RCMAR – HEALTHY AND UNHEALTHY BRAIN AGING

NAD-RCMAR EVENT

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Overview

- Learning Objectives/Overview

  - Dementia statistics

  - Context

  - Normal, age related cognitive changes

    - Western, biomedical framework of cognition

Dementia Overview

- "Umbrella" term that includes a variety of neurodegenerative diseases and conditions that cause progressive cognitive and behavioral impairments affecting ADLs (Cooper & Greene, 2005).

  - Chronic and persistent, with no cure

  - Caused by damage to brain cells

  - Type of dementia and symptoms depend on which regions of the brain are damaged.

- Dementia is not part of the normal aging process.

- Some symptoms of dementia are potentially caused by treatable conditions

Key Points

- Most forms of dementia come on slowly and may be preceded by mild cognitive impairment (MCI). MCI does not include functional losses.

- Alzheimer's disease is the most common but not the only type of dementia.

- Diagnosis of dementia requires impairment in two or more core cognitive functions

- Dementia of Alzheimer's disease has been described as progressing through three stages: early, middle, and late stage.

- Diagnosis is predominantly made by primary care provider (PCP), geriatrician, neuropsychologist, or neurologist.

- Not all memory issues are indicative of Alzheimer's disease or another type of dementia.

Alzheimer's and Dementia Worldwide
(Population = 7.6 billion)
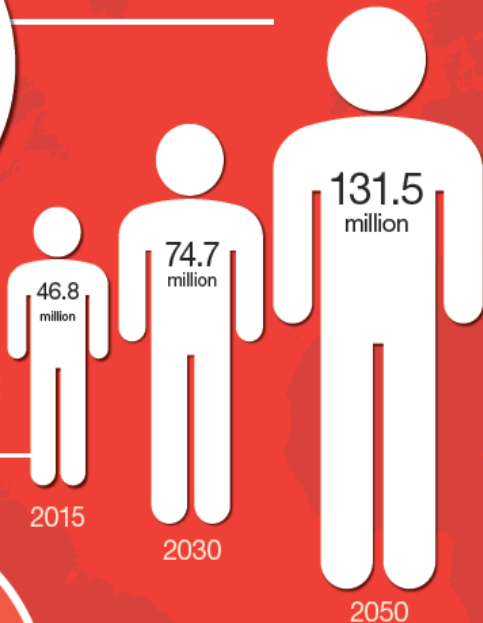
The global impact of dementia

Around the world, there will be 9.9 million new cases of dementia in 2015, **one every 3 seconds**

46.8 million people worldwide are living with dementia in 2015. **This number will almost double every 20 years.**

46.8 million
2015

74.7 million
2030

131.5 million
2050

68% 2050

Much of the increase will take place in low and middle income countries (LMICs): in 2015, 58% of all people with dementia live in LMICs, rising to 63% in 2030 and 68% in 2050.

US$ 818 BILLION
2015

US$ 1 TRILLION
2018

The total estimated worldwide cost of dementia in 2015 is US$ 818 billion. By 2018, dementia will become a trillion dollar disease, rising to **US$ 2 trillion by 2030**

If global dementia care were a country, it would be the **18th largest economy** in the world exceeding the market values of companies such as Apple and Google

Apple $742 billion

Google $368 billion

Dementia $818 billion
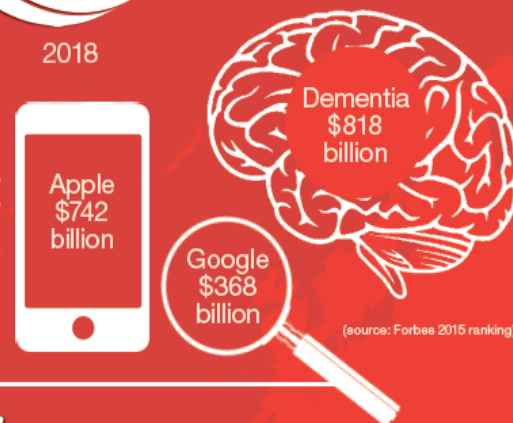
(source: Forbes 2015 ranking).

This map shows the estimated number of people living with dementia in each world region in 2015.

EUROPE 10.5 MILLION

THE AMERICAS 9.4 MILLION

AFRICA 4.0 MILLION

ASIA 22.9 MILLION

We must now involve more countries and regions in the global action on dementia.

The World Alzheimer Report 2015 was independently researched by King's College London and supported by Bupa.

Alzheimer's Disease International
The global voice on dementia

Alzheimer's Disease International, 2018.

2019 Facts and Figures

- 58% in low and middle income countries
  - 68% in 2050
- Three quarters of people with dementia are undiagnosed
  - 55% in the US
  - 90% in India
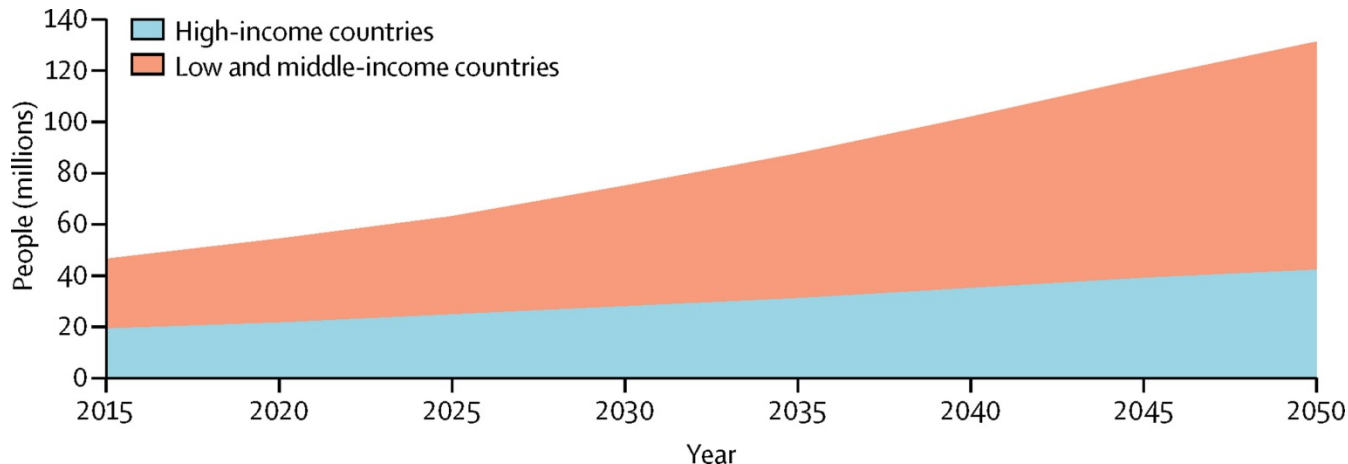
Growth in numbers of people with dementia in high-income and low and middle-income countries

Alzheimer's in the United States
(Population = 326 million)

Increased Life Expectancy and Epidemic of Alzheimer's/Dementia

- 10,000 Americans reach 65 each day

- Current life expectancy 78 years
  - 35 in 1776
  - 47 years in 1900

- **Age** is single greatest risk factor for Alzheimer's disease

- 80 million Baby Boomers (born 1946-1964)

- 6.8 million AI/AN in 2017 census
  - 10.4% over the age of 65
    - 7.6% in 2007
    - 18% by 2050

THE SILVER TSUNAMI IS COMING!
SAVE SENIOR AND DISABILITY COMMUNITY SERVICES!

