Interface between Normal Aging and Mild Cognitive Impairment

Diane Howieson, PhD

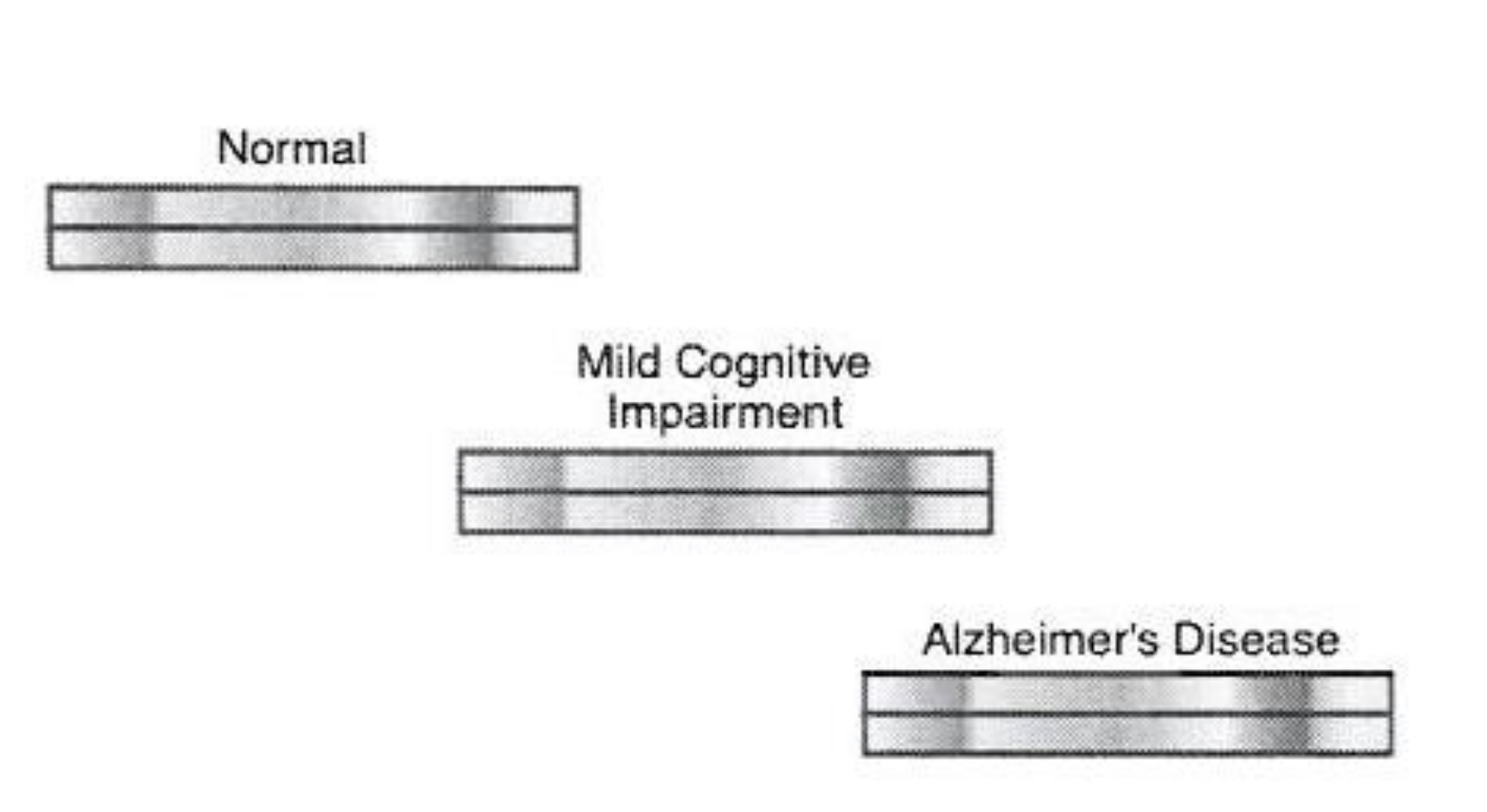
Neuropsychologist

Layton Aging and Alzheimer's Disease Center

Oregon Health & Science Center

Cognitive continuum showing the overlaps

Adapter from Petersen, 2004



Diagnostic criteria for dementia of the Alzheimer's type

- Development of multiple cognitive deficits manifested by both
  - 1) memory impairment
  - 2) one or more of the following cognitive disturbances: aphasia, apraxia, agnosia, or disturbance in executive functioning
- Cognitive deficits in (1) and (2) each cause significant impairment in social or occupational functioning and represent a decline from a previous level of functioning
- Gradual onset and progressive course

