Alzheimer Disease

Conflict of Interest Disclosure

- Consultant for: Western RHA, Norman RHA, Winnipeg RHA
- Speaker for: Pfizer, Alzheimer Society of MB, WRHA
- Received grant/research support from: no one
- Received honoraria from: Pfizer, NOW CMHA

Objectives

- 1. The attendees will be able to describe the ways that dementia is more than memory impairment.
- 2. The attendee will be able to describe the importance of early diagnosis and their roles and responsibilities in medicolegal issues such as Powers of Attorney and Driver Vehicle Licensing.
- 3. The attendees will be able to understand when to start a cognitive enhancer and how to monitor it's use.

President 1981 – 1989
Diagnosed 1994

I have recently been told that I am one of the millions of Americans who will be afflicted with Alzheimer's.

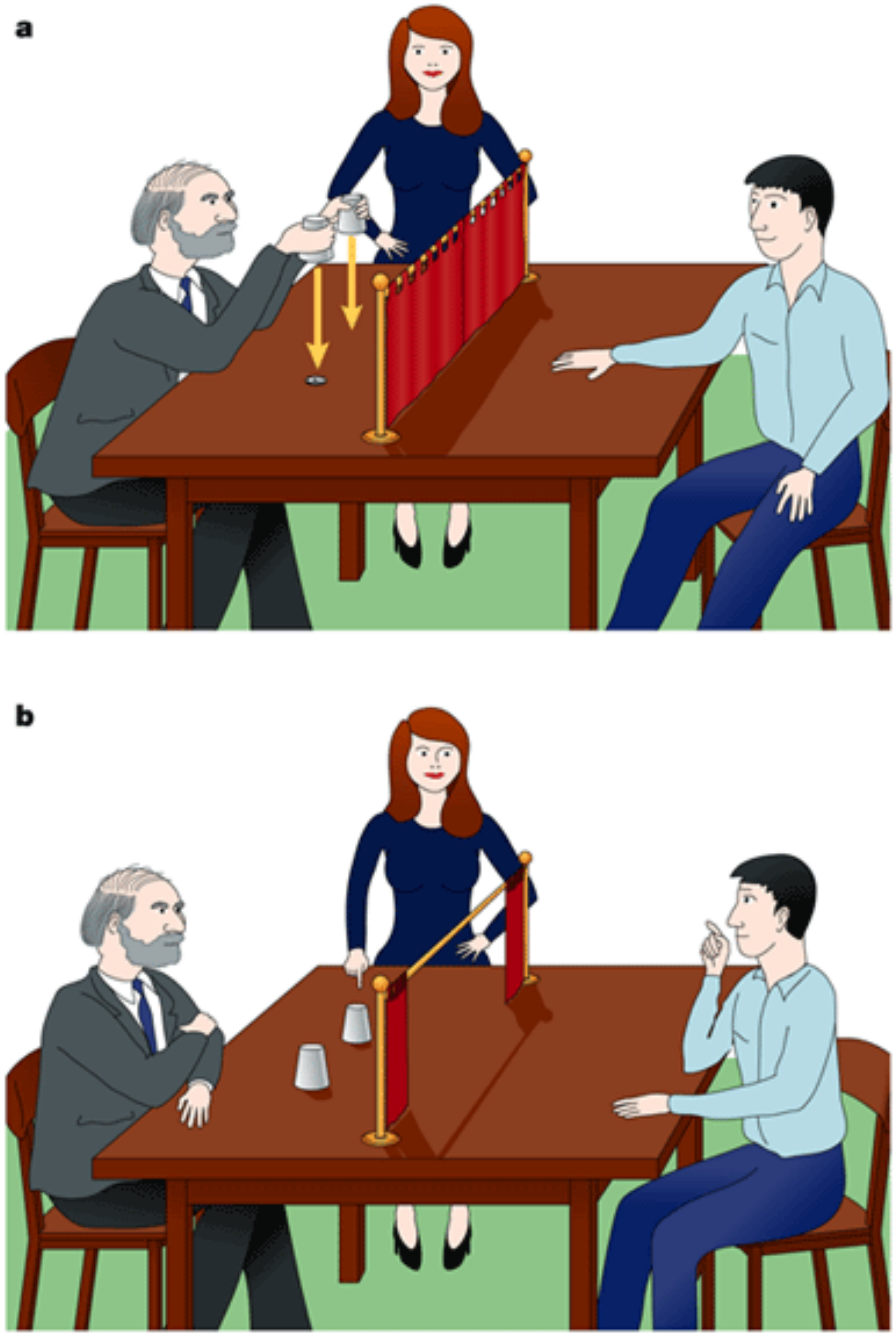
At the moment I feel just fine. I intend to live the remainder of the years God gives me on this earth doing the things I have always done. I will continue to share life's journey with my beloved Nancy and my family. I plan to enjoy the great outdoors and stay in touch with my friends and supporters.

Unfortunately, as Alzheimer's disease progresses, the family often bears a heavy burden. I only wish there was some way I could spare Nancy from this painful experience. When the time comes, I am confident that with your help she will face it with faith and courage.

Born 1911- Died 2004

Response Inhibition

- **RED BLUE YELLOW**
- **XXXX XXXX XXXX**
- **RED BLUE YELLOW**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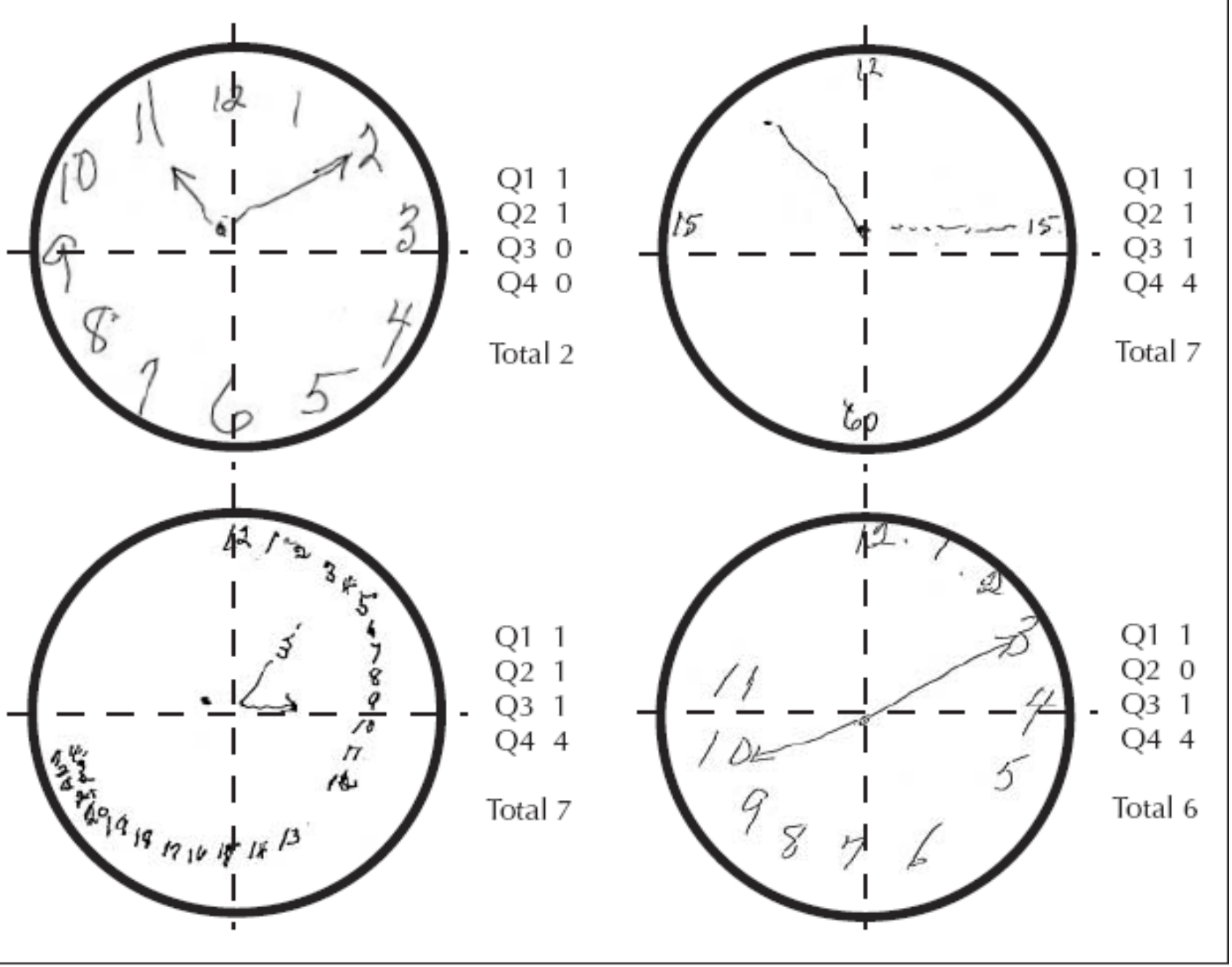
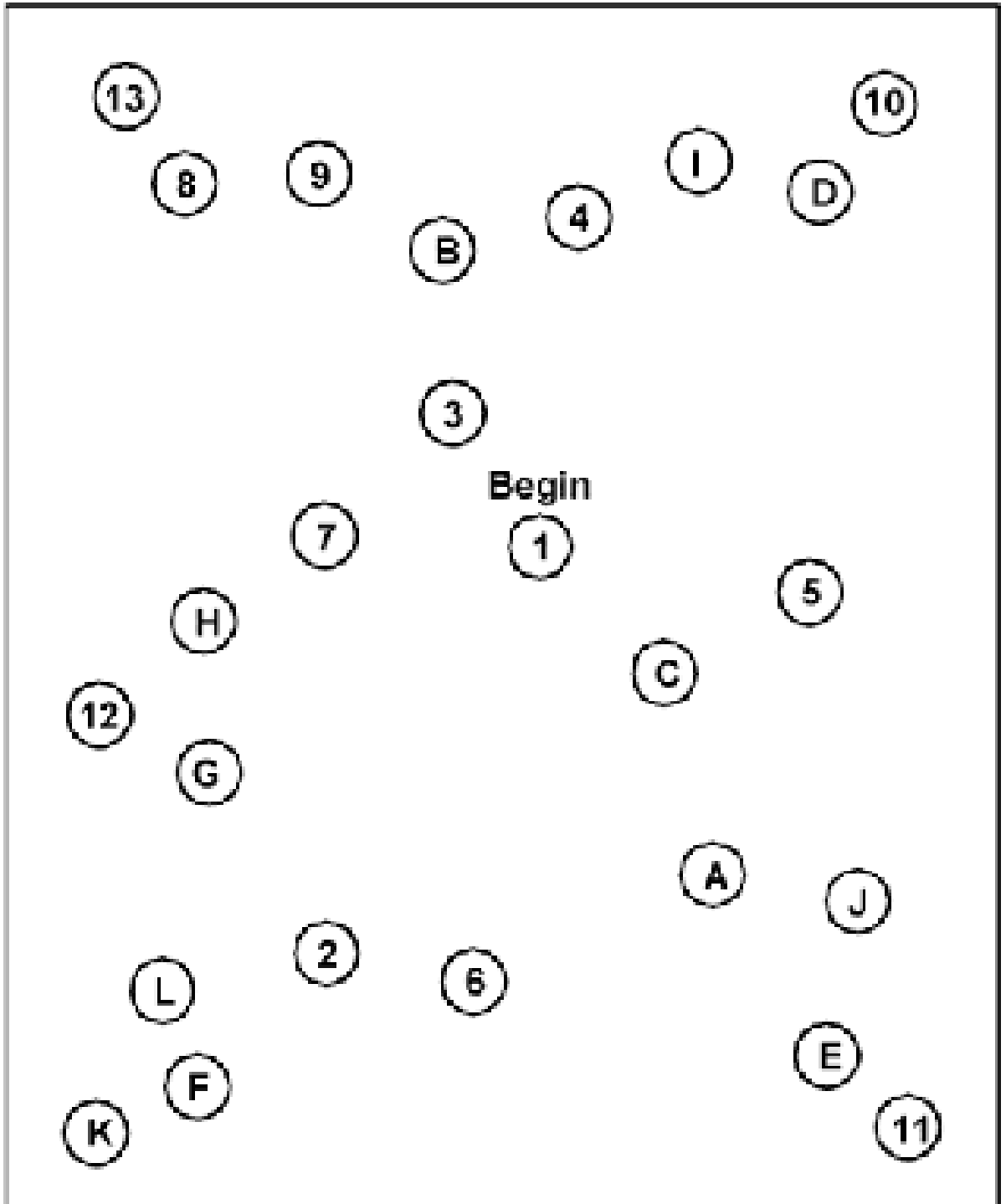