2019 Facts and Figures

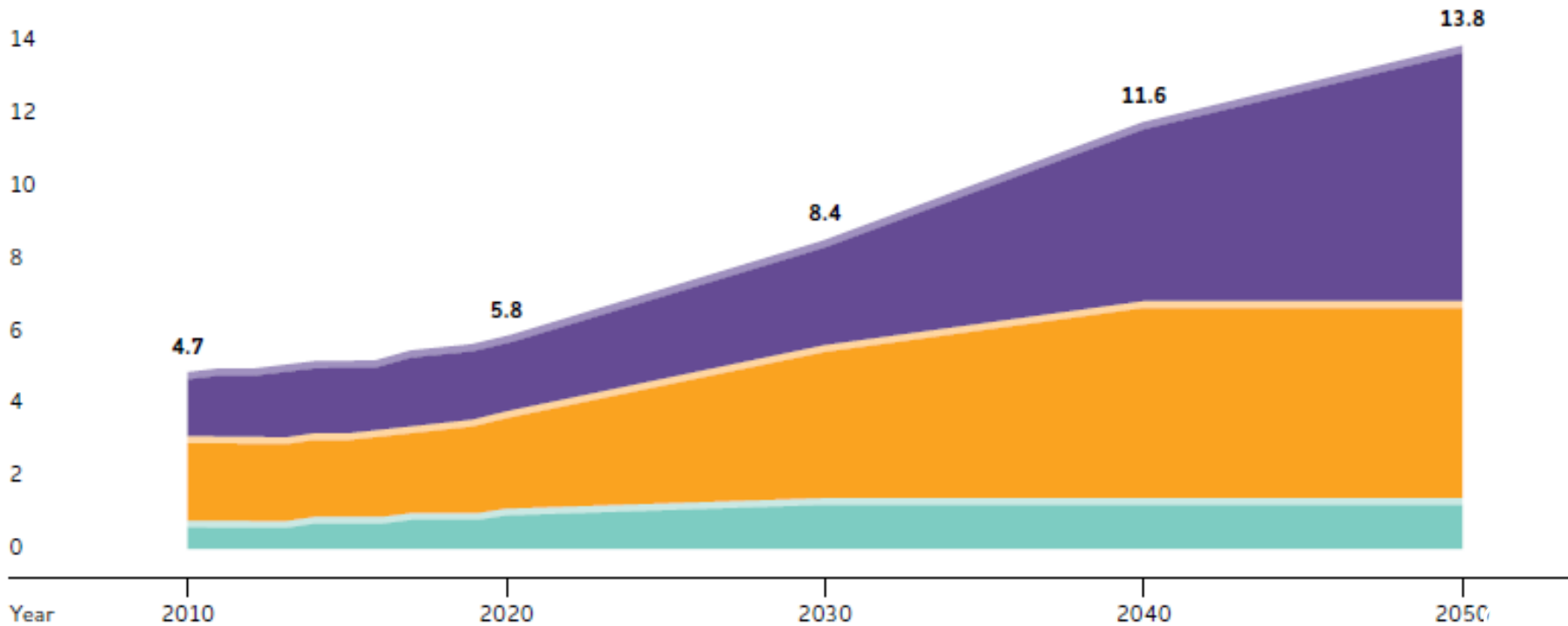**Projected Number of People Age 65 and Older (Total and by Age Group) in the U.S. Population with Alzheimer's Dementia, 2010 to 2050**

Alzheimer's Association. 2019 Alzheimer's Disease Facts and Figures. Alzheimers Dement 2019;14(3):367-429.

- $604 Billion worldwide in 2010 Wimo & Price 2010
  - $238 billion/year = (T2DM+CAD+HTN+CVA)

- Third most costly health condition in 2018
  - Annual cost ~ $259 billion
  - $172 billion in 2010 Davis, J, Hsiung, GY, Lui-Ambrose, T. Br. J of Sports Med, May 2011, Bateman et al. NEJM 2012

- Projected 2050 prevalence of 100,980 AI/AN with dementia
  - $2.6 billion Garrett et al, Mental Health Disorders Among an Invisible Minority: Depression and Dementia Among American Indian and Alaska Native Elders, The Gerontologist, Volume 55, Issue 2, April 2015, Pages 227–236,

- $7.9 trillion cost savings with early detection

DEMENTIA, HEALTHCARE & ECONOMIC BURDEN

FIGURE 13

Hospital Stays per 1,000 Medicare Beneficiaries Age 65 and Older with Specified Coexisting Medical Conditions, with and without Alzheimer's or Other Dementias, 2014

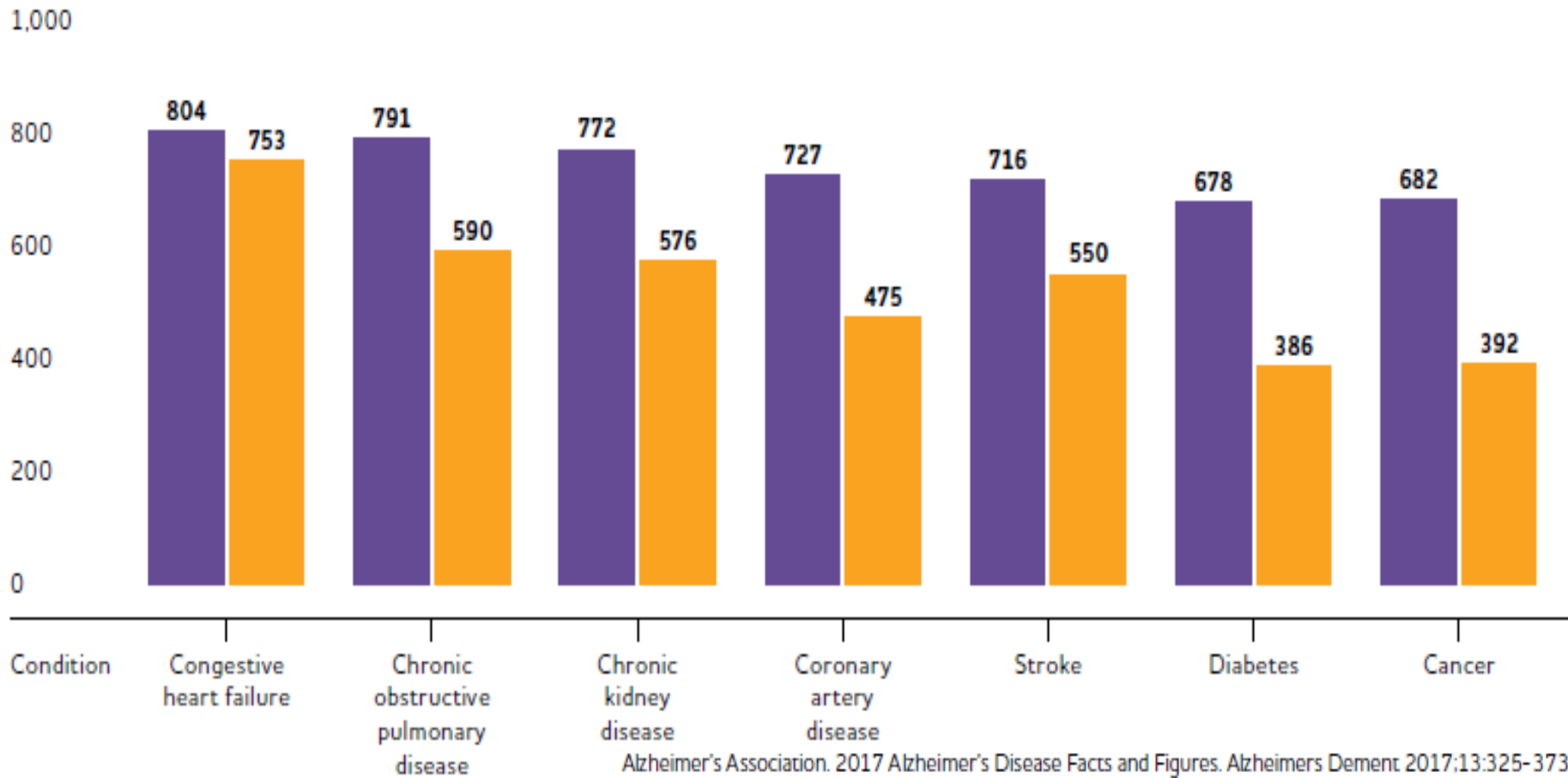Hospital stays   ■ With Alzheimer's or other dementias   ■ Without Alzheimer's or other dementias