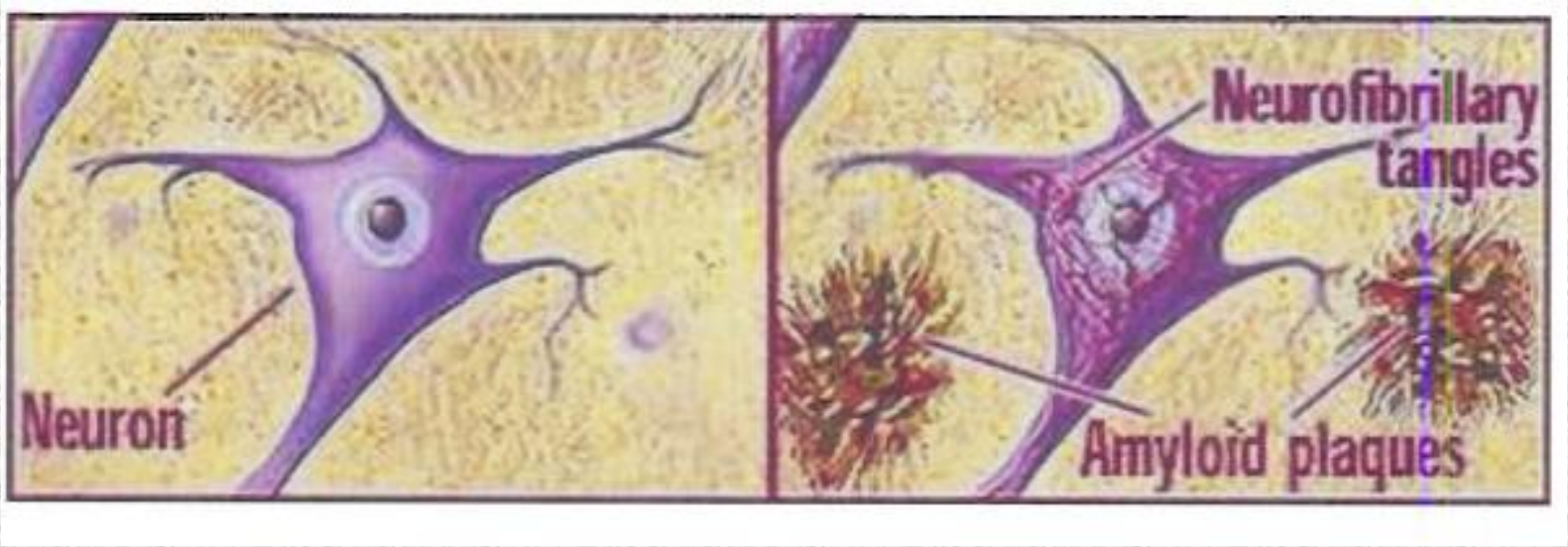
DSM-IV

Diagnostic criteria for MCI*

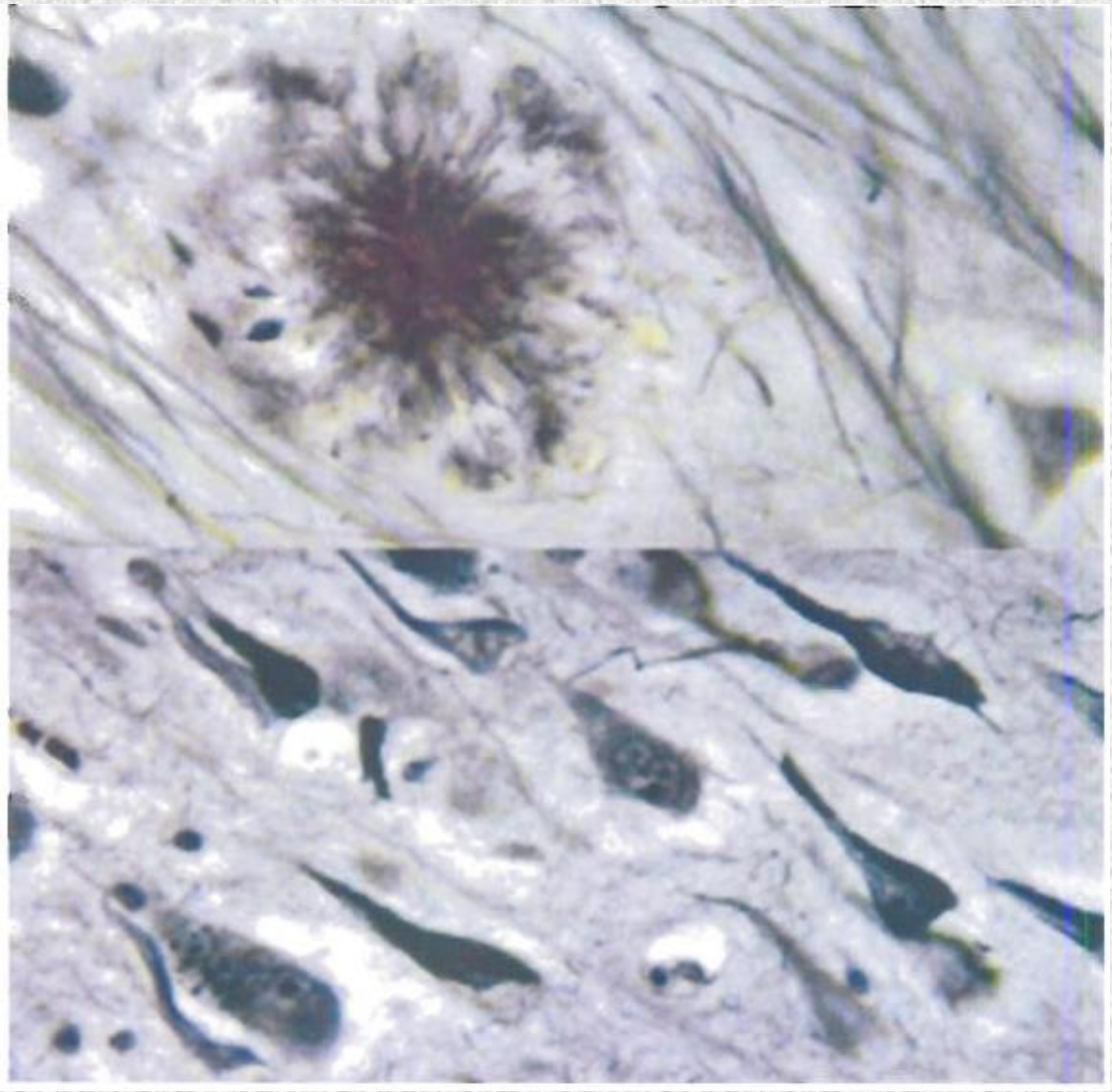
- Not cognitively normal for age
- Does not meet criteria for a dementia diagnosis
- Evidence of cognitive decline
  - Self and/or informant report a decline
  - **and** impairment on objective cognitive tasks
  - **and/or** decline over time on cognitive tasks
- Preserved basic activities of daily living/ minimal impairment in complex activities

*Minor neurocognitive disorder DSM-V

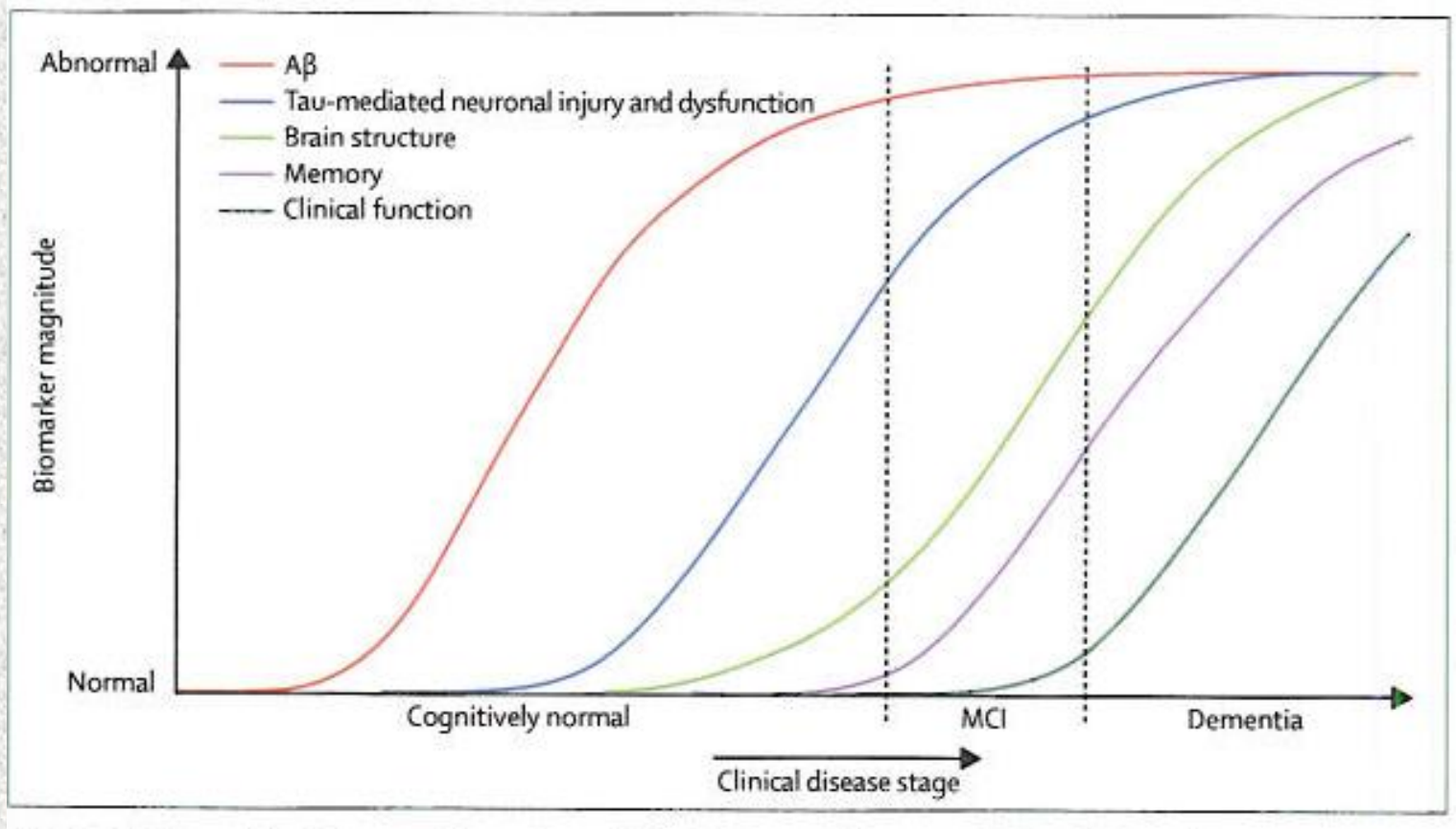
Winblad et al, J Int Med, 2004, 256, 240-246



