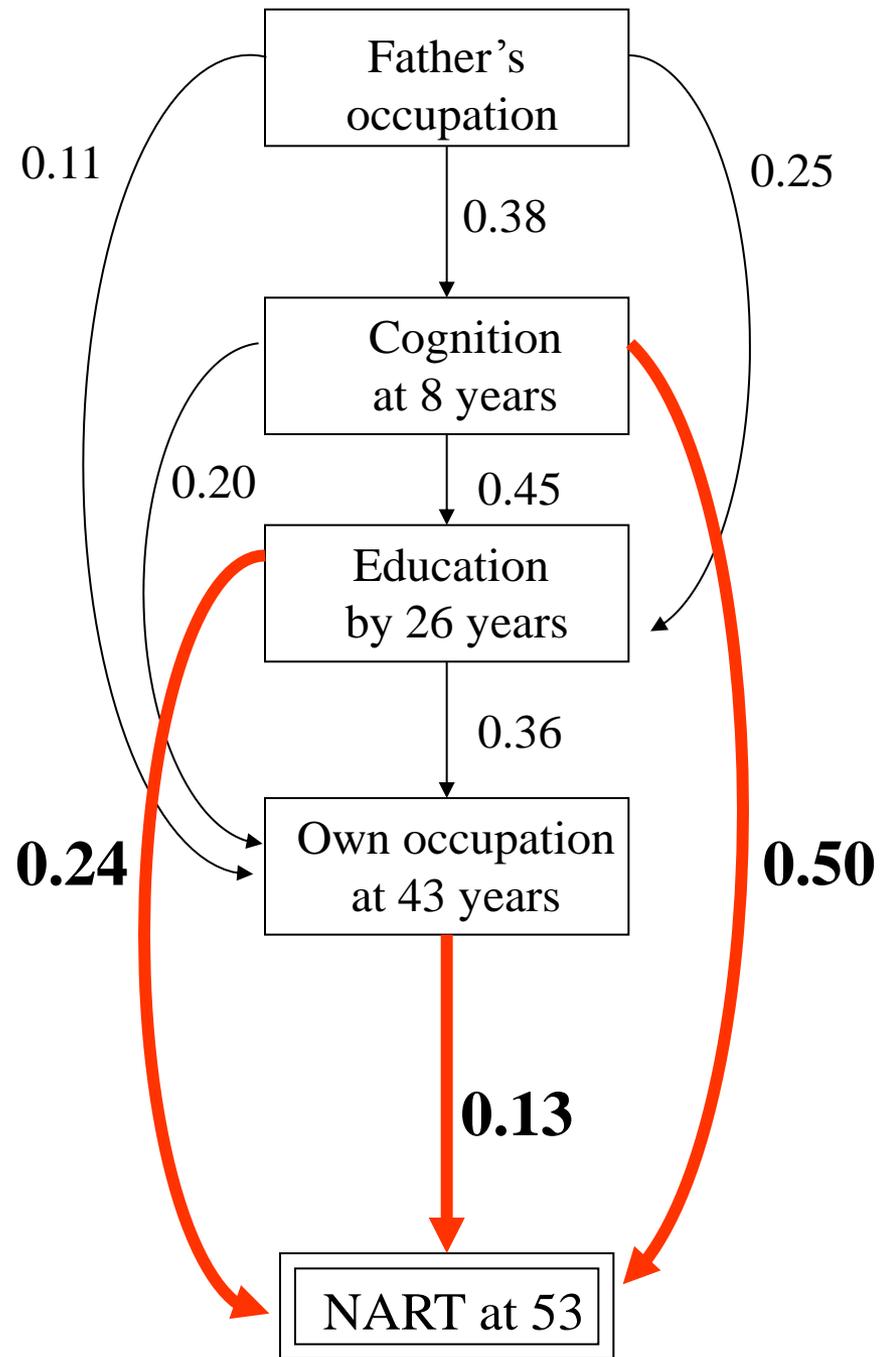


Activation Task Performance
Cognitive Domains
Function / ADL
Cognitive decline over time/
Incident MCI/AD

Measured IQ
Education/Literacy
Leisure Activity
CR Network

How Would Reserve-based Interventions Work?