Condition	Congestive heart failure	Chronic obstructive pulmonary disease	Chronic kidney disease	Coronary artery disease	Stroke	Diabetes	Cancer
With Alzheimer's or other dementias	804	791	772	727	716	678	682
Without Alzheimer's or other dementias	753	590	576	475	550	386	392

Alzheimer's Association. 2017 Alzheimer's Disease Facts and Figures. Alzheimers Dement 2017;13:325-373.

TABLE 13

Average Annual Per-Person Payments by Type of Service and Coexisting Medical Condition for Medicare Beneficiaries Age 65 and Older, with and without Alzheimer's or Other Dementias, in 2016 Dollars*

Medical Condition by Alzheimer's/Dementia (A/D) Status	Average Per-Person Medicare Payment					
	Total Medicare Payments	Hospital Care	Physician Care	Skilled Nursing Facility Care	Home Health Care	Hospice Care
Coronary artery disease						
With A/D	$26,223	$7,853	$2,199	$4,386	$2,343	$3,092
Without A/D	16,366	5,656	1,565	1,410	971	374
Diabetes						
With A/D	25,385	7,472	2,154	4,242	2,267	2,590
Without A/D	14,014	4,681	1,380	1,225	844	255
Congestive heart failure						
With A/D	28,773	8,825	2,310	4,794	2,455	3,452
Without A/D	24,412	8,960	2,075	2,596	1,742	807
Chronic kidney disease						
With A/D	28,002	8,457	2,255	4,666	2,319	3,075
Without A/D	20,077	6,989	1,779	1,883	1,201	473
Chronic obstructive pulmonary disease						
With A/D	27,797	8,481	2,283	4,624	2,399	3,189
Without A/D	18,962	6,792	1,725	1,749	1,201	602
Stroke						
With A/D	26,608	7,751	2,177	4,564	2,254	3,199
Without A/D	19,169	6,305	1,753	2,294	1,455	605
Cancer						
With A/D	25,207	7,352	2,109	3,934	2,074	2,862
Without A/D	15,987	4,833	1,447	1,050	692	484

*This table does not include payments for all kinds of Medicare services, and as a result the average per-person payments for specific Medicare services do not sum to the total per-person Medicare payments.

Created from unpublished data from the National 5% Sample Medicare Fee-for-Service Beneficiaries for 2014.[188]

Normal Aging Versus Dementia: Identifying the Differences

Suspicion and recognition of dementia versus normal aging are based on changes that occur across the following capabilities:

- Cognitive function
  - Memory
  - Executive function
  - Information processing
- Visuospatial function
- Other sensory changes
- Language skills
- Ability to perform basic and instrumental activities of daily living (ADLs and IADLs, respectively)
- Appearance of specific behavioral and psychologic symptoms

Cognitive Function

- Cognitive function refers to how a person becomes aware of, perceives, or comprehends ideas (Anstey et al., 2004).

- It declines gradually while young and more rapidly among older adults (>60s) (Anstey et al., 2004).

- Many other medical and psychological factors can influence cognitive function (Pankratz et al., 2015; Mayo Clinic, 2017b; UCSF Memory and Aging Center, 2017; Heaton et al., 2010; Karakis et al., 2016; Emory Alzheimer's Disease Research Center, 2017; HelpGuide.org, n.d.; Pagoria et al., 2011).

Domains of Cognitive Functioning

- Intelligence/Premorbid Functioning
- Memory (Verbal and Visual)
- Executive Functioning
- Attention/Concentration
- Reasoning/Judgment
- Language
- Visuospatial/constructional
- Sensory/Perceptual
- Motor
- Academic

Executive Function

- Executive function refers to a set of mental or cognitive skills believed to be controlled by the frontal lobe, anterior cingulate, prefrontal cortex, basal ganglia, and thalamus.

- There are 2 main types of executive functions :

  o Organization: attention, managing time, planning and organizing, remembering details, sequencing, and working memory

  o Regulation: self-control, emotional regulation, decision-making, and moral reasoning

- Impairments in executive function can lead to difficulty planning, emotional swings and changes, loss of fine motor skills, apathy, and socially inappropriate behaviors

Memory Loss

- Many different types of memory (Arlt, 2013; Atkinson & Shiffrin, 1968)

- General types of memory (Arlt, 2013; UCSF Memory and Aging Center, 2018d):
  - Short-term (or working) memory (<1 min)
  - Long-term (lifetime) memory

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Memory - Systems

- Working
  - Short term storage
  - Manipulation
- Semantic
  - Permanent, general knowledge, context free
- Episodic
  - Personal events, contextual
- Perceptual representational
  - Presemantic, modality specific
- Procedural
  - Motor/cognitive skills
- Sensory
  - Visual (iconic), auditory (echoic), smell-based (olfactory), taste-based, or haptic (touch-based) memory