Brain changes characteristic of Alzheimer’s disease

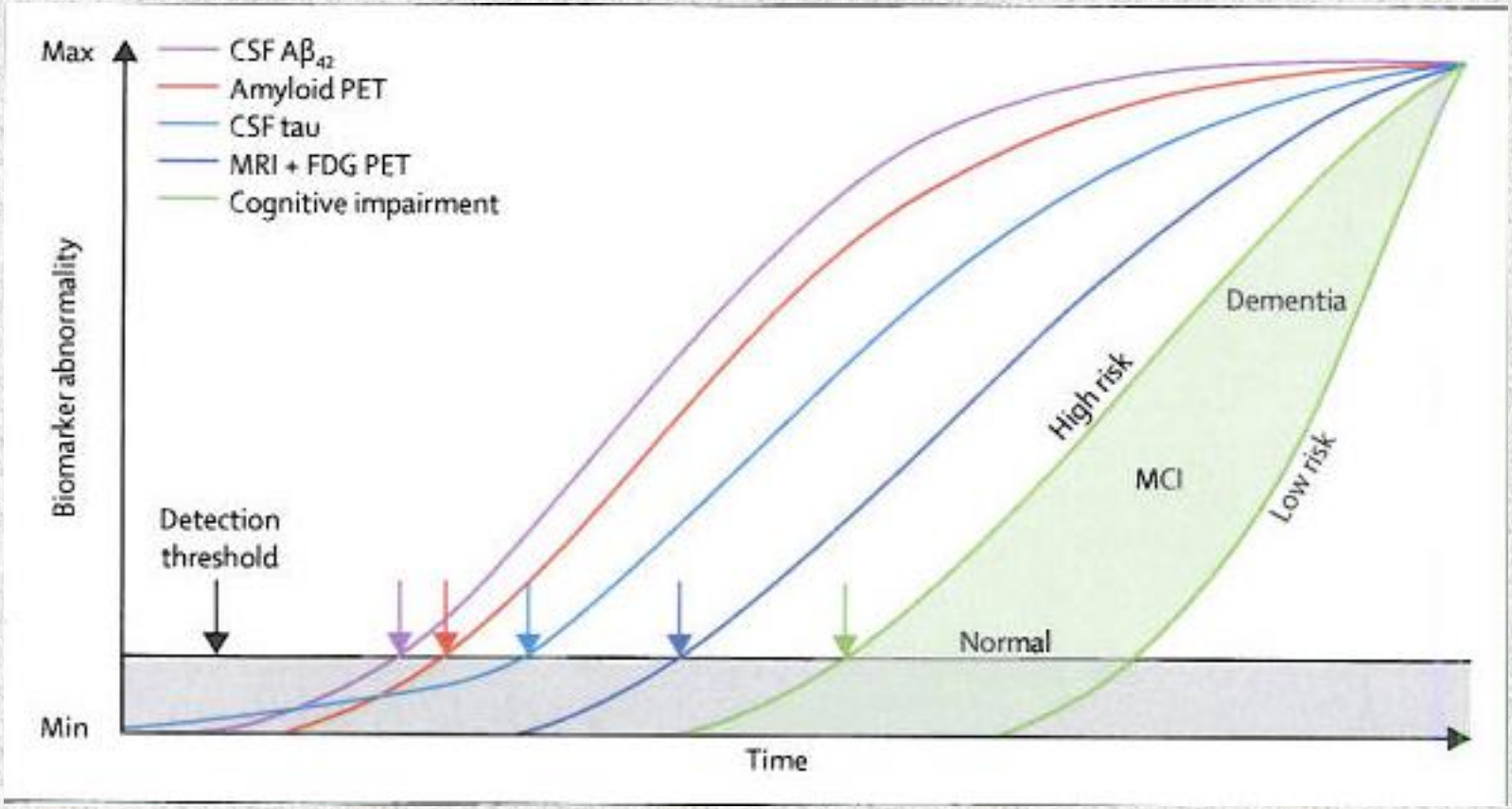


Plaque above and tangles below



2010 Model of dynamic biomarkers of the Alzheimer's disease pathological cascade

Jack Lancet Neurology, 2013



2013 Model of temporal order of Alzheimer's disease biomarkers

Jack Lancet Neurology, 2013

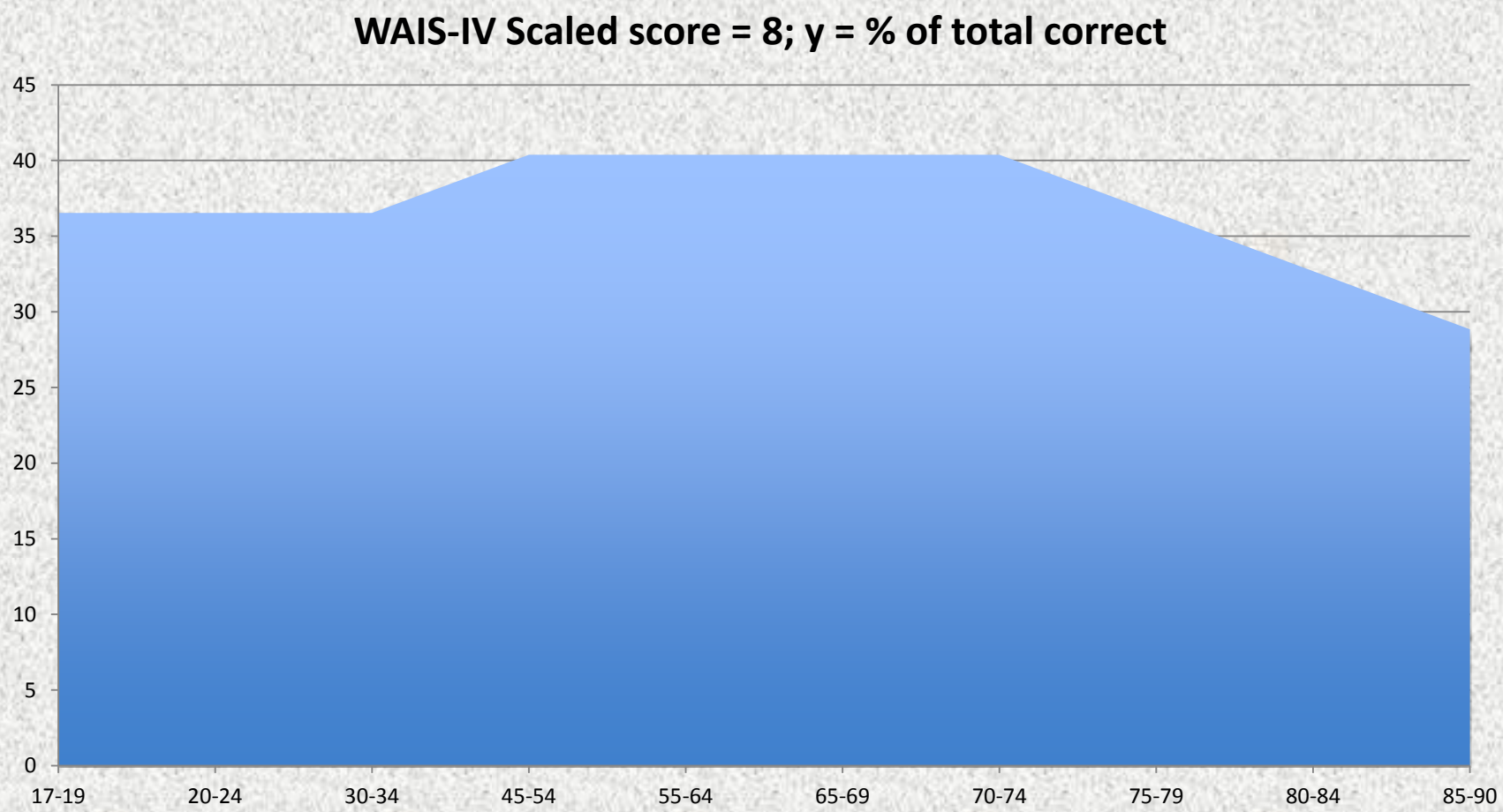
What are age-related changes in cognition?

What is causing these changes?

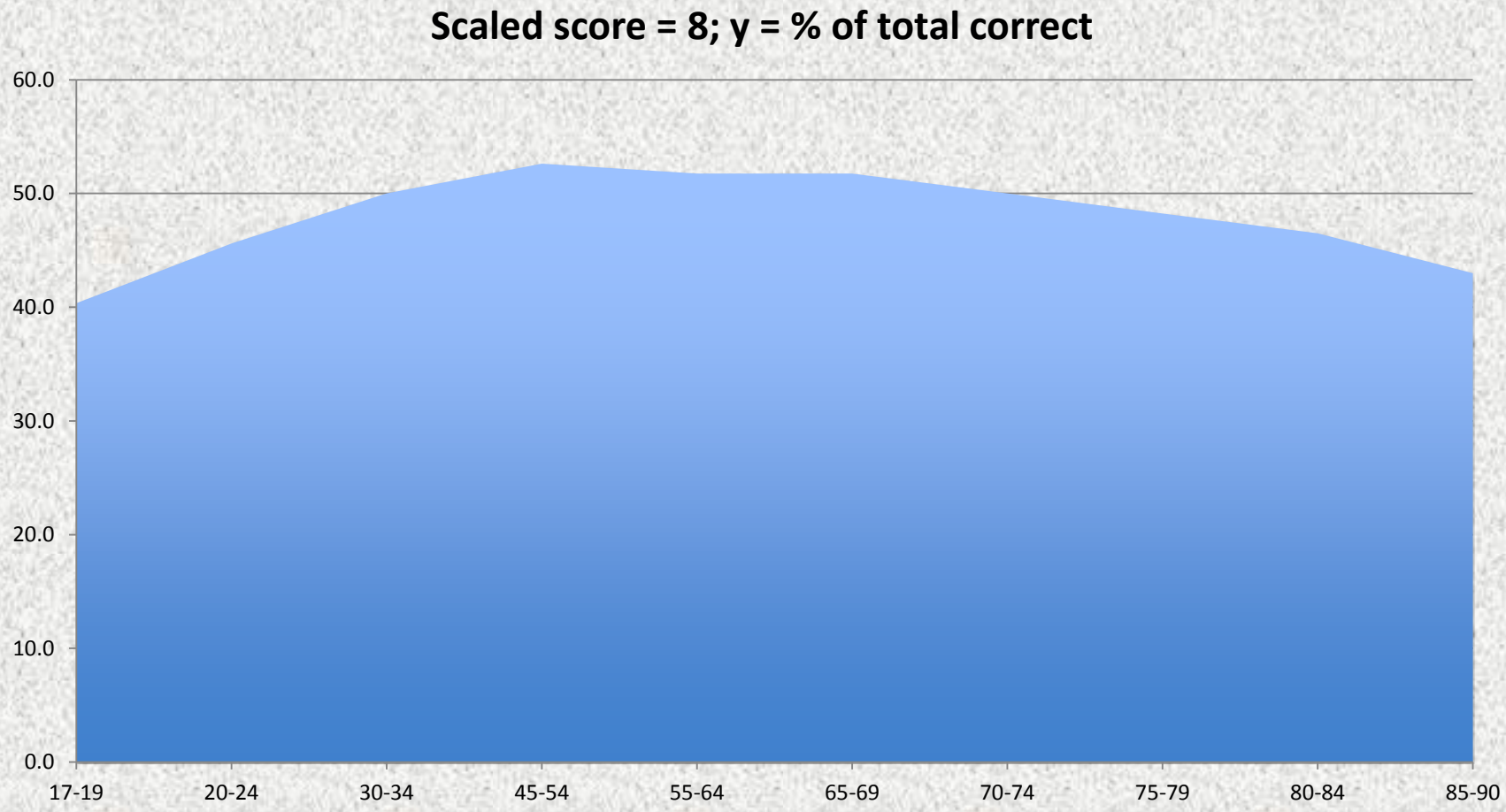
Cognitive functions that show little change with age