Cochrane Review: Physical activity and enhanced fitness to improve cognitive function in older people without known cognitive impairment

Eight out of 11 studies reported that aerobic exercise interventions resulted in ... improvements in cognitive capacity.

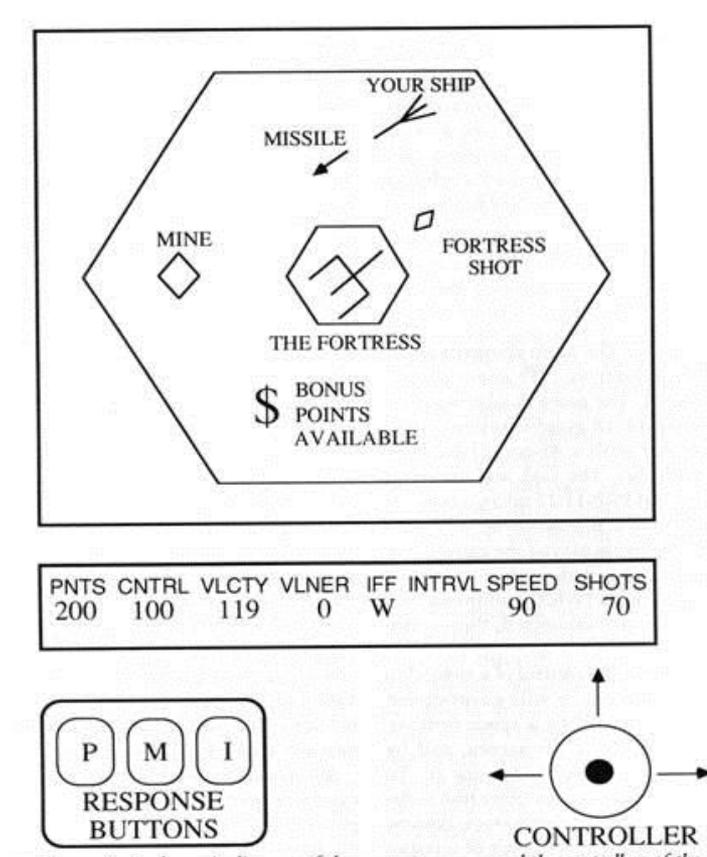
The largest effects on cognitive function were found on motor function and auditory attention (effect sizes of 1.17 and 0.50 respectively).

Moderate effects were observed for cognitive speed (effect size 0.26) and visual attention (effect size 0.26).

Problems With Cognitive Interventions to Date

- Small effect size
- Poor generalization to other cognitive domains
- Poor generalization day-to-day functions or IADLs
- Questionable sustainability of effects
- Relation to rate of aging or dementia onset not established