Schacter & Tulving, 1994

The multi-store model of memory (Atkinson & Shiffrin, 1968)
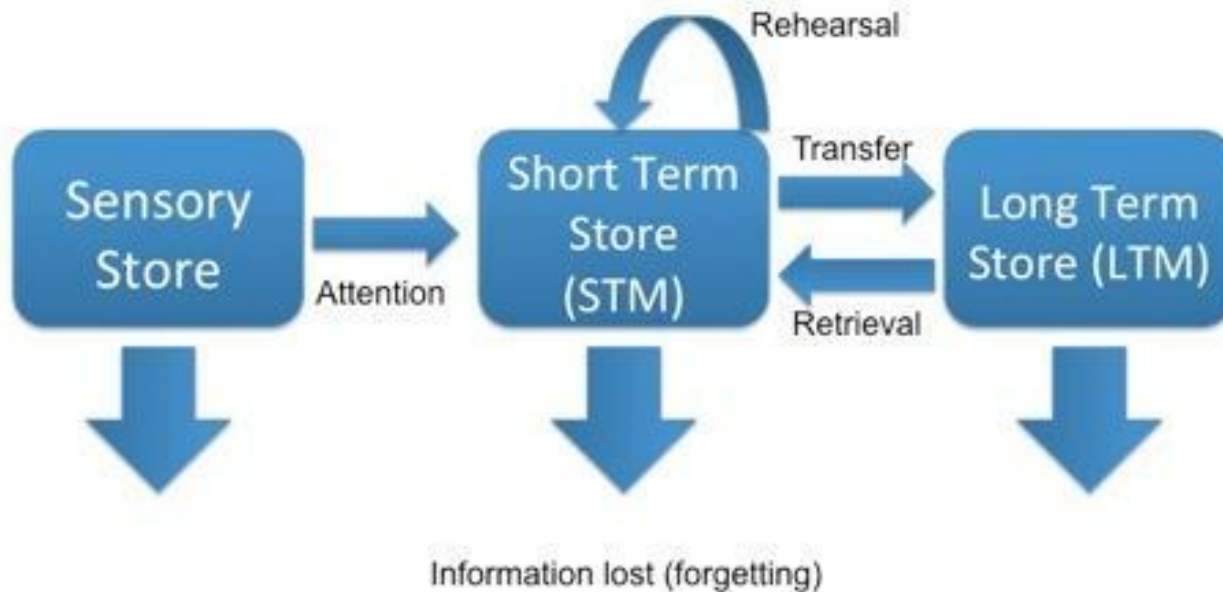
Normal Aging, continued

- As people age, they retain their ability to perform basic ADL without needing assistance (Galvin, 2012; Gold, 2012).

  o Inability to perform IADL typically precedes inability to perform basic ADL (Galvin, 2012).

  o Inability to manage finances may be one of the earlier IADL changes suggestive of dementia (Gold, 2012).

Visual Perception, Language Skills, Sensory Impairments

Normal aging leads to changes in all 5 senses:

- Visuoperceptual difficulties (Macknik et al., 2016; Staudinger et al., 2011; NEI, n.d.)

- Auditory problems (Tun et al., 2012)

- Speech and language impairments (Sörös et al., 2009; Tun et al., 2012)

- Changes in taste (NIA, n.d.)