Normal 3 or less


13
10
8
9
I
D
4
B
3
Begin
7
1
5
H
C
12
G
A
J
2
6
L
E
F
K
11

Trails B

Age	Time in seconds
18-24	49
25-34	51
35-44	58
45-54	64
85-89	141

100 metres

Usain Bolt 23yo	9.58 (200m 19.19s)
70-74	14.4
90-94	18.08
95-99	22.04

9.58/22.04 = 0.43

49/141 = 0.35

- Heterogeneity increases with age (eg Trails B SD at age 24 is 13 and at age 84 is 65)

Dementia

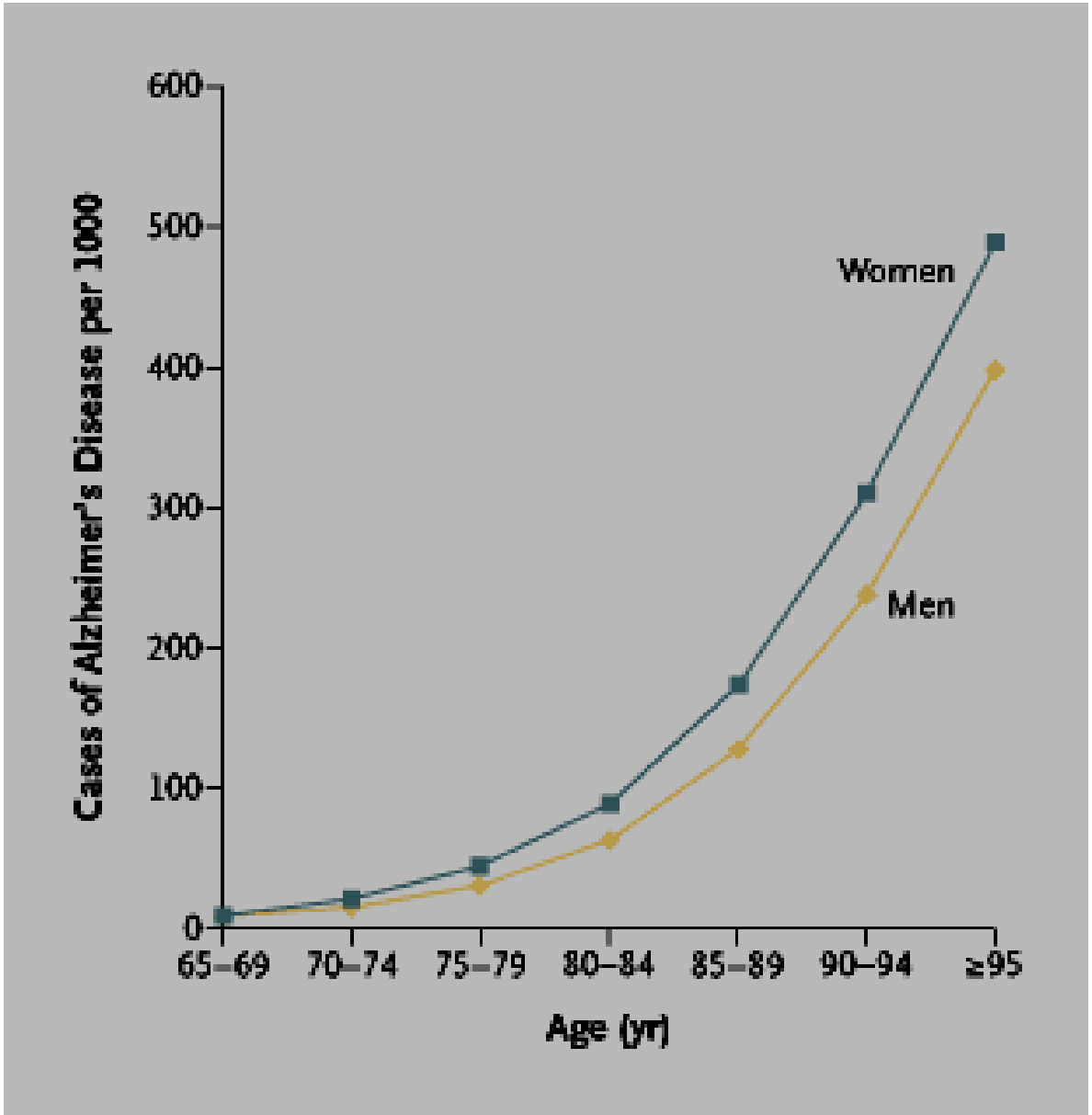
- Most feared disease of seniors and families.
- “Old” is defined not by age but by decreased function/dependence on others (usually driven by dementia)
- Cost estimates to the system are $5.5 billion per year now in Canada ($140 billion US)
- “Stresses” health care “pseudo-system” collaboration/integration at all seams

The Rising Tide

- Alzheimer Society of Canada – Jan. 2010
- Incidence 103,728 new cases per year in 2008 (257,811 by 2038)
- Prevalance of 480,618 people in 2008 (1,125,184 people by 2038)

- Delay onset by 2 years would decrease the prevalence by over 400,000 people by 2038