"Hold" tests or "crystallized intelligence"

Information performance at 25th percentile by age



Vocabulary performance at 25th percentile by age

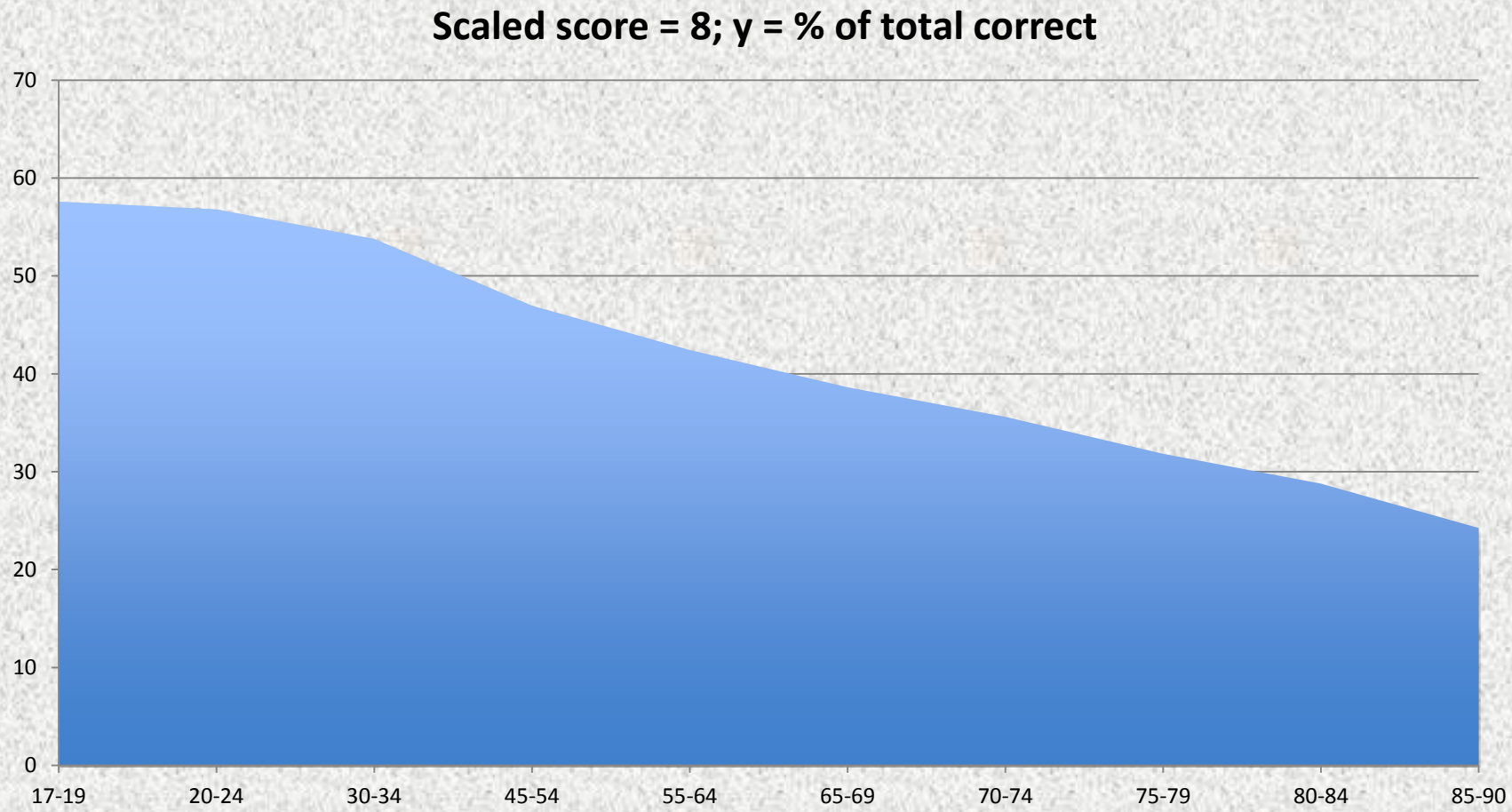


Cognitive functions that decline with advanced age

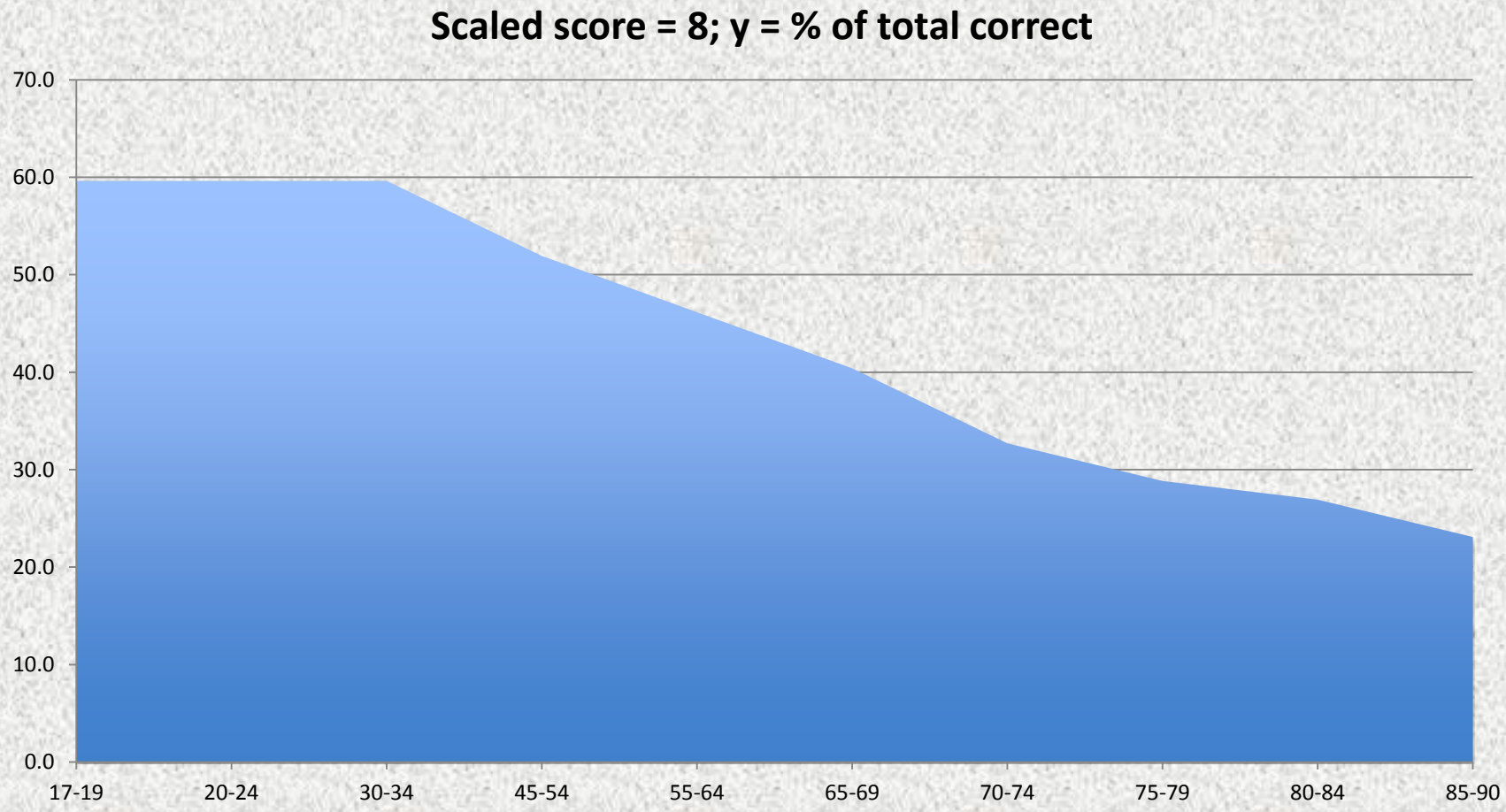
"Fluid intelligence"