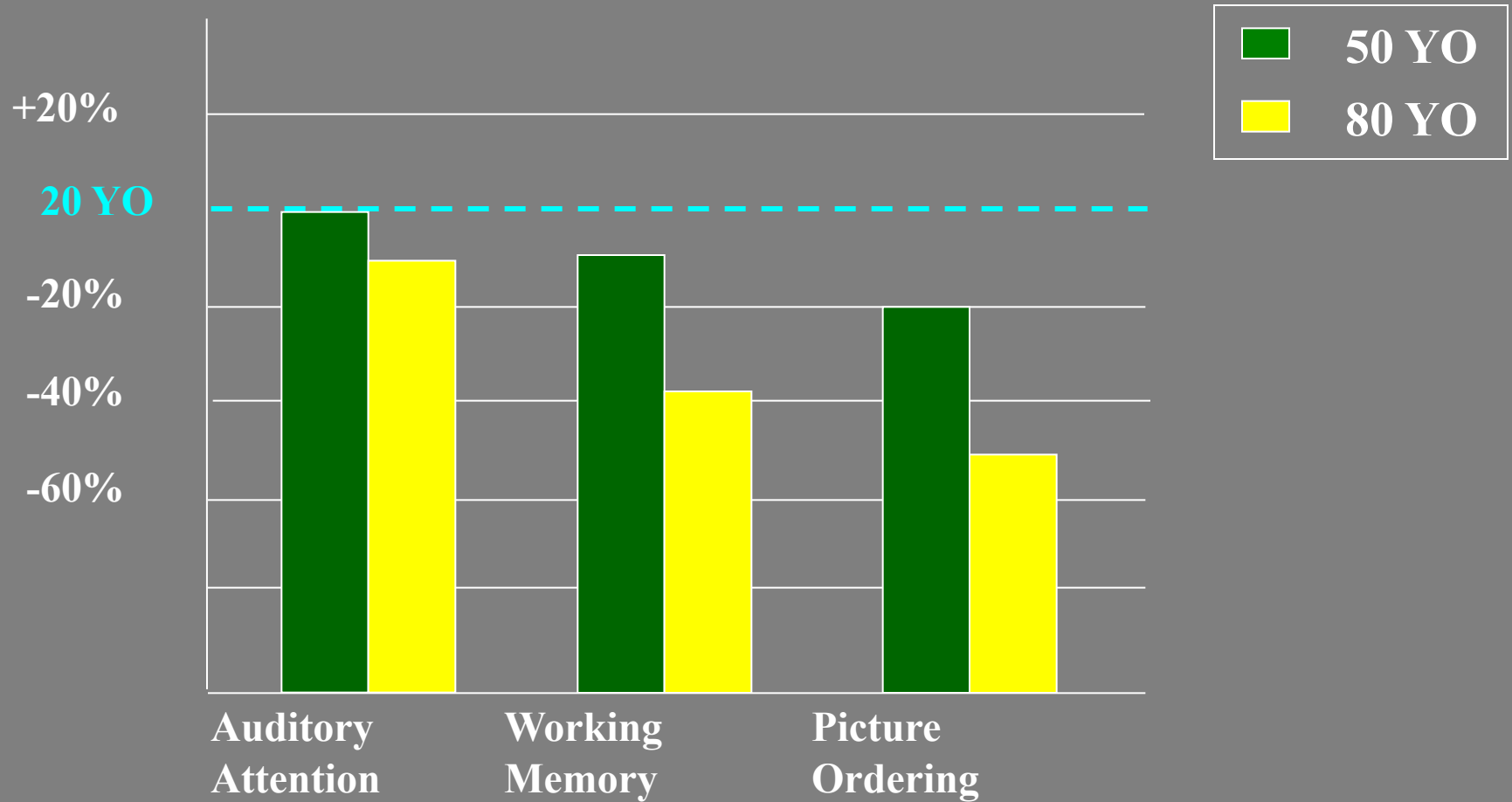- Changes in smell (Vasavada et al., 2015)
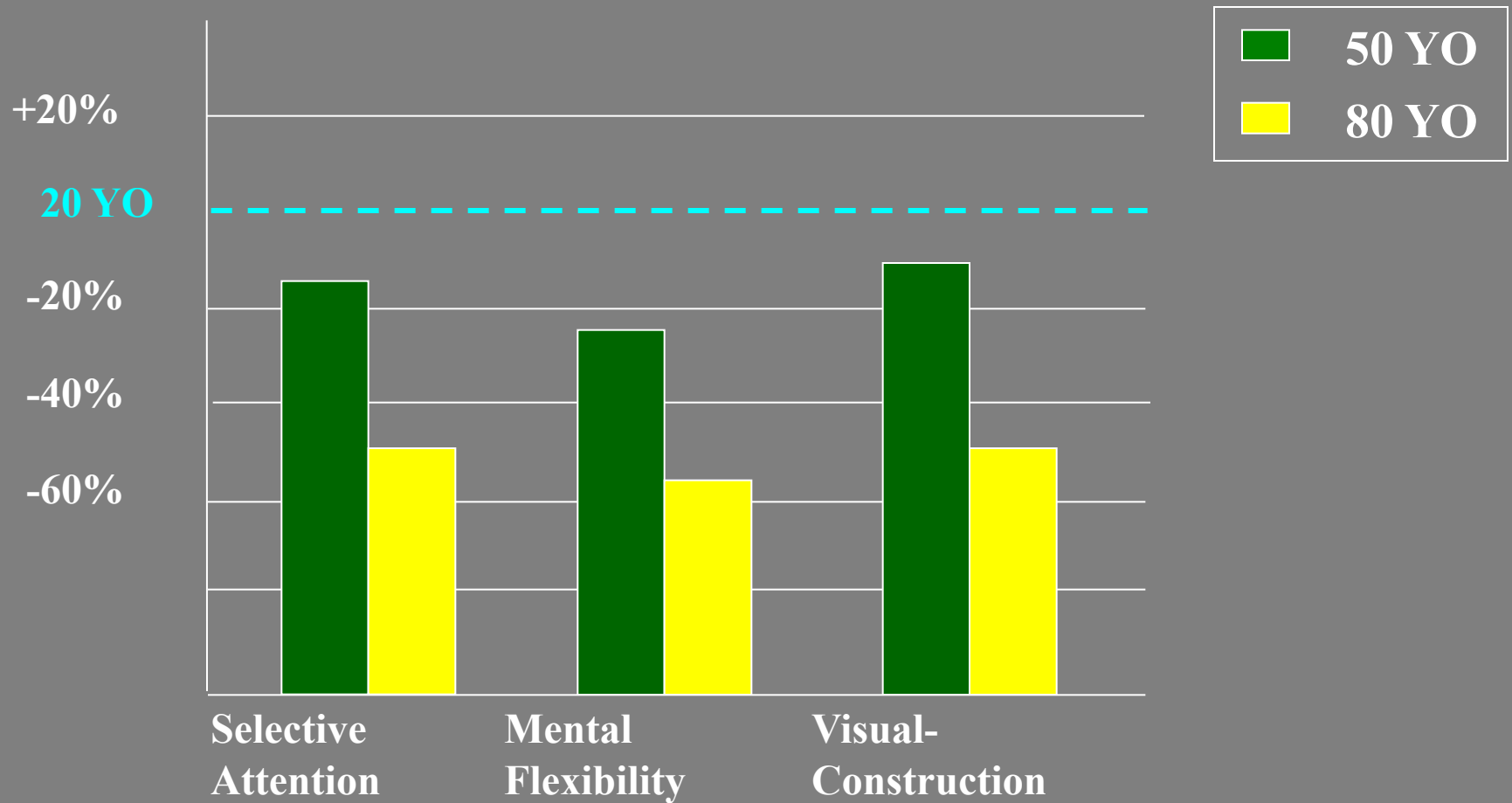
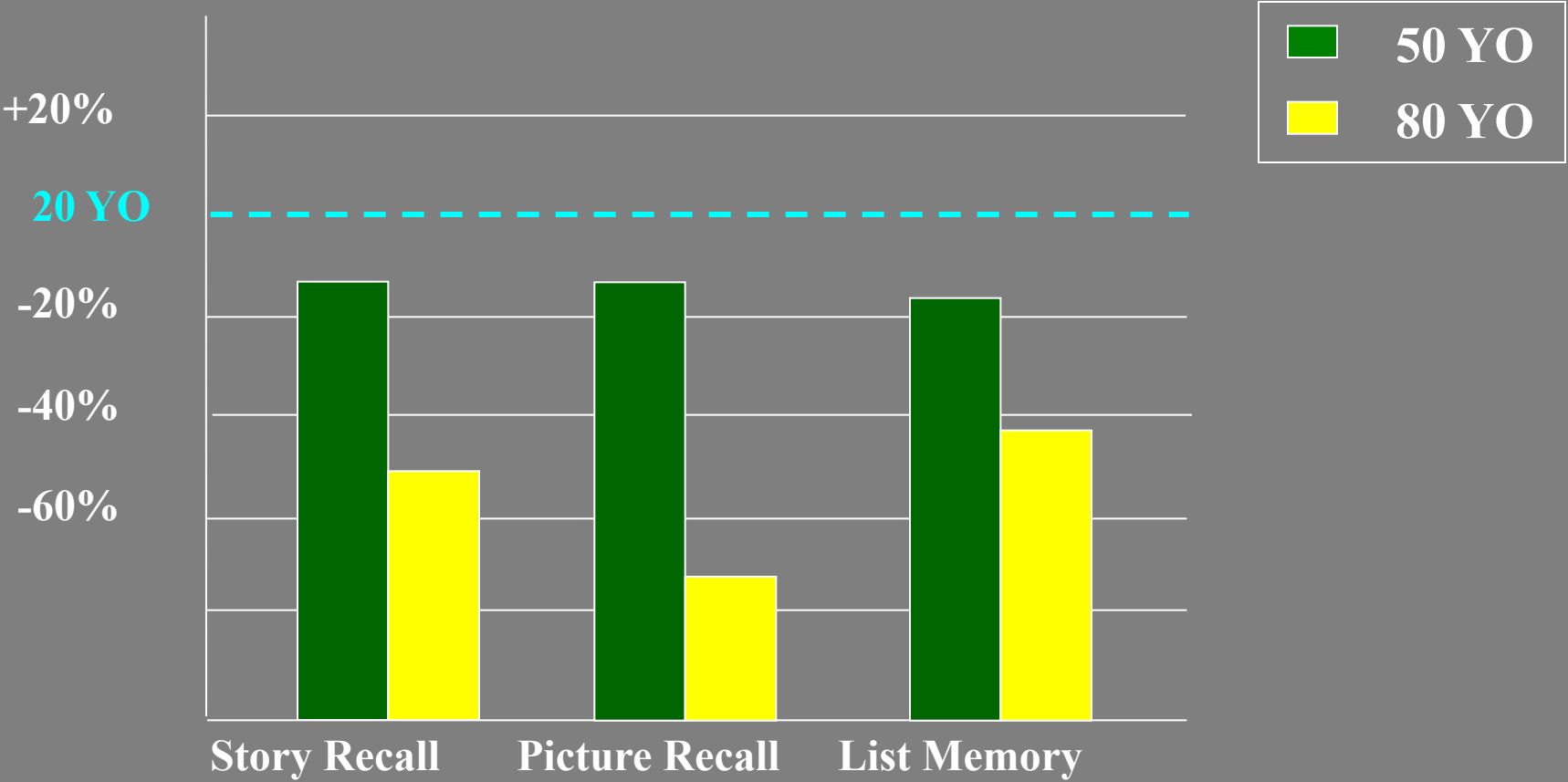# What's Normal, What's Not?
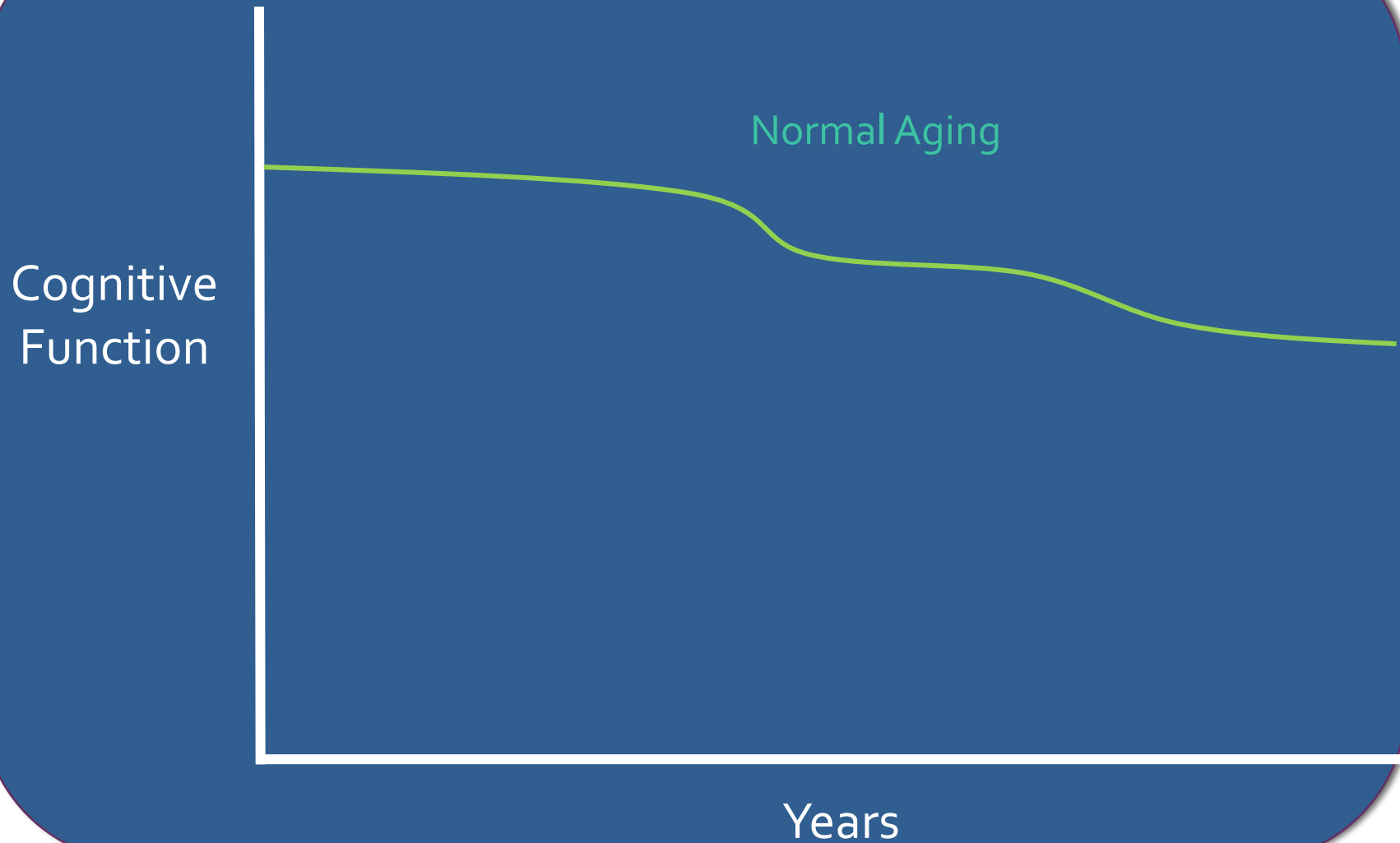
Normal Aging