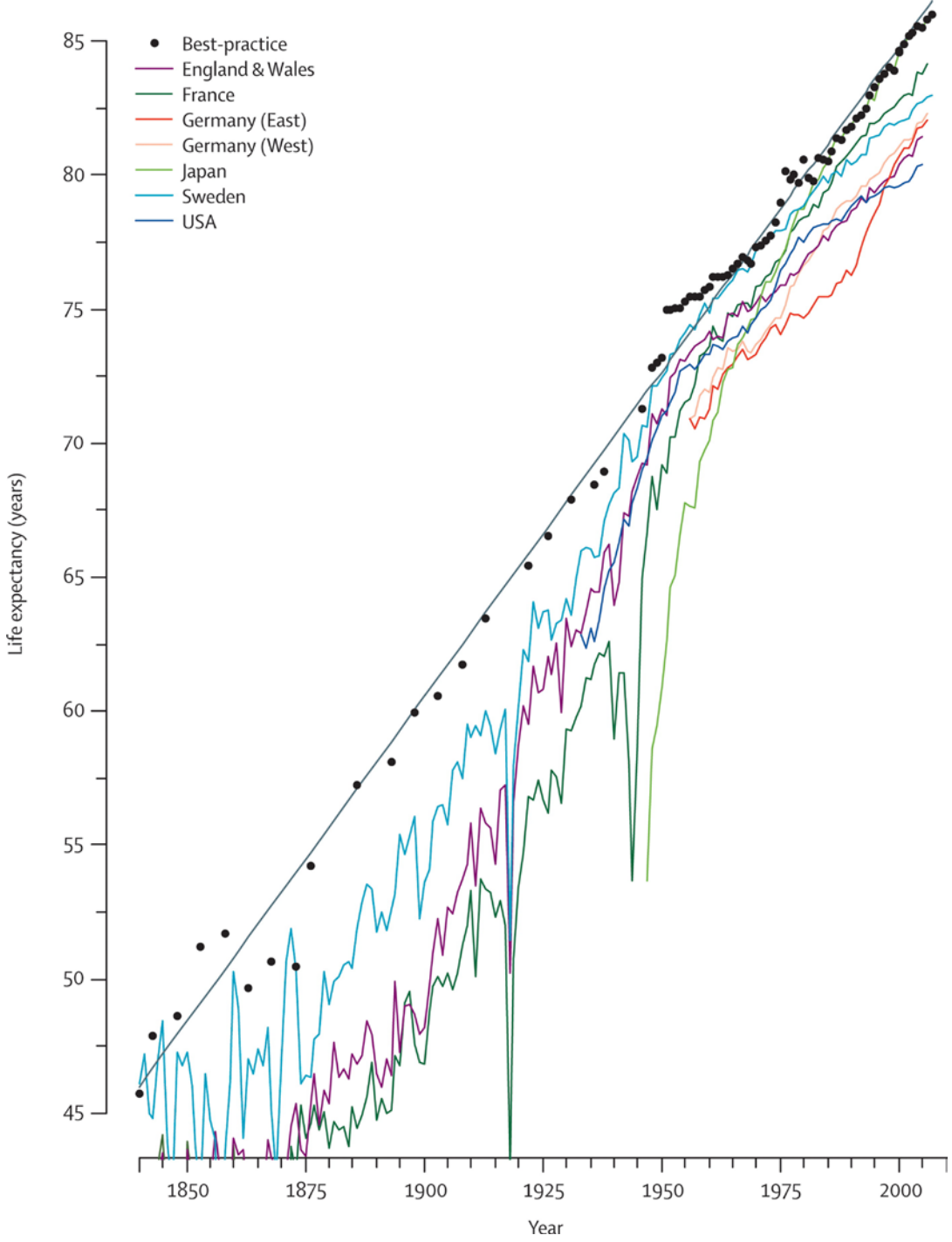
Dementia is an Age associated illness



Dementia

- Prevalence doubles for every increase of age of 5 years after age 65
- Prevalence of 1% at age 65
- 10% of those over age 65
- 25% of those age 85

- Depends upon definition and cut points

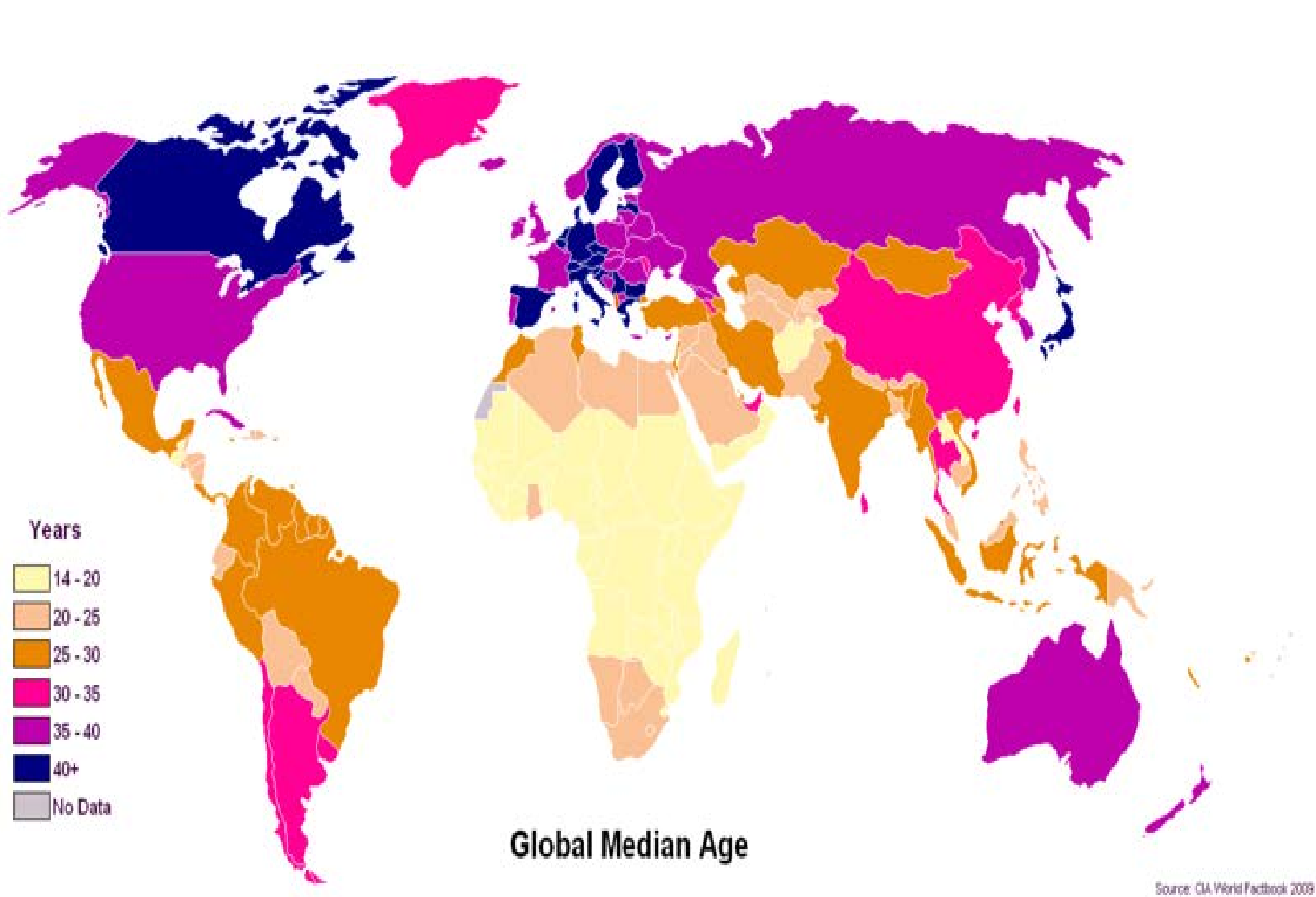


Lancet Vol 374

Demographics (2006 Census)

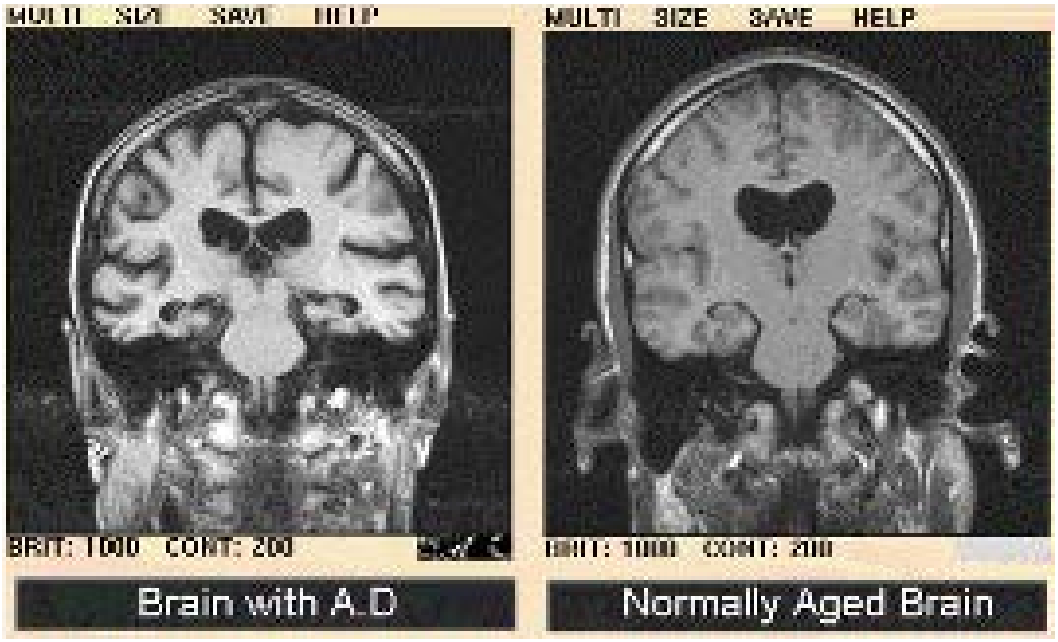
- Manitoba 161,890/1,148,400 = 0.141
- Canada 4,335,250/31,612,895 = 0.137
- Winnipeg 95,930/694,670 = 0.138