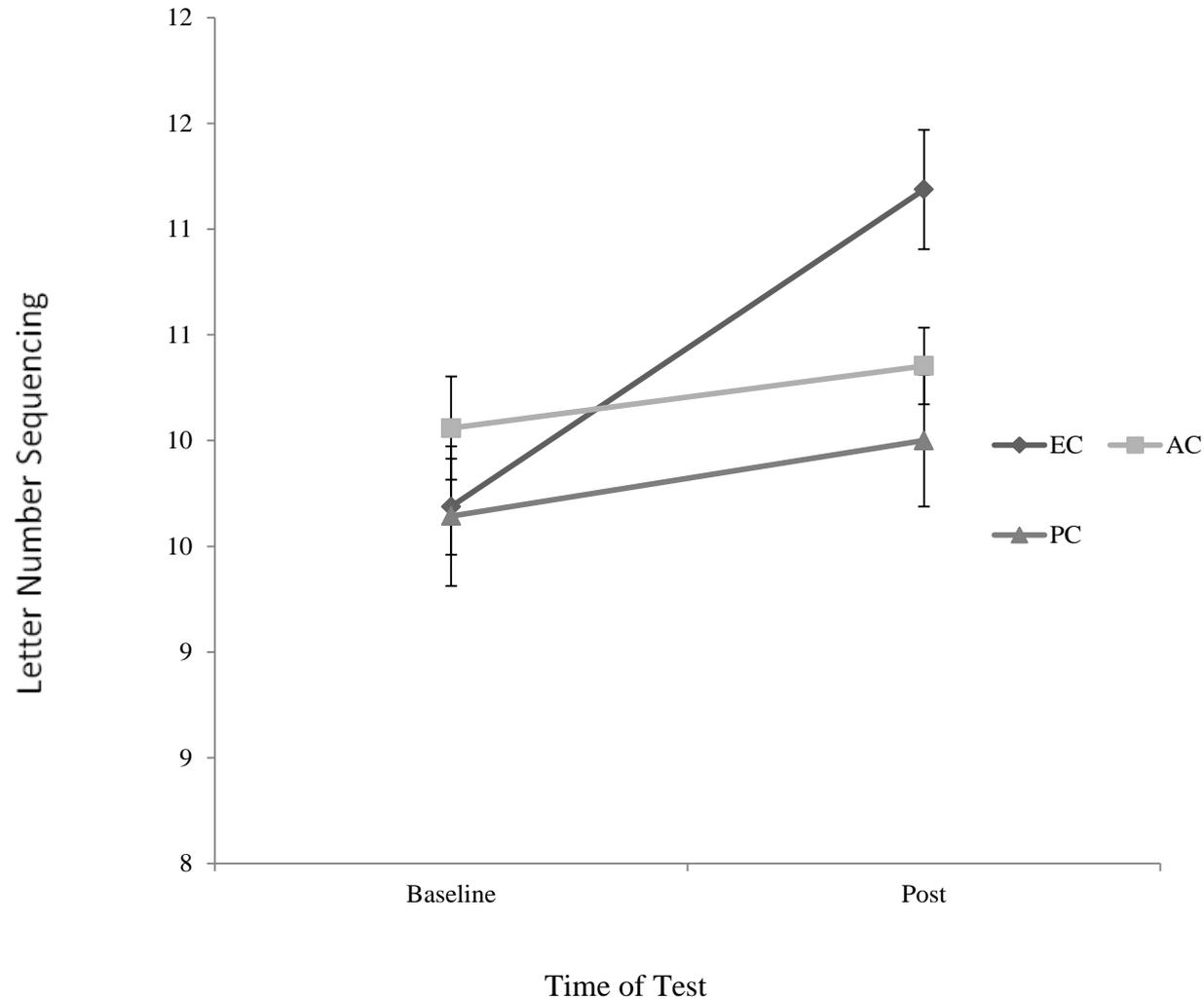
Space Fortress Intervention Study



The Space Fortress Game

- **Emphasis Change Training:**
 - Subjects perform the whole task during training, but are required to systematically change their emphasis on major sub-components of the task.
 - Encourages subjects to explore the response alternative space
 - Promotes executive control
 - Is associated with improved transfer of training
- Our study had 3 groups: 12 weeks of game play with and without emphasis change training, and a no gameplay control group

Space Fortress: Cognitive Outcome



Ongoing Intervention Trials

We have two ongoing intervention trials in healthy, cognitively intact individuals:

- Combined space fortress and aerobic exercise
 - Age 60-75
 - 3 conditions (N=30/condition): space fortress +aerobic exercise; SF + stretching/toning; computer games + S/T
 - 3 months with 12-month followup
- Long-term aerobic exercise
 - Ages 30-45 and 50-65 (N=130 for each)
 - 2 conditions: aerobic exercise vs. stretching/toning
 - 6 months with 12-month followup

What will the large-scale project to enhance CR look like?

- Healthy elderly population
- Intensive, extensive, combined interventions
- Long-term follow-up
- Outcomes:
 - Rapidity of cognitive/functional decline
 - Incident dementia

Conclusions

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