Cognitive Function

Years

Normal Aging: Cognitive Changes
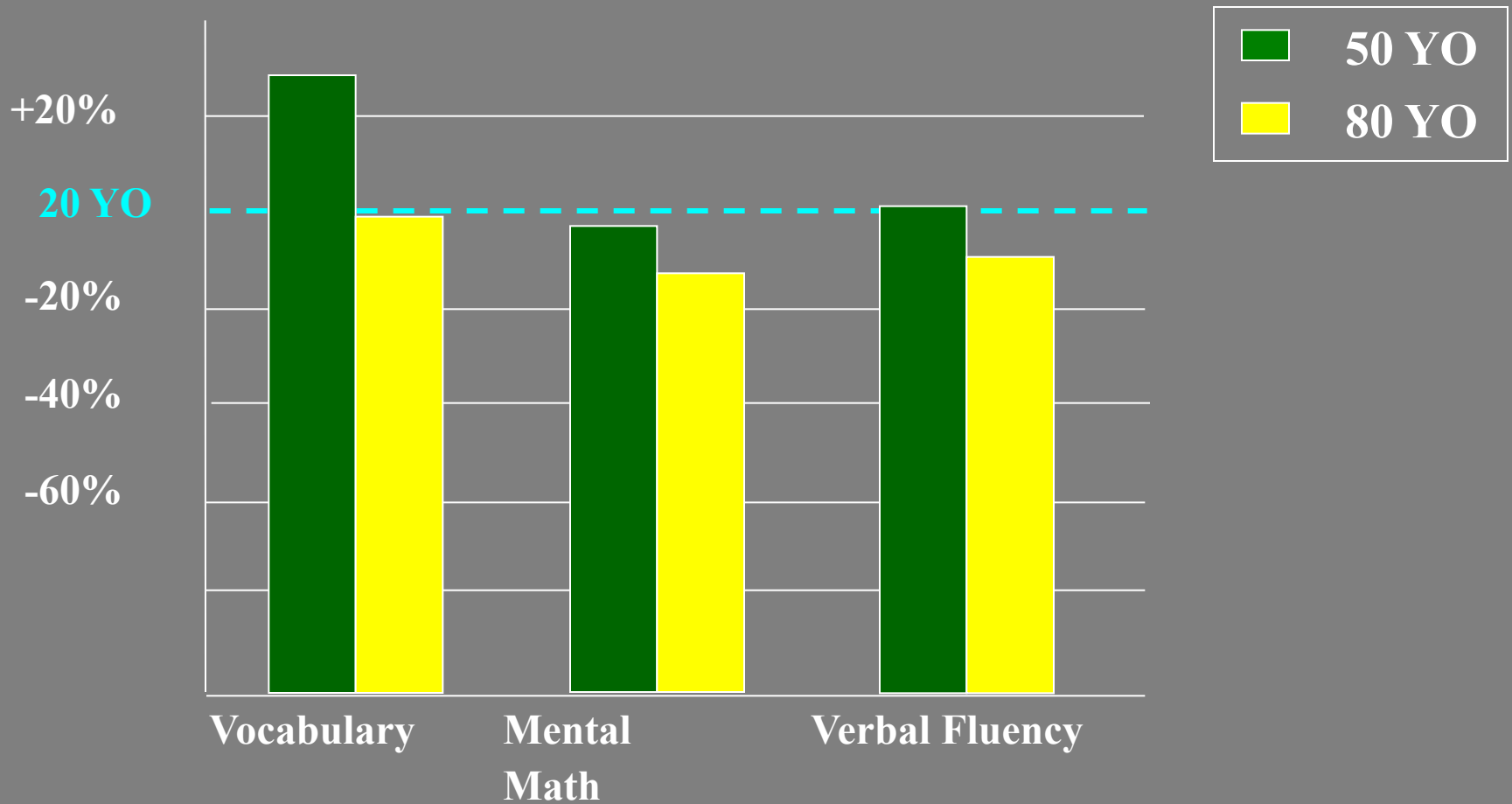
Normal Aging: Cognitive Changes