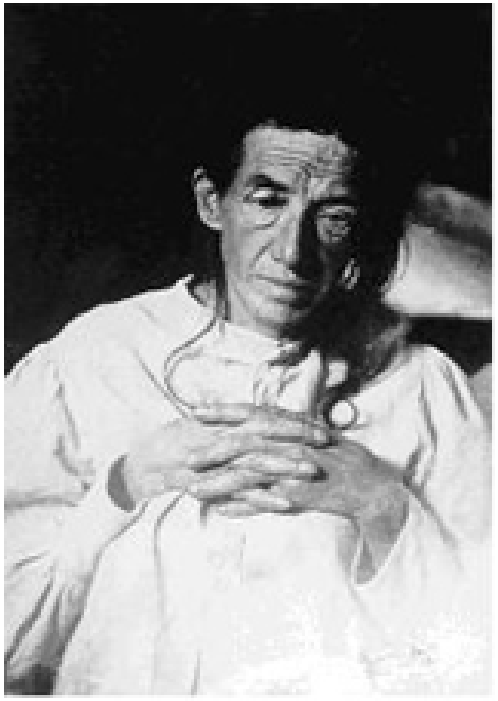
The new 65 is 87


Years
14 - 20
20 - 25
25 - 30
30 - 35
35 - 40
40+
No Data
Global Median Age
Source: CIA World Factbook 2009

Alois Alzheimer 1864-1915

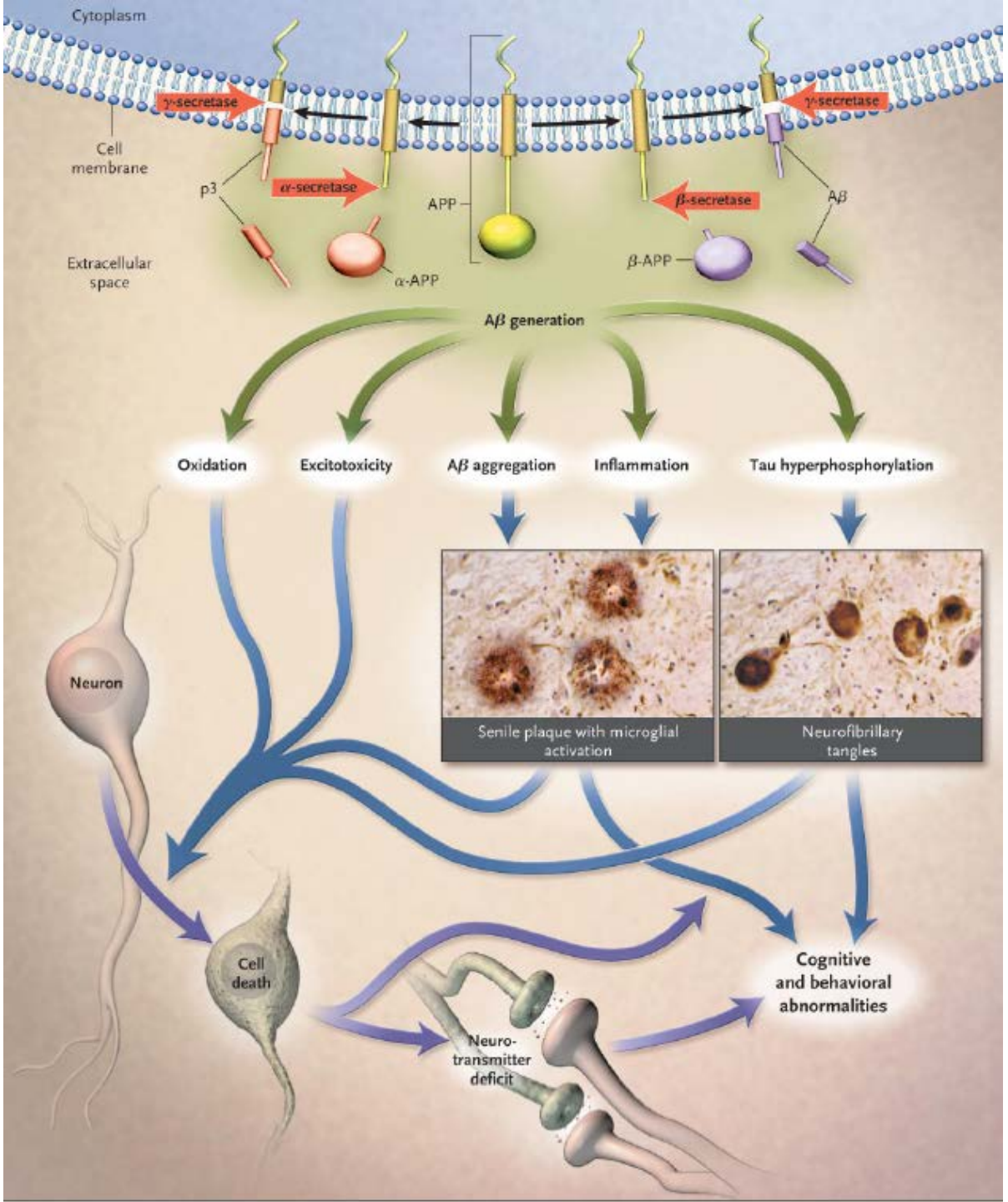
German neuropathologist & psychiatrist who described in 1906 the clinical and neuropathological features of a woman aged 51 years, with atrophied cerebral cortex, senile plaques and neurofibrillary tangles