Processing speed

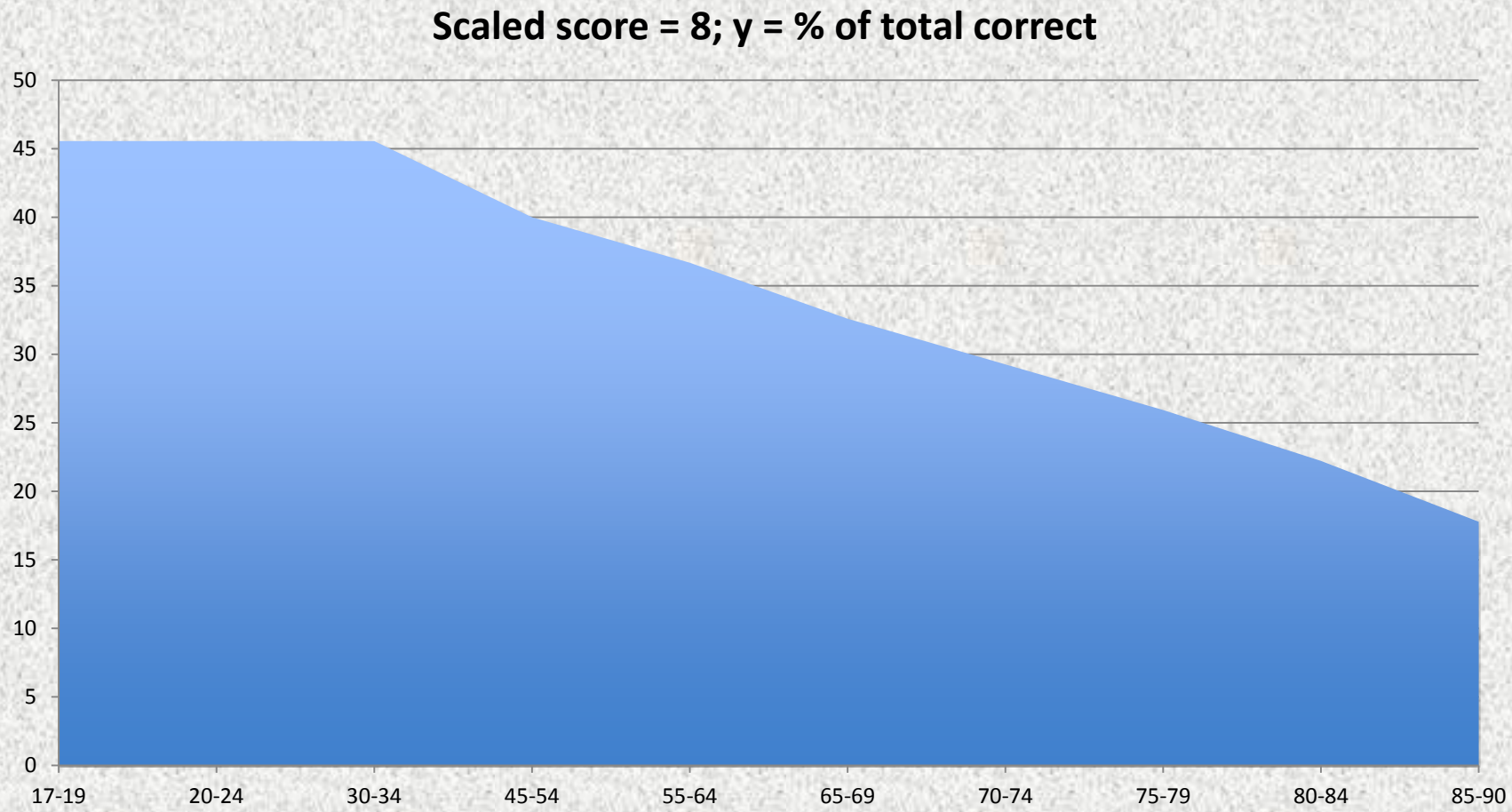
Block Design performance at 25th percentile by age



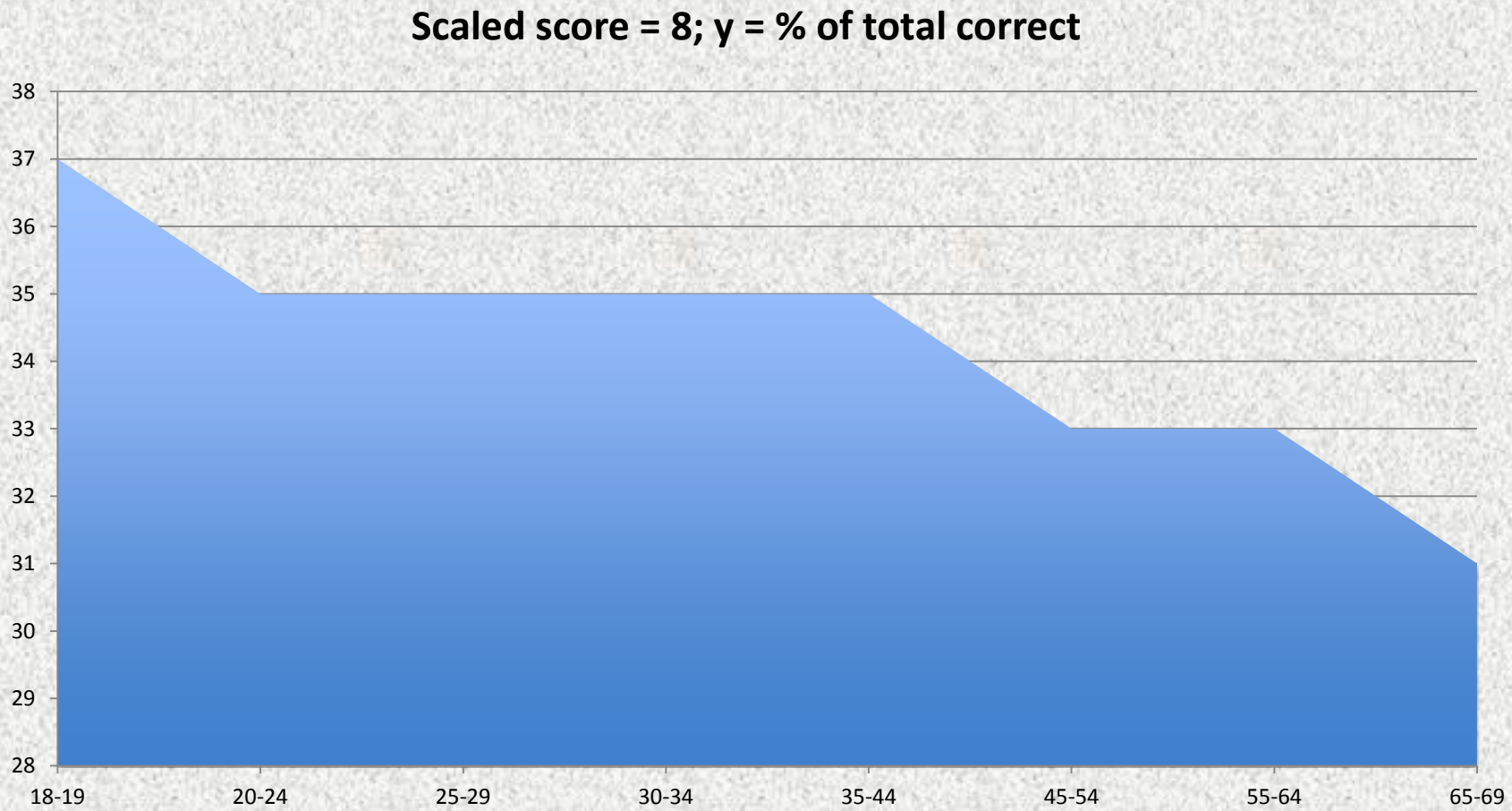
Matrix Reasoning performance at 25th percentile by age



Coding performance at 25th percentile by age



Logical Memory II performance at 25th percentile by age



Factors affecting individual differences

- Genetics
- Experience
- Cognitive reserve
- Health and brain disease

Genetic influence

- In twin studies of elders, heritability estimated at:
  - .60 for verbal abilities
  - .50 for spatial abilities and speed
  - .40 for memory

Plomin et al., Behav Genet, 1994, 24, 207-215

- More than 50 genes have been implicated.

•Payton, Neuropsychol Rev, 2009, 19, 451-477

Experience

- Early childhood experiences
- Education and occupation

- Le Carret et al., Dev Neuropsychol, 2003, 23, 317-337

Cognitive reserve

The ability to perform cognitive tasks effectively despite brain injury or disruption.

Stern, JINS, 2002, 8, 448-460

May operate through additional synapses or recruitment of redundant or alternative brain networks.