Normal Aging: Cognitive Changes

Normal Aging: Memory Changes

Age-Related Memory/Cognitive Changes
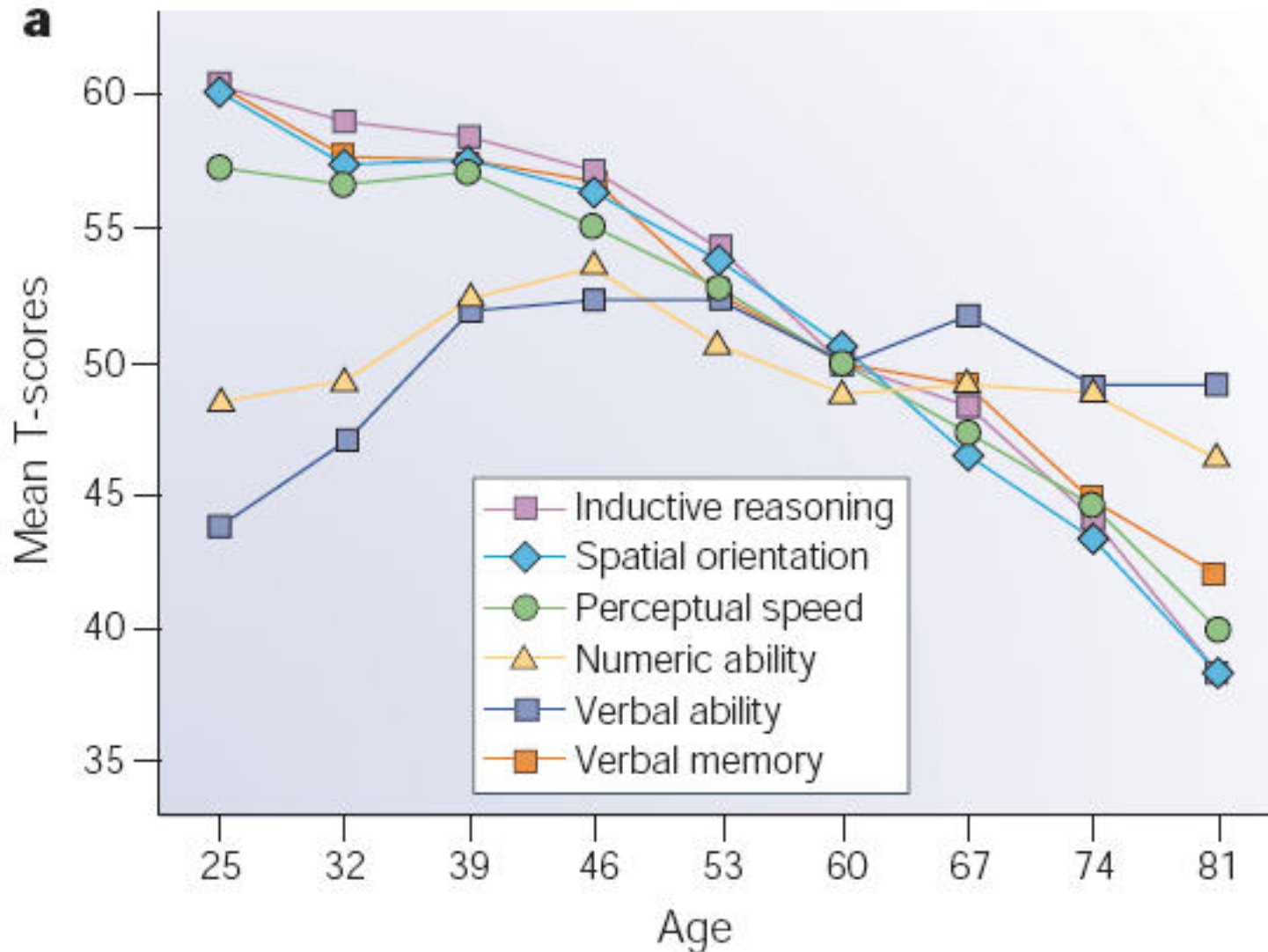
- **Few changes:**

  - **Crystallized Intelligence**

  - **Procedural Memory**

  - **Long-term Memory**

  - **Auditory Attention**

  - **Verbal Fluency**

  - **Working Memory?**

- **Declines:**

  - **Sensory Memory**

  - **Short-term Memory**

  - **Complex/Selective Attention**

  - **Executive Skills**

  - **Processing Speed**

  - **Motor Tasks**

  - **Working Memory?**

Normal Aging: Cognitive Changes

Cognitive Changes: Physiological Theory

- Shrinkage of neurons

- Decreases in:

  - myelination

  - number of synaptic connections

  - neurotransmitter availability

  - perfusion

- Location Specific:

  - » Hypothalamus vs. prefrontal cortex

Cognitive Changes: Physiological Theory

Related health conditions:

- Smoking

- Alcohol

- Sitting disease/Sedentary life style

- Depression

- Sleep apnea

- Delirium

- Hospitalization/Sepsis

- Head Injury

- Low level of education

- Type 2 Diabetes

- Obesity

- High blood pressure

- Hyperlipidemia

- Cerebrovascular risk

Differential Risk Factors: AI/AN

- High prevalence of vascular risk factors
  - Strong Heart and Cerebrovascular Disease and Consequences studies
  - Cholerton et al 2017
    - 80% with hypertension
    - 48% with diabetes
    - 40% with dyslipidemia
    - Reduced whole brain/hippocampal volumes associated with decreased processing speed
    - Total brain volume associated with verbal learning (not recall)

- Environmental factors
  - Chronic low level arsenic exposure associated with decreased processing speed and fine motor speed (Carrol et al, 2017)
  - Chronic low level domoic acid exposure (Tracy et al, 2016)
  - PCB exposure effect in older Mohawk, but not younger (Haase et al, 2009)

Differential Risk Factors: AI/AN

- Diabetes prevalence in white populations= 6.2% (Mokdad et al., 2000)
  - blacks (10.8%)
  - Mexican Americans (10.6%)
  - AIANs (9.0%)

- Increase in hypertension and diabetes with age (Rhoades et al, 2007)
  - Despite decreases in smoking

- High prevalence of multiple vascular risk factors in AI veterans without diagnosed cognitive impairment (Kirkpatrick et al, 2019)
  - 44% with abnormal MoCA scores
  - 15 received comprehensive workup
    - normal ($N = 4$)
    - non-amnestic MCI ($N = 4$)
    - vascular MCI ($N = 5$)
    - vascular dementia ($N = 2$)

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Kirkpatrick, A. C., Stoner, J. A., Donna-Ferreira, F., Malatinszky, G. C., Guthery, L. D., Scott, J., & Prodan, C. I. (2019). High rates of undiagnosed vascular cognitive impairment among American Indian veterans. GeroScience, 41(1), 69–76. doi:10.1007/s11357-019-00055-5