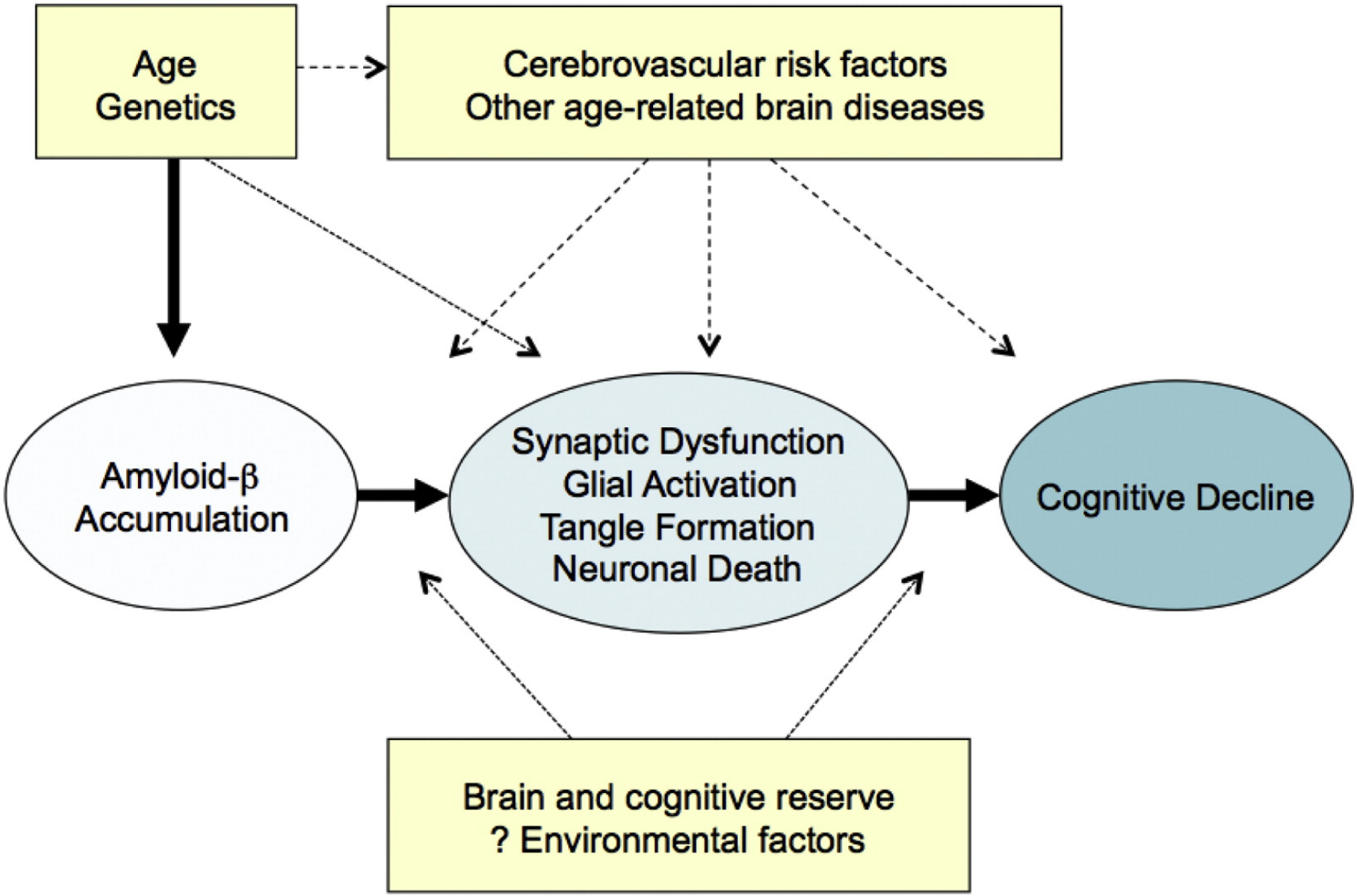


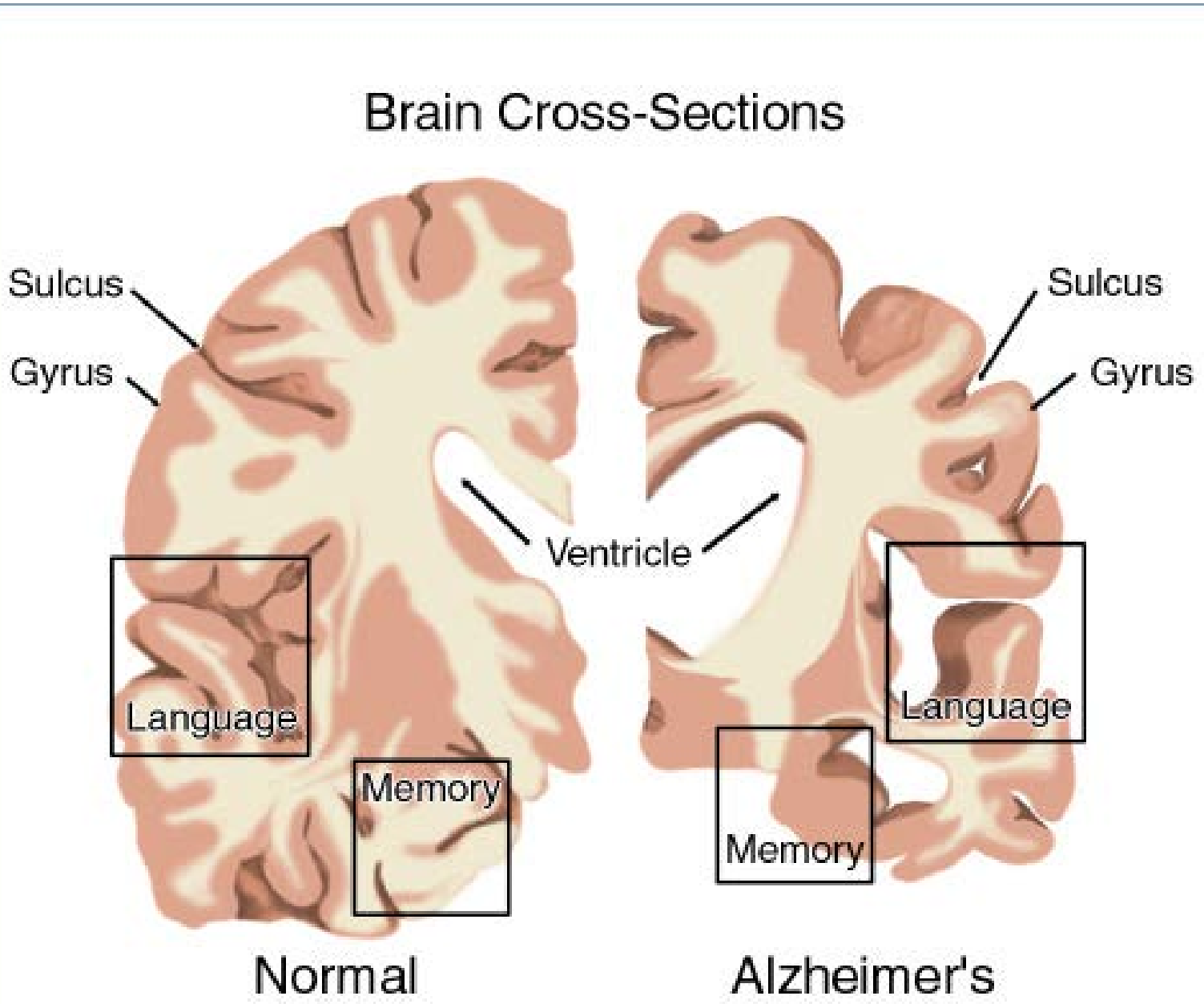
What is Alzheimer's Disease

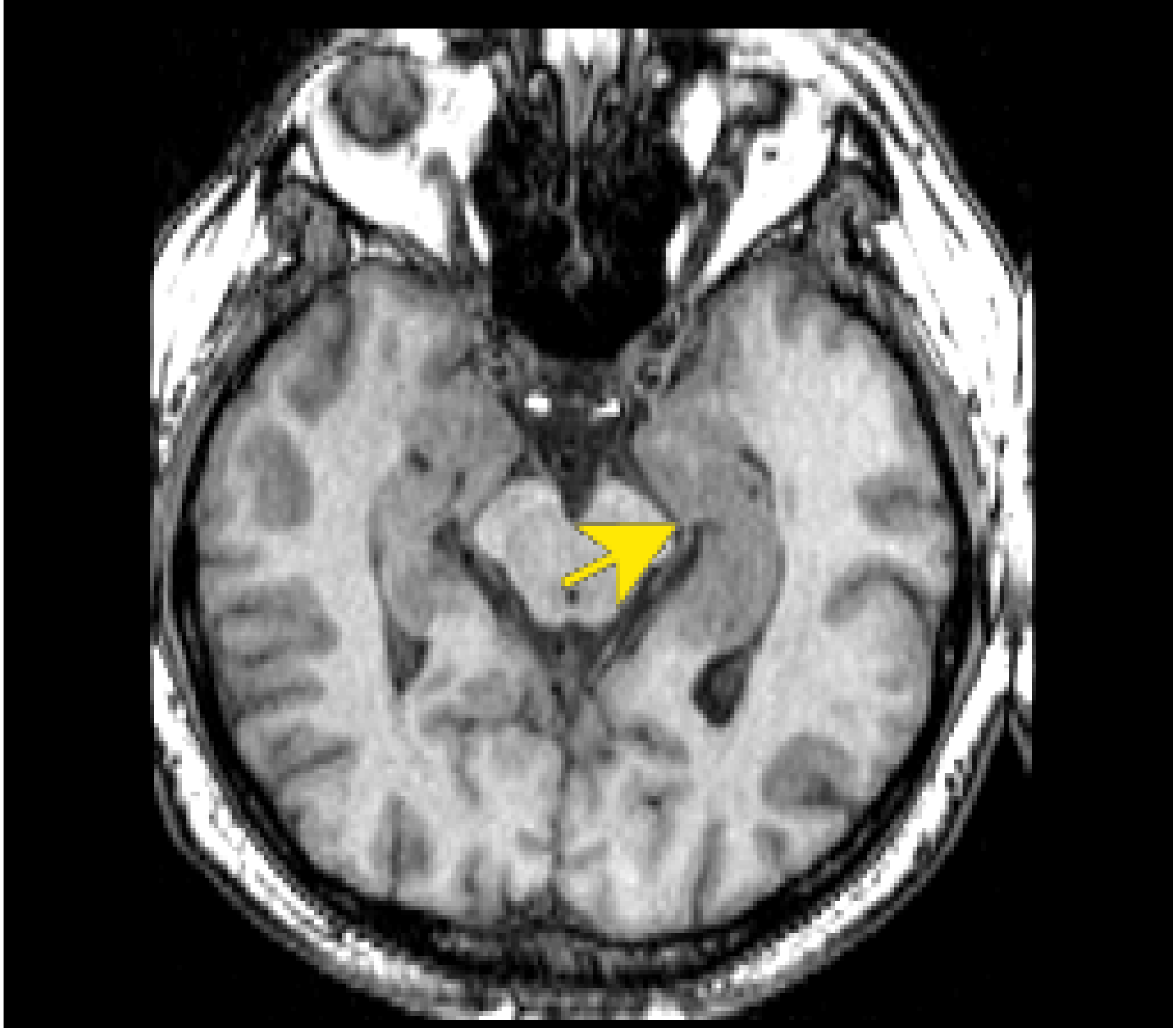
- NINCDS- ADRDA criteria
- Gradual onset
- Progressive impairment
- Memory AND word finding problems and difficulty strategizing/planning
- Easiest to diagnose when otherwise completely healthy