Influenced by genetics and experience

Health

- Systemic illness
  - E.g., thyroid, anemia, infections

    Spiro III, A. and Brady, CB. J Gerontol B Psychol Sci Soc Sci, 2011, 66B(S1), i17-25
- Cerebrovascular risk factors
  - diabetes, hypertension, hypercholestremia, smoking
- Drugs and alcohol
- Mood

  Kook et al., J Affect Disord, 2012, Jul 25

Health cont'd

- Exercise

  Sofi et al., J Internal Med, 2010, 269, 107-117

- Nutrition

  Bowman et al., Neurology, 2012, 78, 241-249

- Social activity

  James et al., JINS, 2011, 17, 998-1005

Brain changes with aging

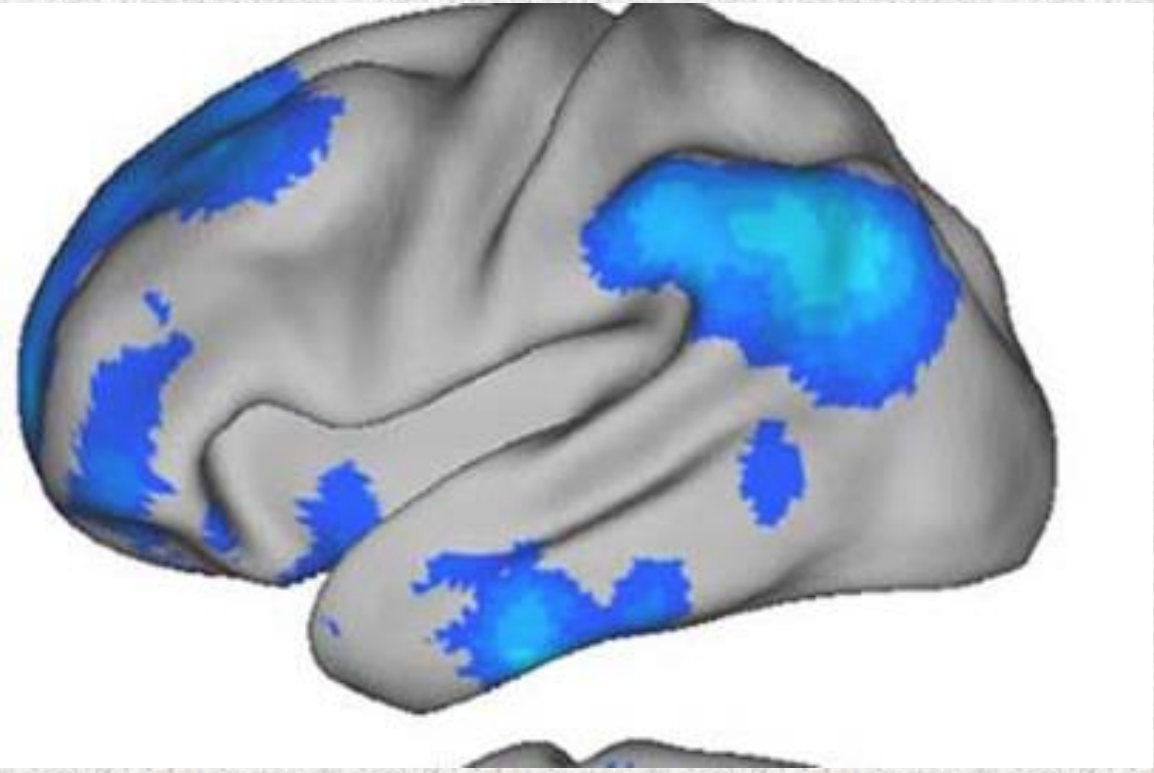
- Structures
  - Brain's volume at peak in early 20s
  - Atrophy prefrontal > temporal > parietal = occipital

    Raz and Rodrigue, Neurosci Biobeh Rev, 2006, 30, 730-748
  - White matter deterioration

    Johansen-Berg , Curr Opin Neurol, 2010, 23, 351-358
- Distributed networks
  - Alterations in connectivity of distributed neural systems

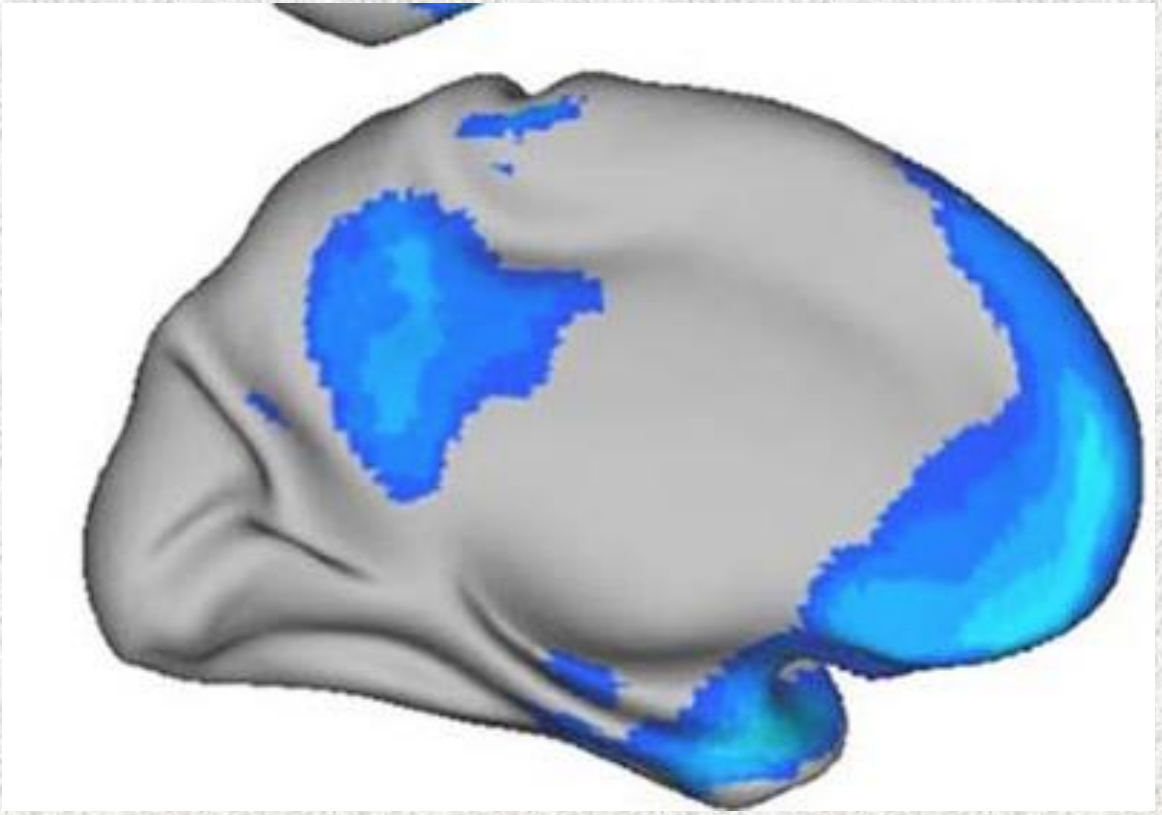
    Ystad et al., Neuroimage, 2011, 55, 24-31

    Seeley et al., Neuron, 2009, 62, 42-52



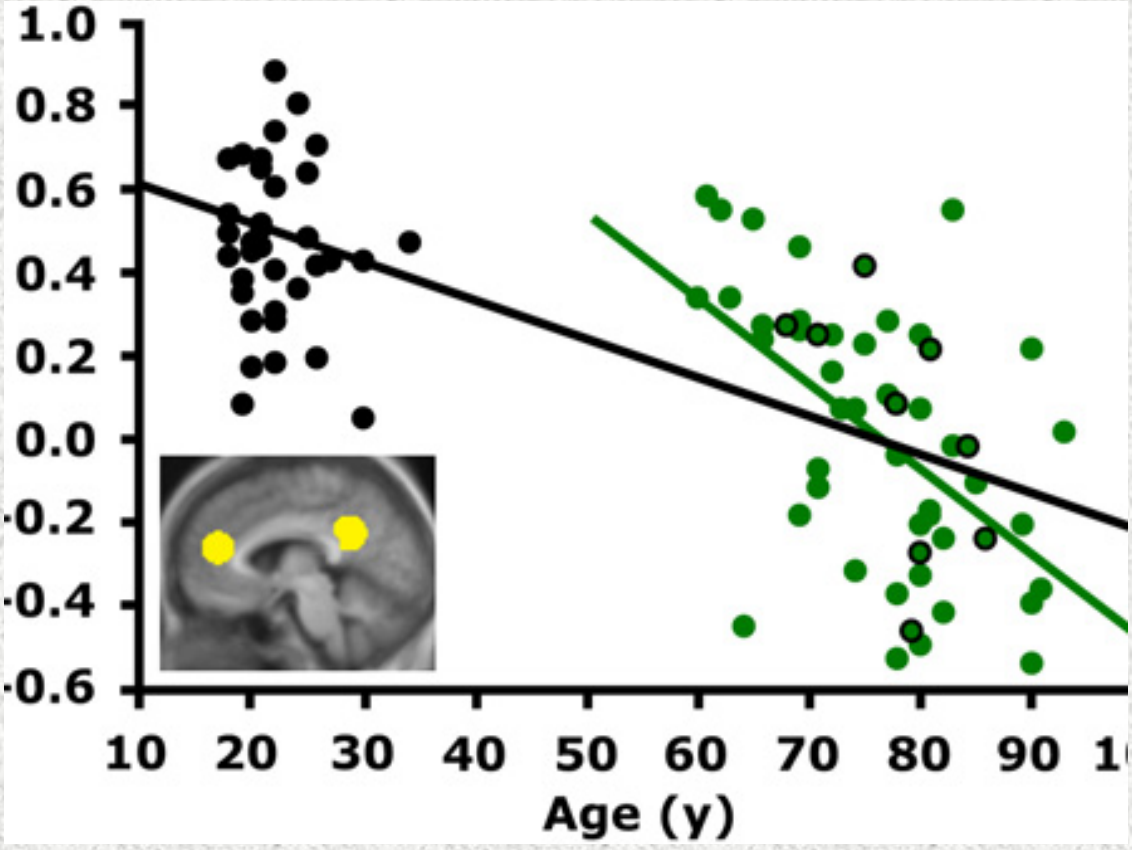
Default network, lateral view

Buckner et al., 2008, Ann NY Acad Sci, 1124, 1-38



Default network, medial view

Buckner et al., 2008, Ann NY Acad Sci, 1124, 1-38



Default network. Anterior correlations to posterior functional correlations are markedly reduced in advanced aging.