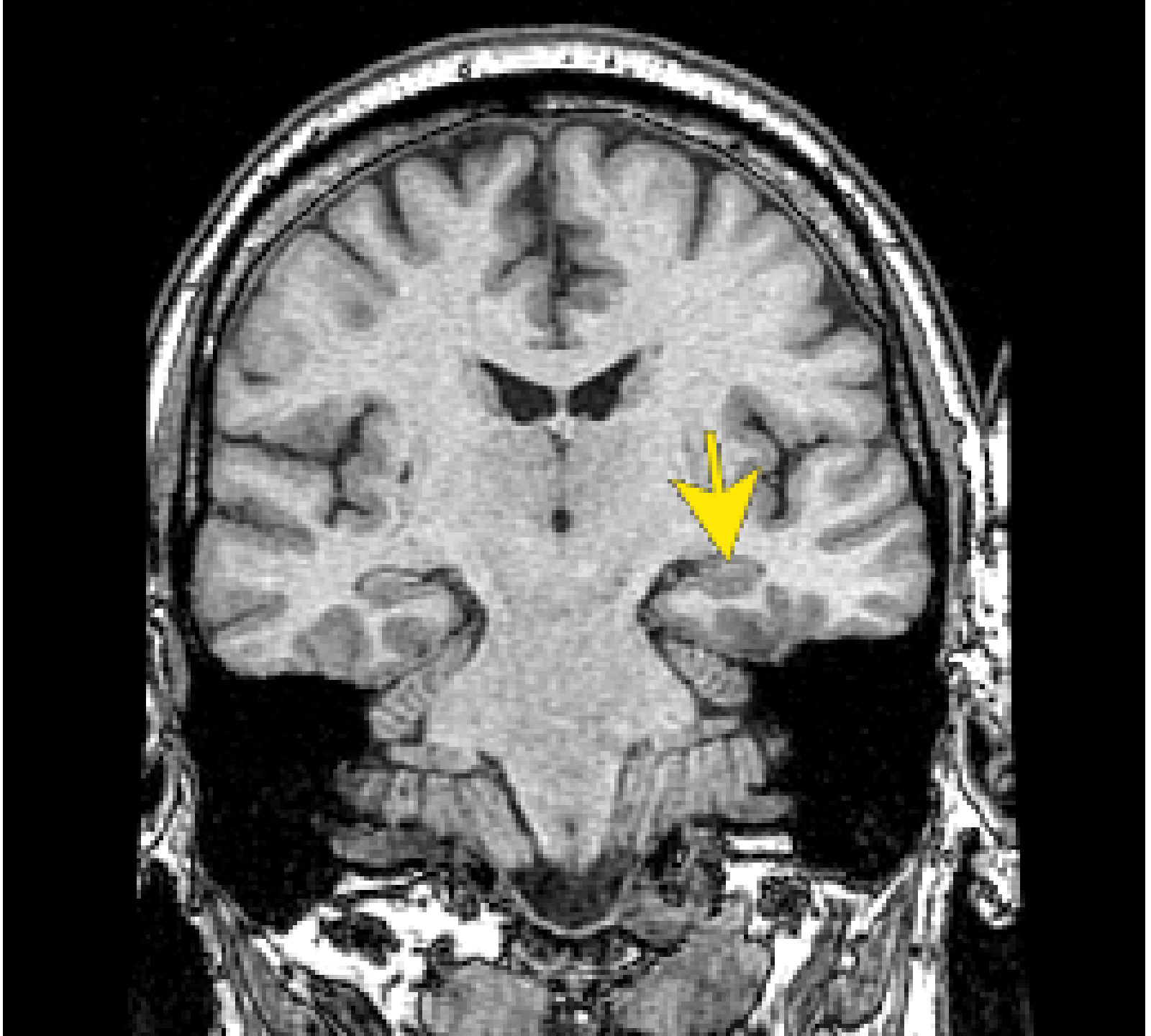

Cytoplasm
γ-secretase
Cell membrane
p3
α-secretase
APP
β-secretase
Aβ
γ-secretase
Extracellular space
α-APP
β-APP
Aβ generation
Oxidation
Excitotoxicity
Aβ aggregation
Inflammation
Tau hyperphosphorylation
Neuron
Senile plaque with microglial activation
Neurofibrillary tangles
Cell death
Neuro-transmitter deficit
Cognitive and behavioral abnormalities

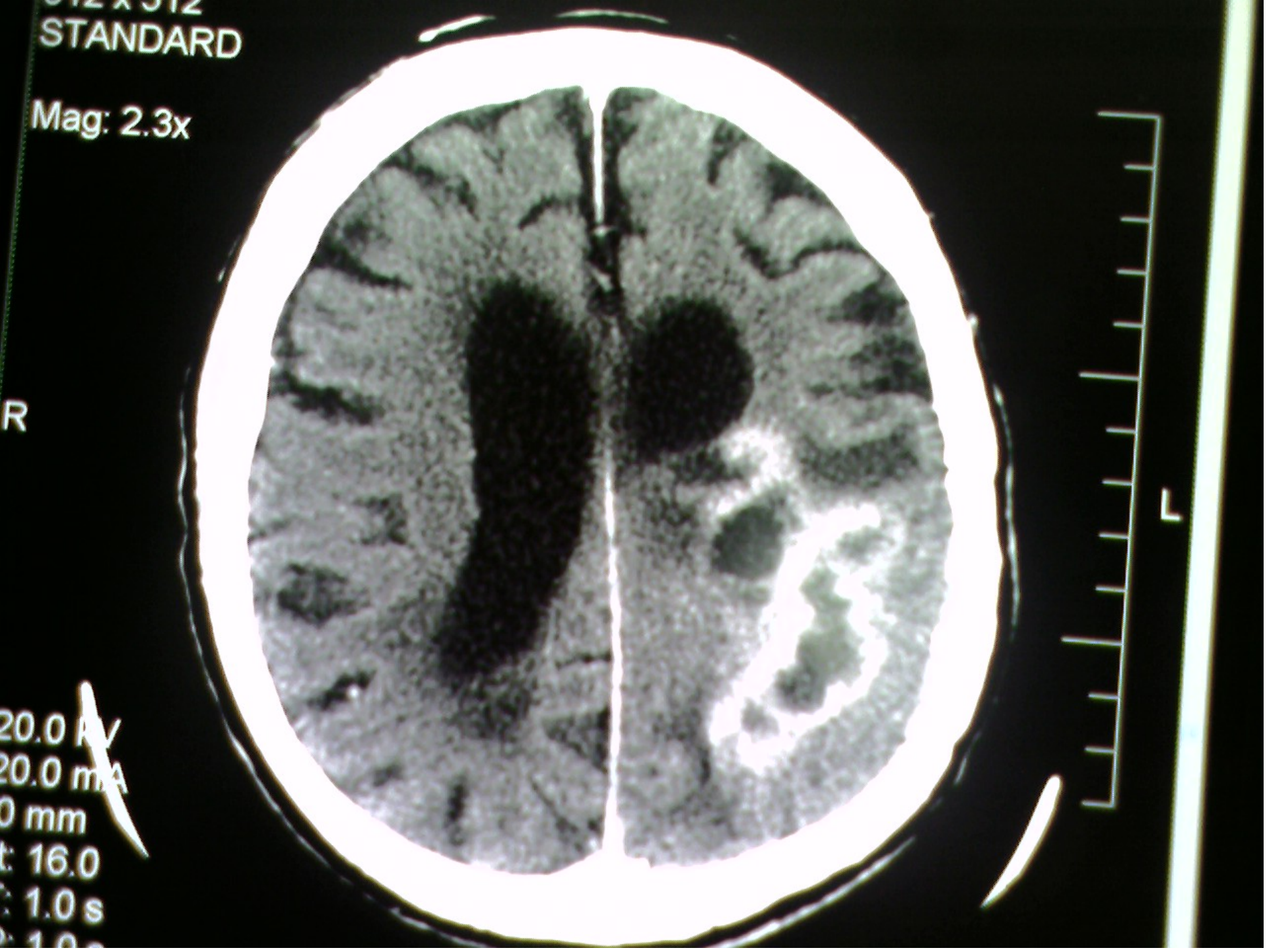
Hypothetical model of AD pathophysiological cascade




Brain Cross-Sections
Sulcus
Gyrus
Ventricle
Language
Memory
Sulcus
Gyrus
Language
Memory
Normal
Alzheimer's






STANDARD
Mag: 2.3x
R
L

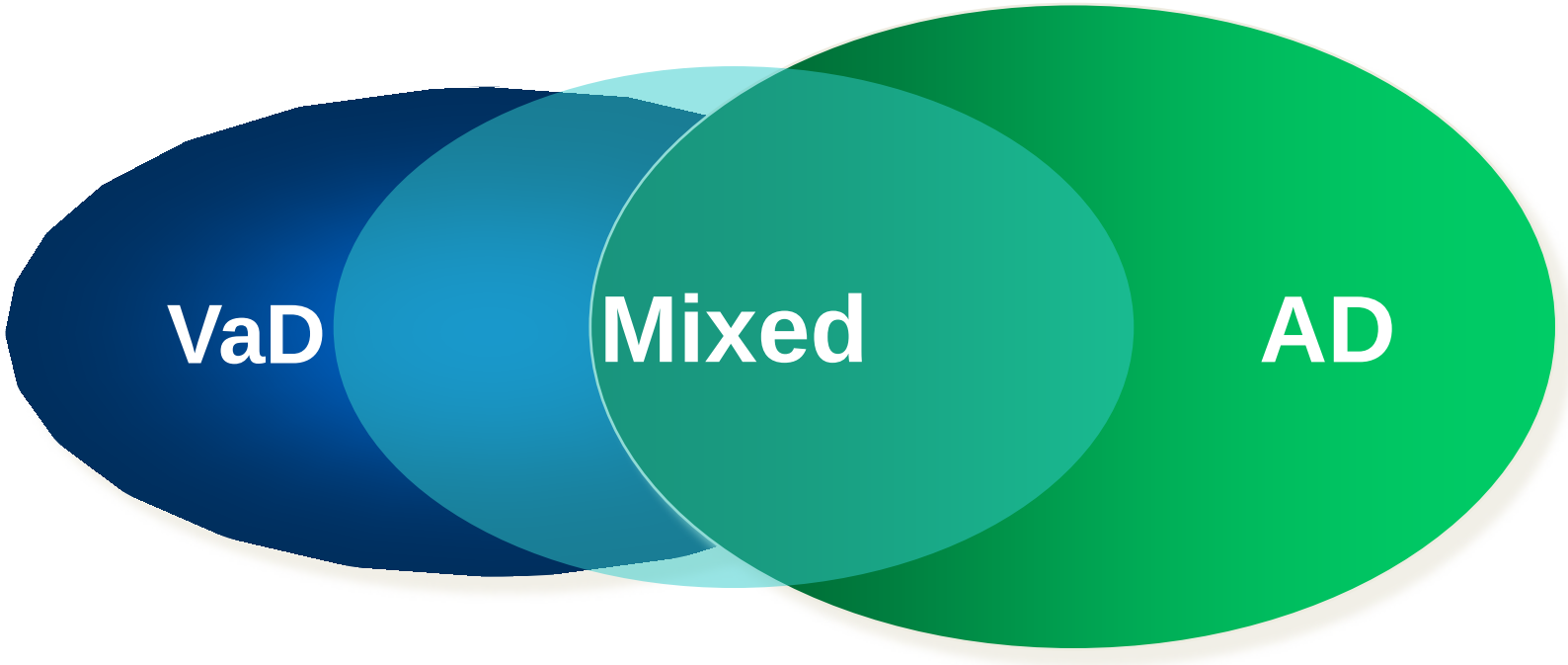
Defining Dementia

- A decline from a previous level of function
- Demonstrable impairment of memory (DSM-3)
- Other impairment in at least one of:
  - Language (naming)
  - Judgment / frontal lobe function
  - Construction / visuo-spatial function
  - Abstraction
  - Personality
- Impairment is sufficient to interfere with function and Activities of Daily Living.
- Insidious, and > 6 months (ICD-10)

What are the types of Dementia

- AD
- FTD
- VaD
- LBD
- Parkinson’s Dementia
- others

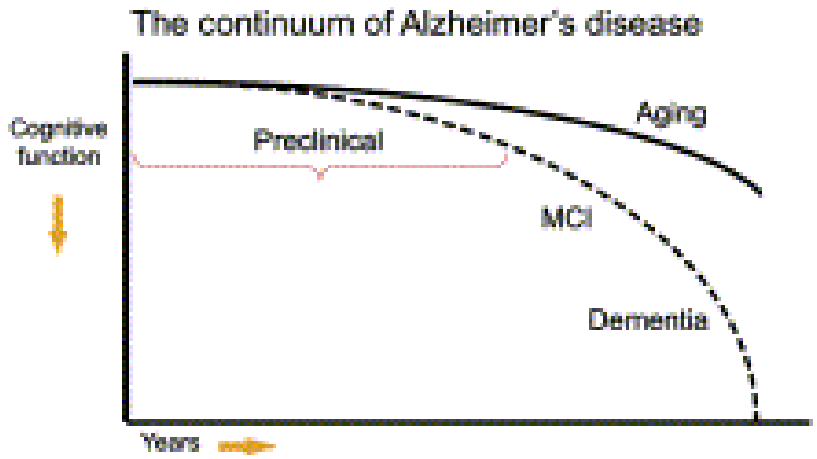
But sometimes it is more than one thing…



80% of all Dementias

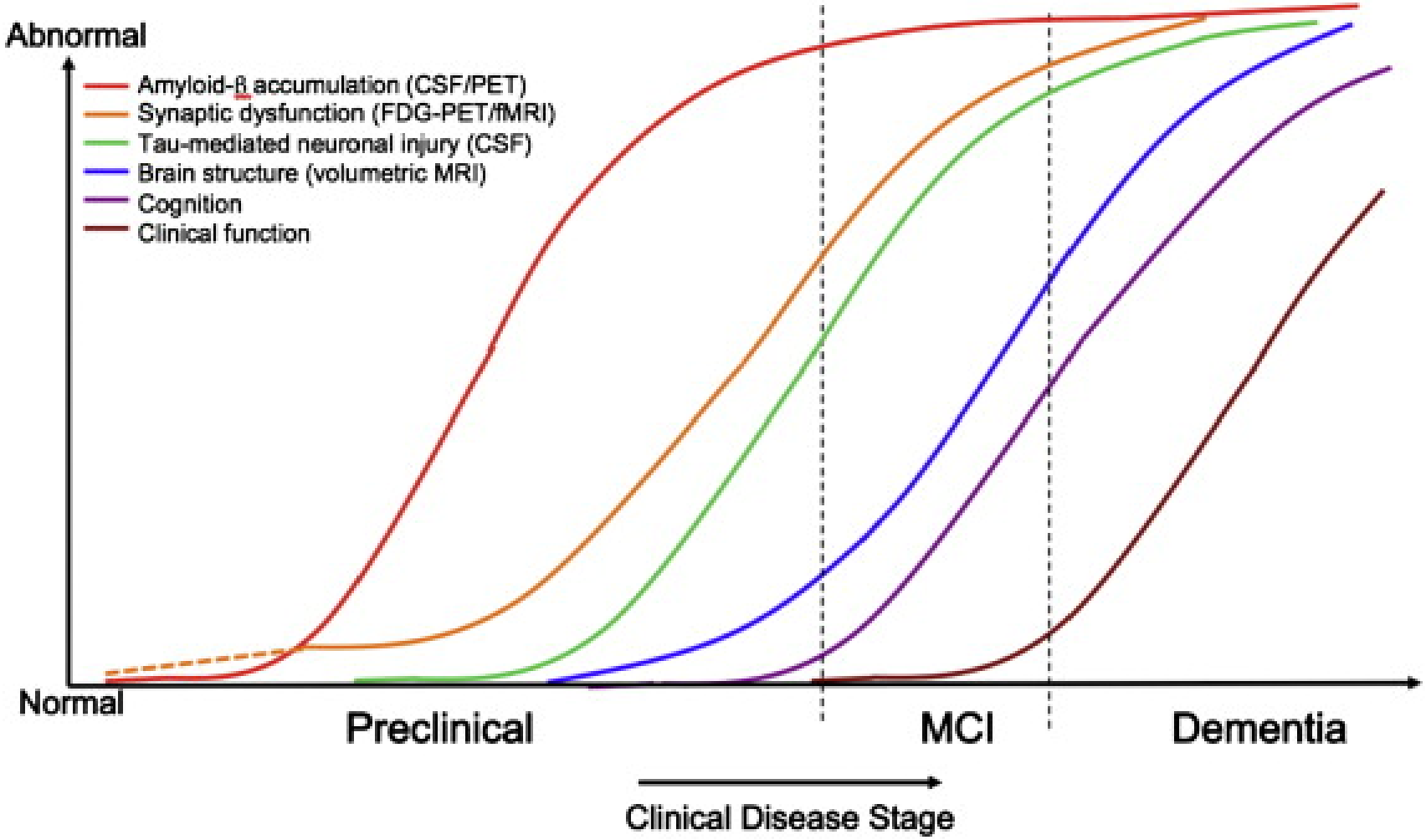
Continuum

- Gradation even within pre-clinical stage
- Normal, to “not normal but not MCI”, to MCI



New Criteria:

- Reflect better understanding of other less common types of Dementia such as Lewy Body Dementia, Fronto-temporal dementia and Vascular dementia
- More research focused (pre-clinical, histopathological correlates)


Abnormal
Amyloid-β accumulation (CSF/PET)
Synaptic dysfunction (FDG-PET/fMRI)
Tau-mediated neuronal injury (CSF)
Brain structure (volumetric MRI)
Cognition
Clinical function
Normal
Preclinical
MCI
Dementia
Clinical Disease Stage

The Doubling Rule (Think 2) For Dementia Risk

< 65	1%
65	2%
70	4%
75	8%
80	16%
85	32%

- **Risk Doubles every 5 years.**
- **But each additional risk factor approximately doubles the risk**
  - **+ve family history doubles the risk.**

Based on Kivipelto, M. et al. Arch Neurol 2005;62:1556-1560.