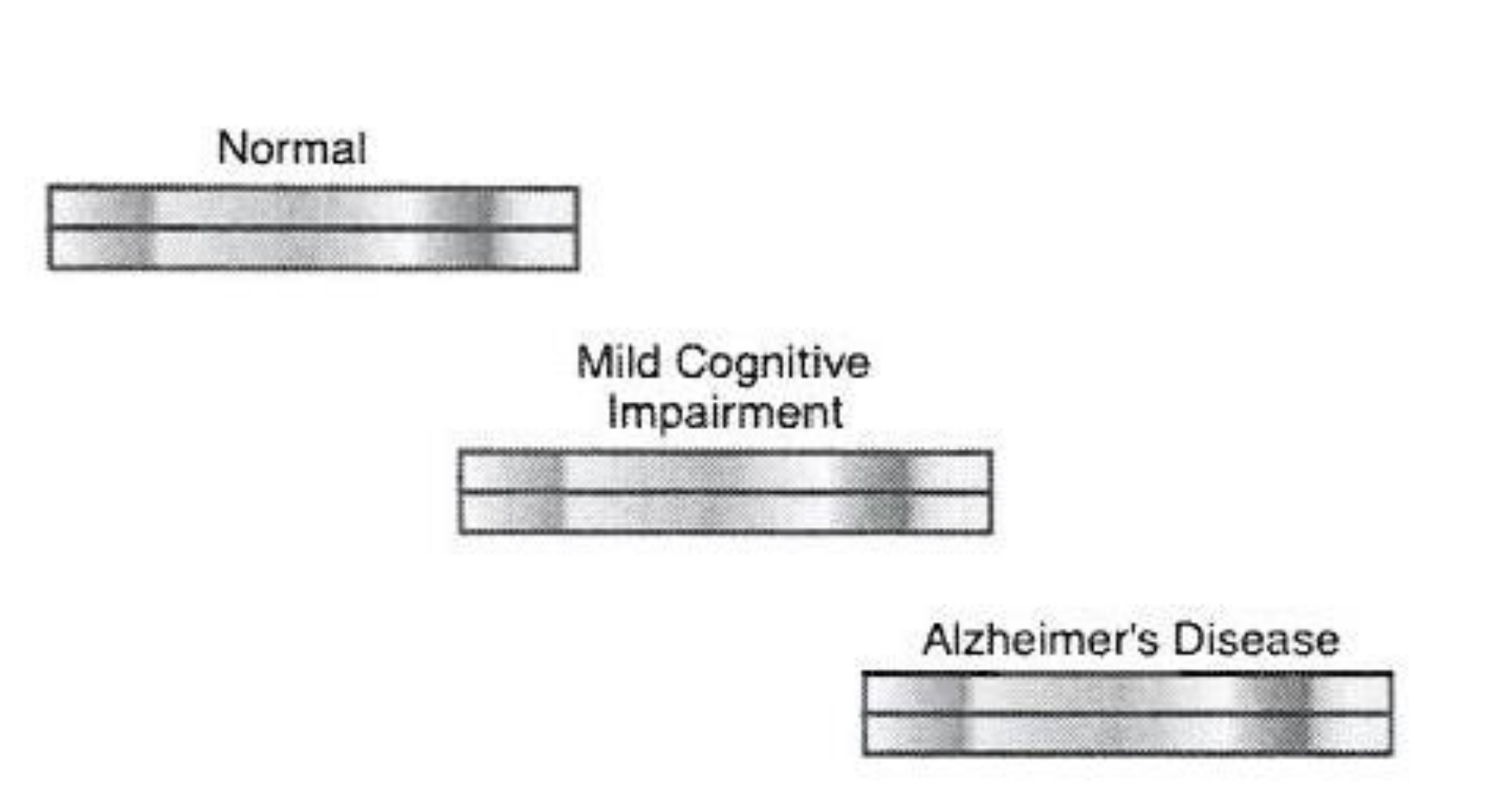
Y axis is temporal correlation between medial prefrontal cortex and posterior cingulate/retrosplenial cortex.

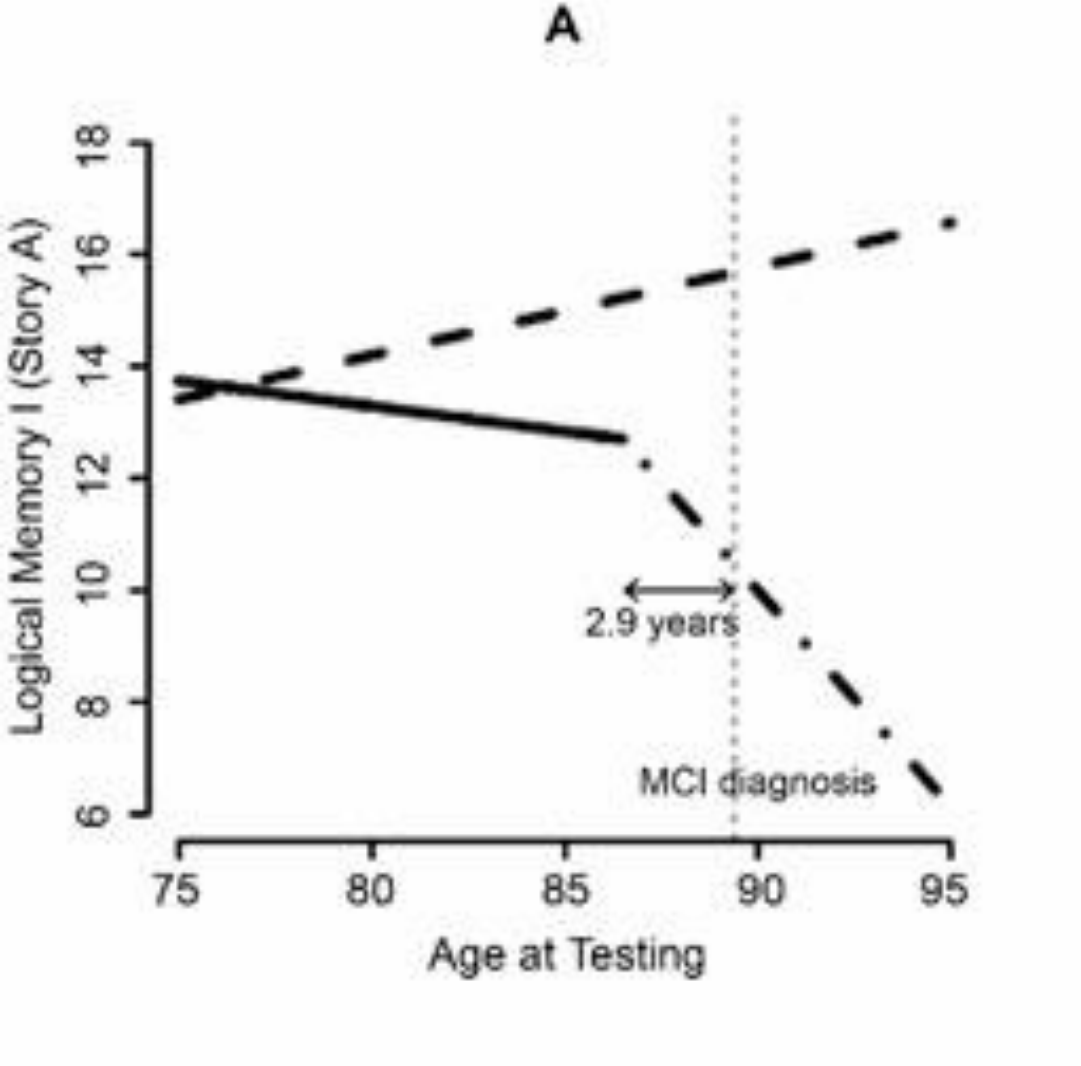
Black = young adults. Green = older adults.

Andrews-Hanna et al., 2007, Neuron, 56, 2924-935

Cognitive continuum showing the overlaps

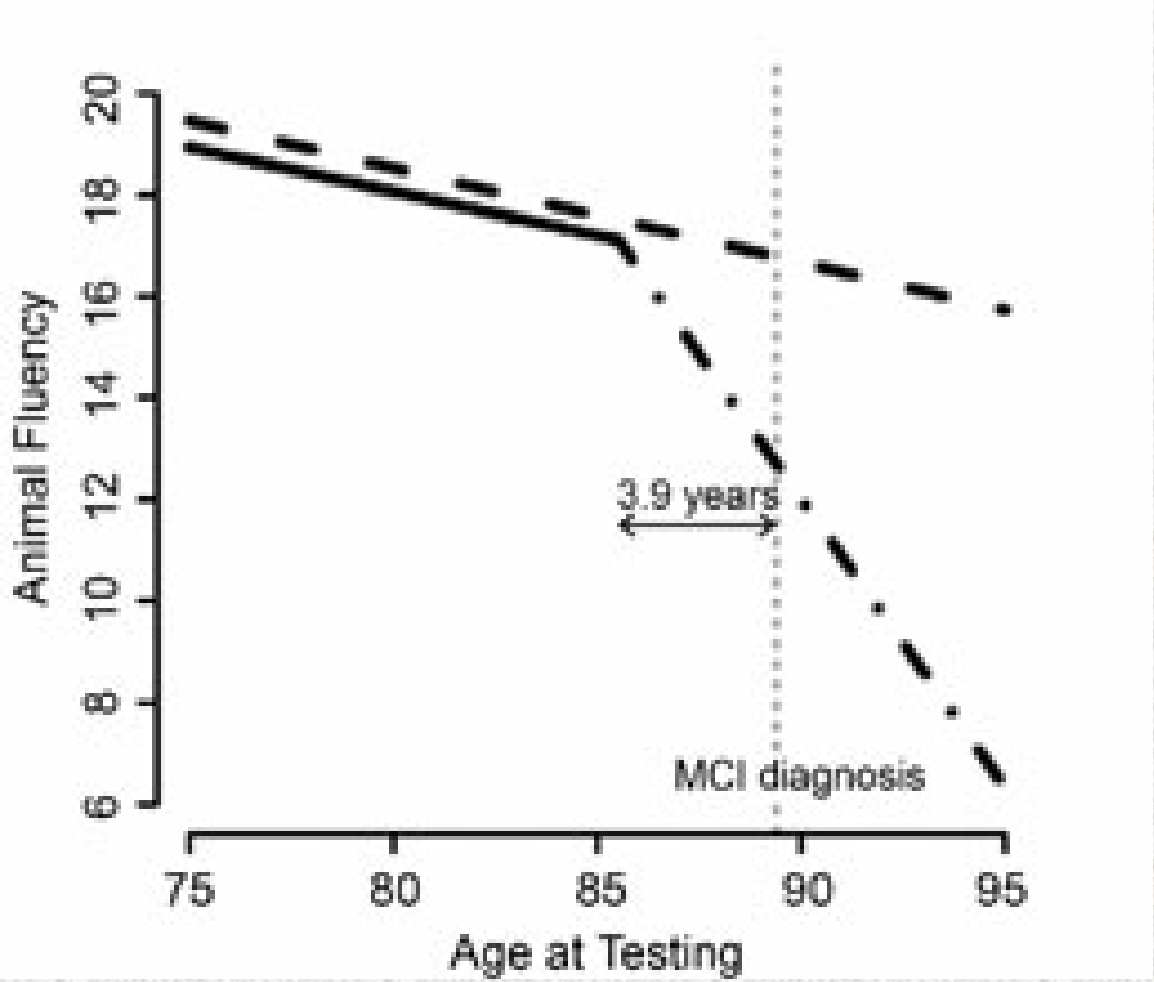
Adapter from Petersen, 2004





Logical Memory and Pre-MCI

Howieson et al., JINS 2008



Animal Fluency and Pre-MCI

Howieson et al., JINS 2008

Cognitive impairment in MCI

Deficit	**%**
Memory only	30
Memory and visuospatial	14
Memory and executive	7
Memory, visuospatial, and executive	10
Visuospatial only	11
Executive only	19
Visuospatial and executive	9

"This illustrates that AD need not begin as a memory problem." Storandt et al, Neurol, 2006, 67, 467-473

Risk Factors for MCI

- Age
- APOE4 allele
- Lower educational level
  - » Manly et al, Arch Neurol, 2005, 62, 1739-46
- Midlife elevated serum cholesterol level
  - » Kivipelto et al, Neurology, 2001, 56, 1683-9
- Vascular disease
- Depression

Conclusions about prognosis of MCI

- Prevalence in the general elderly population is 3 – 19%.
- The risk of developing dementia is 11- 33% over two years.
- A sizable proportion (e.g., 44%) of patients with MCI returned to normal a year later.

» Ritchie, Dialogues Clin Neurosci, 2004, 6, 401-08

Conditions affecting prognosis from MCI

- Age
- How long MCI has existed
- Whether amnestic MCI or other subtype of MCI
- APOE allele (2 or 3 vs. 4)
- Vascular risk factors
- Hippocampal atrophy

Problem identifying MCI

- A low score on a test may be normal for that individual: 26% of healthy adults have 1 or 2 scores 1 SD below mean on the WAIS-III/WMS-III battery.

  Binder et al., Arch Clin Neuropsychol, 2009

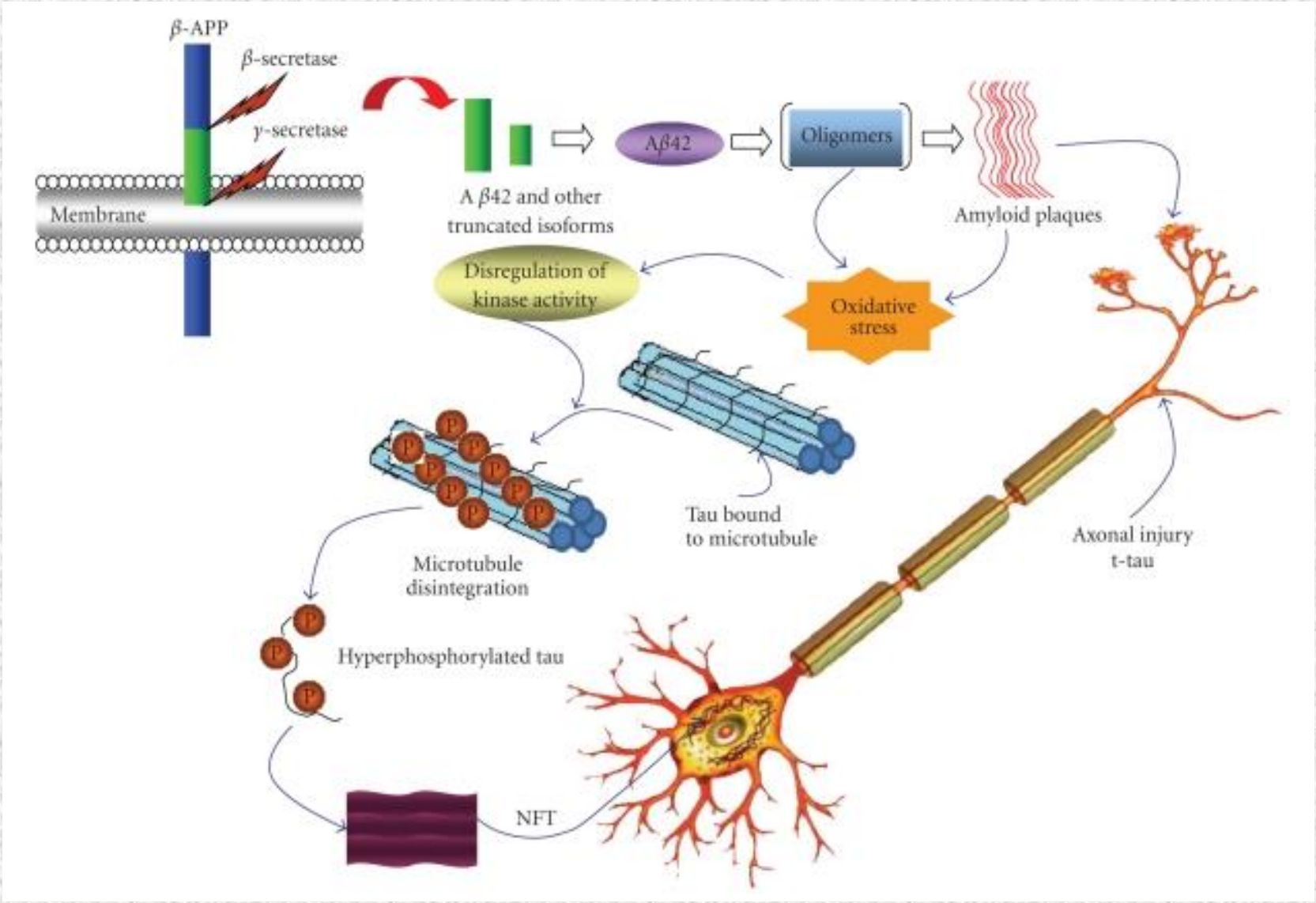
- For some people average scores represent a decline from a previous higher level of functioning.

Recommendations for diagnosis

- Take a careful history including premorbid cognition, lifestyle, and vascular risk factors.
- Get detailed functional information from an informant.
- Assess for depression, medication side-effects, alcohol abuse, etc.
- Use the best age- and education-corrected norms available.
- Try to assess the individual at two time points.

Clinical recommendations

- Elders and MCI patients should keep physically and cognitively active.
- They should reduce vascular risk factors as much as possible.
- MCI patients may benefit cognitive-behavioral treatment to improve daily functioning. More studies are needed.



AD pathological cascade

Anoop et al., Int J Alzheimer Dis. 2010