Dementia Risk Calculator

AGE	%
<65	1
65	2
70	4
75	8
80	16
85	32

Risk = 4%

(age)

Family history (Risk doubles for each first degree relative)

- ☐ XX Mother
- ☐ Father
- ☐ Brother
- ☐ Sister

- ☐ X 1 (no family history)
- ☐ X 2 (1 relative)
- ☐ X 4 (2 relatives)

Risk = 8% (age + family history)

Vascular risk factors (Risk doubles for each vascular risk factor)

- ☐ Atrial Fibrillation
- ☐ Diabetes
- ☐ Heart Disease (MI/CAD)
- ☐ Hyperlipidemia
- ☐ XX Hypertension
- ☐ Smoking
- ☐ Stroke
- ☐ Obesity

- ☐ X 1 (no vascular risk factors)
- ☐ X 2 (1 vascular risk factor)
- ☐ X 4 (2 vascular risk factor2)

Risk = 16% (age + family history + vascular risk factors)

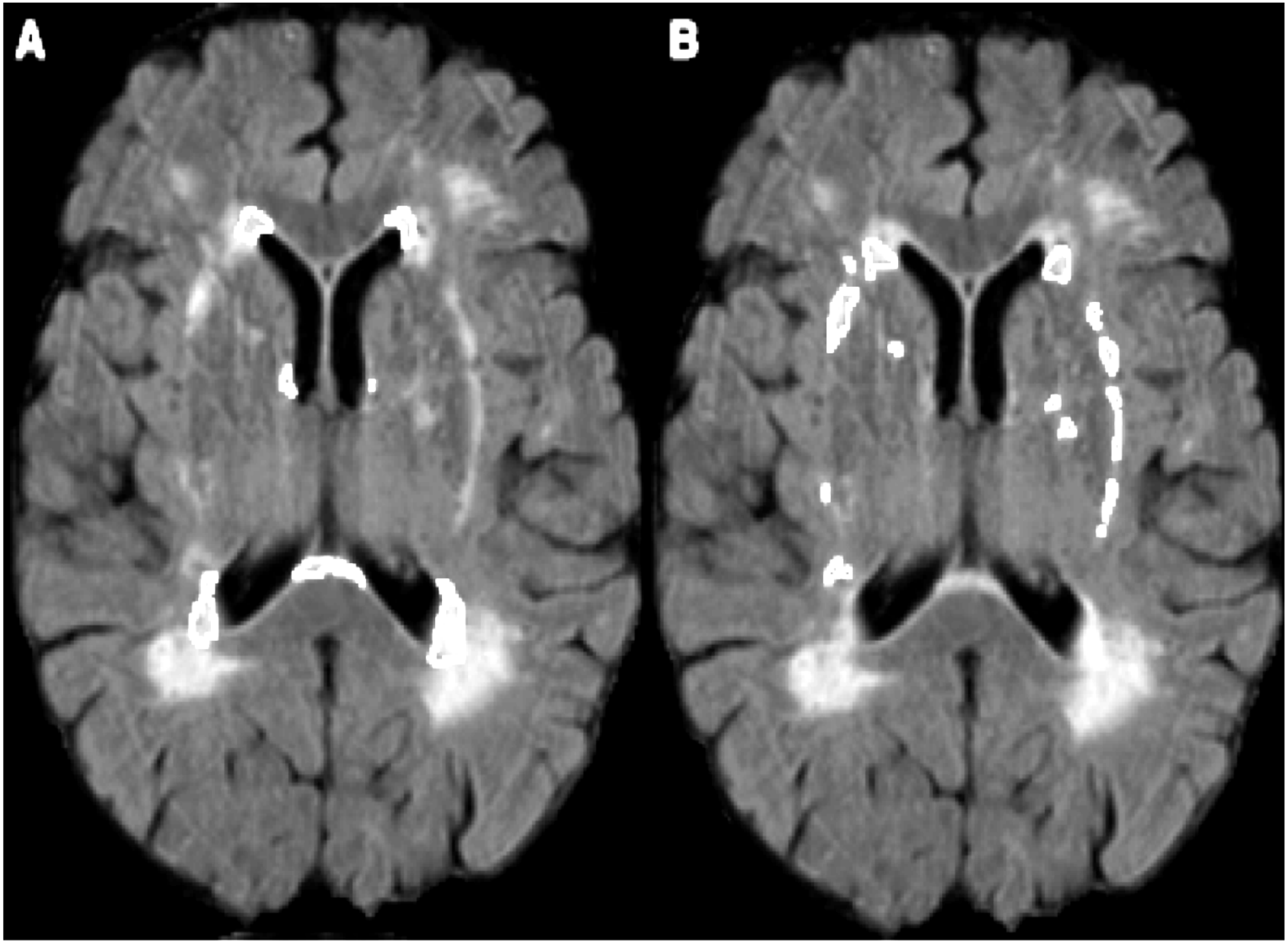
Overall risk = 16 %

Independent Effects of Midlife Vascular Risk Factors for Risk for Dementia

Risk Factor	Dementia OR (95% CI)
BMI> 30	2.09 (1.16-3.77)
SBP> 140 mmHg	1.97 (1.03-3.77)
Total cholesterol> 251 mg/dL	1.89 (1.02-3.49)
Age, years	1.18 (1.10-1.27)
Women	0.59 (0.34-1.03)
Years of Education	0.86 (0.78-0.96)
Years of Follow-up time	1.00 (0.94-1.06)

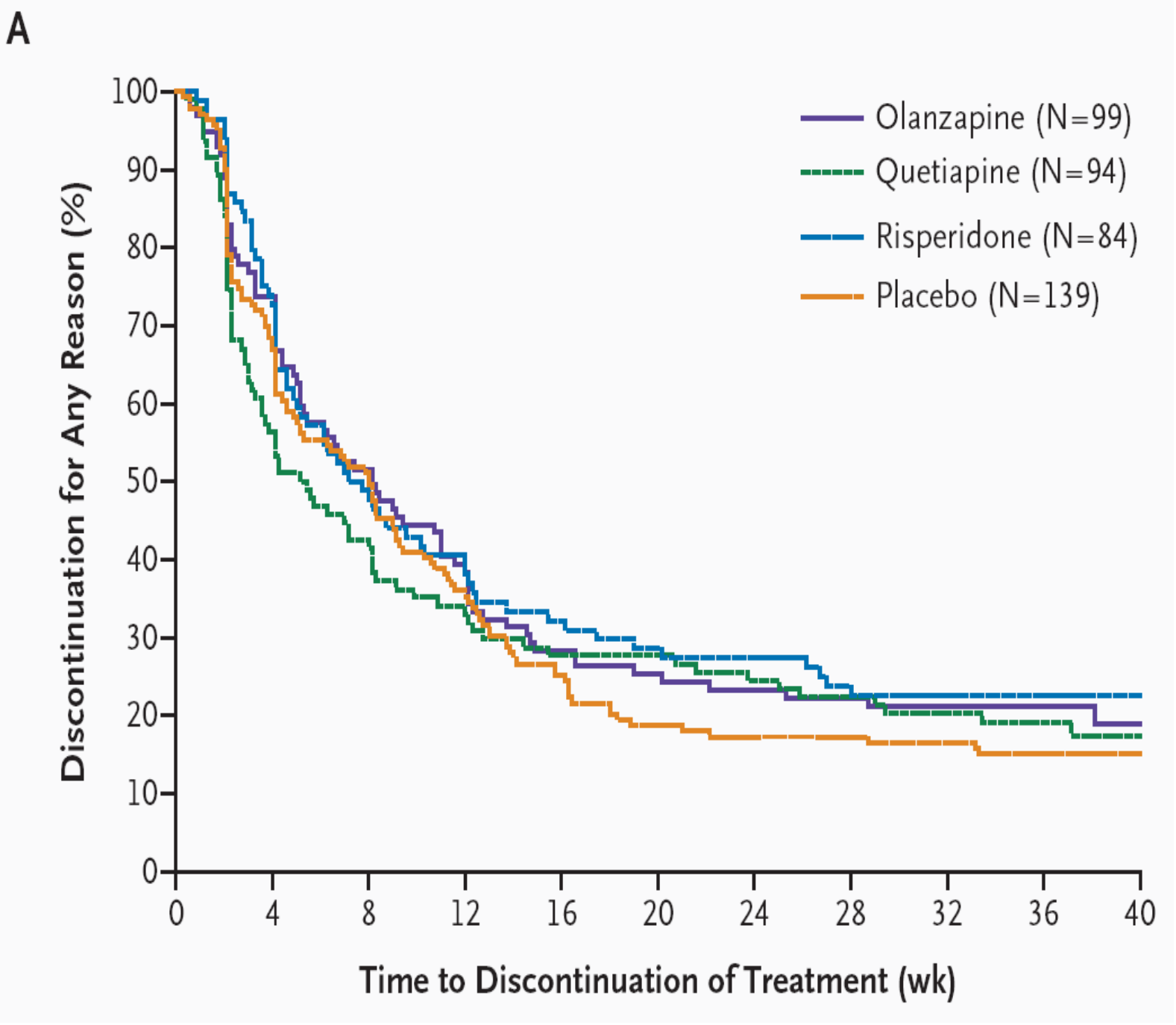
Silent Brain Infarcts (SBI)

- Prevalence of SBI:
  - 60 years of age: 5%
  - 90 years of age: 35%
- Most common risk factors:
  - Age
  - Hypertension
  - History of Coronary Artery Disease


A
B

Management Issues

- Caregiver stress (psychoeducation)
- Substitute Consent (Power of Attorney, etc)
- Driving
- Behavioral and Psychological issues
- Home care, institutional care
- Pharmacotherapy
- Increased risk of delirium


A
Olanzapine (N=99)
Quetiapine (N=94)
Risperidone (N=84)
Placebo (N=139)
Discontinuation for Any Reason (%)
100
90
80
70
60
50
40
30
20
10
0
0
4
8
12
16
20
24
28
32
36
40
Time to Discontinuation of Treatment (wk)

Summary

- Age related illness
- “Rising Tide” of prevalence
- Complex biopsychosocial illness which is common
- Best managed with a team approach