Social Cognitive Theory

Stereotypes ⟶ **Expectations**

↓

Active Strategies ⟶ **Recall**

Expectation impacts performance (Trivia Study)

- Younger vs. Older

- Different instructions

    - "Test of Memory" vs. "Ability to Learn Trivia"

- Outcome: Age differences for "Memory," not "Trivia"

Rahal, Hasher, & Colcombe (2001)

Sociocultural Determinants

- Culturally appropriate definitions of normality and functionality
- Acculturation (Trimble, 2000)
  - Predictor of consistency with normative data (Ferraro et al, 1996, Ferraro et al, 2002, Whyte et al, 2005)
- Socioeconomic status
  - Rural versus urban AI/AN (Jervis & Manson, 2002)
- Linguistic and cultural translation/logic
- Education and task familiarity

- **Critical importance of culturally-appropriate measures as well as norms**

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Cognitive Screening- MMSE

- 30 items, 6 domains, 5-10 minutes
- Standard cutoff of 23-24
  - Sensitivity = 66-73%
  - Specificity = 87-92%
    - Positive Predictive Value= 58-67%

- Misclassification rate = 15%

- Age and education effects/norms
  - Sensitivity = 92%
  - Specificity = 96%

The mini mental state examination

Orientation
Year, month, day, date. season ____/5
Country, county, town, hospital, ward (clinic) ____/5

Registration
Examiner names three objects (for example, apple, pen, and table)
Patient asked to repeat objects, one point for each. ____/3

Attention
Subtract 7 from 100 then repeat from result, stop after
five subtractions. (Answers: 93, 86, 79, 72, 65)
Alternatively if patient errs on subtraction get them to
spell world backwards: D L R O W
Score best performance on either task. ____/5

Recall
Ask for the names of the objects learned earlier. ____/3

Language
Name a pencil and a watch. ____/2
Repeat: 'No ifs, and or buts.' ____/1
Give a three stage command. Score one for each
stage (for example, 'Take this piece of paper in your right
hand, fold it in half and place it on the table.' ____/3
Ask patient to read and obey a written command
on a piece of paper stating: 'Close your eyes.' ____/1
Ask patient to write a sentence. Score correct if
it has a subject and a verb. ____/1

Copying
Ask patient to copy intersecting pentagons.
Score as correct if they overlap and each has five sides. ____/1

Total score: ____/30

Cognitive Screening- MMSE

- SALSA study (MMSE) (Espino et al., 2001 & 2004; JAGS)

  - Internal consistency depends on scoring

  - Education effects

  - Language ability

  - Neighborhood effects

  - Socioeconomic status

- MMSE False Positive Rates

  - 6% for non-impaired majority

 - 42% for non-impaired minority

Cognitive Screening- MMSE/DRS-2

- MMSE and DRS-2 in AI/AN elder populations (Jervis et al., 2007& 2010)

  - Comparison to age norms = 10-27% impairment
    - DRS impairment was 81% for age/ed adjusted norms
  - Education effects
    - Type and character
  - Language ability
  - Socioeconomic status/SSI need
  - Access to necessary health care
  - Pre/peri natal factors?

- In addition to age and overall level of education
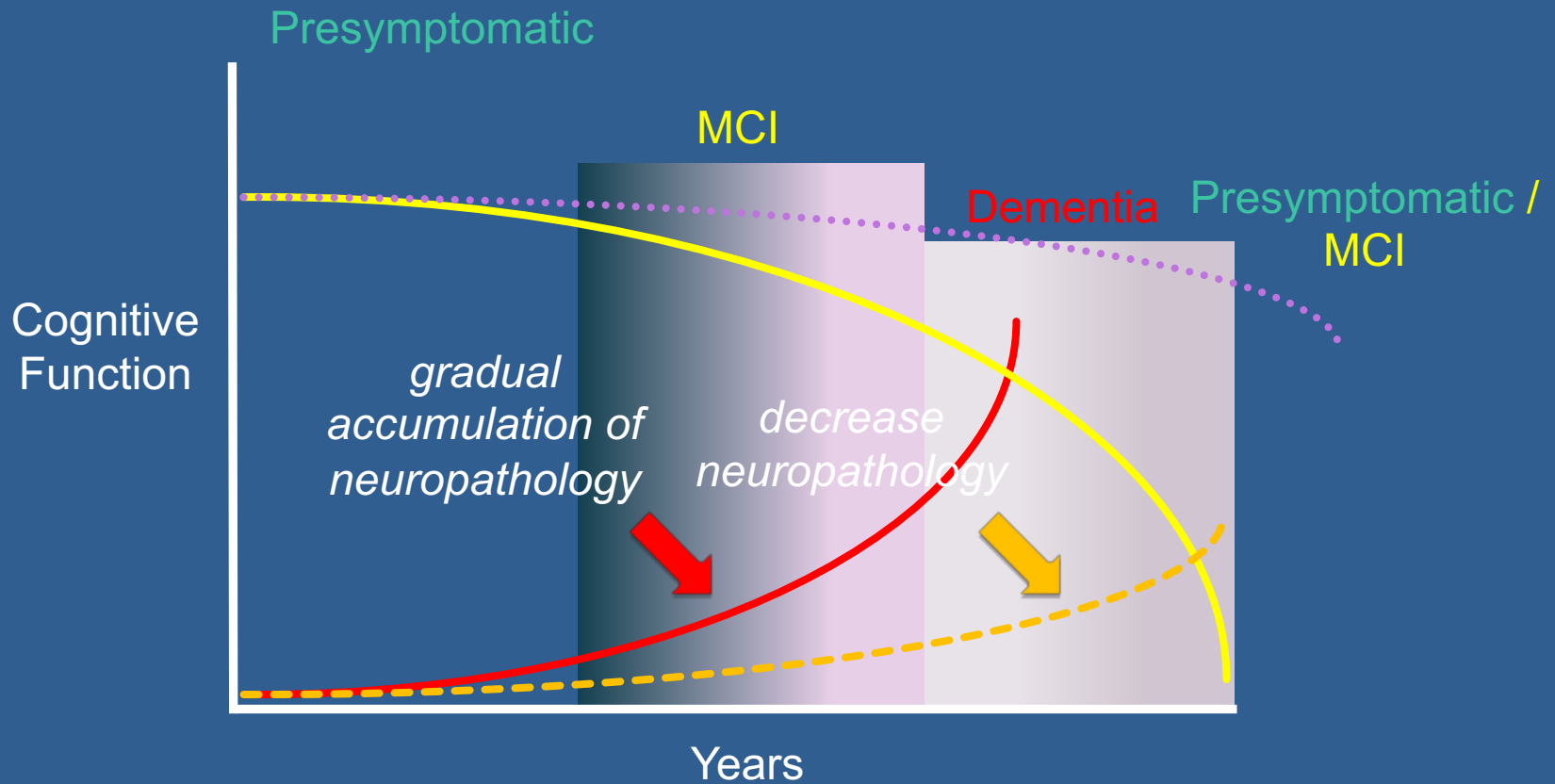- No gender or blood quantum effects (2010)

Brain autopsy results from cognitively healthy individuals
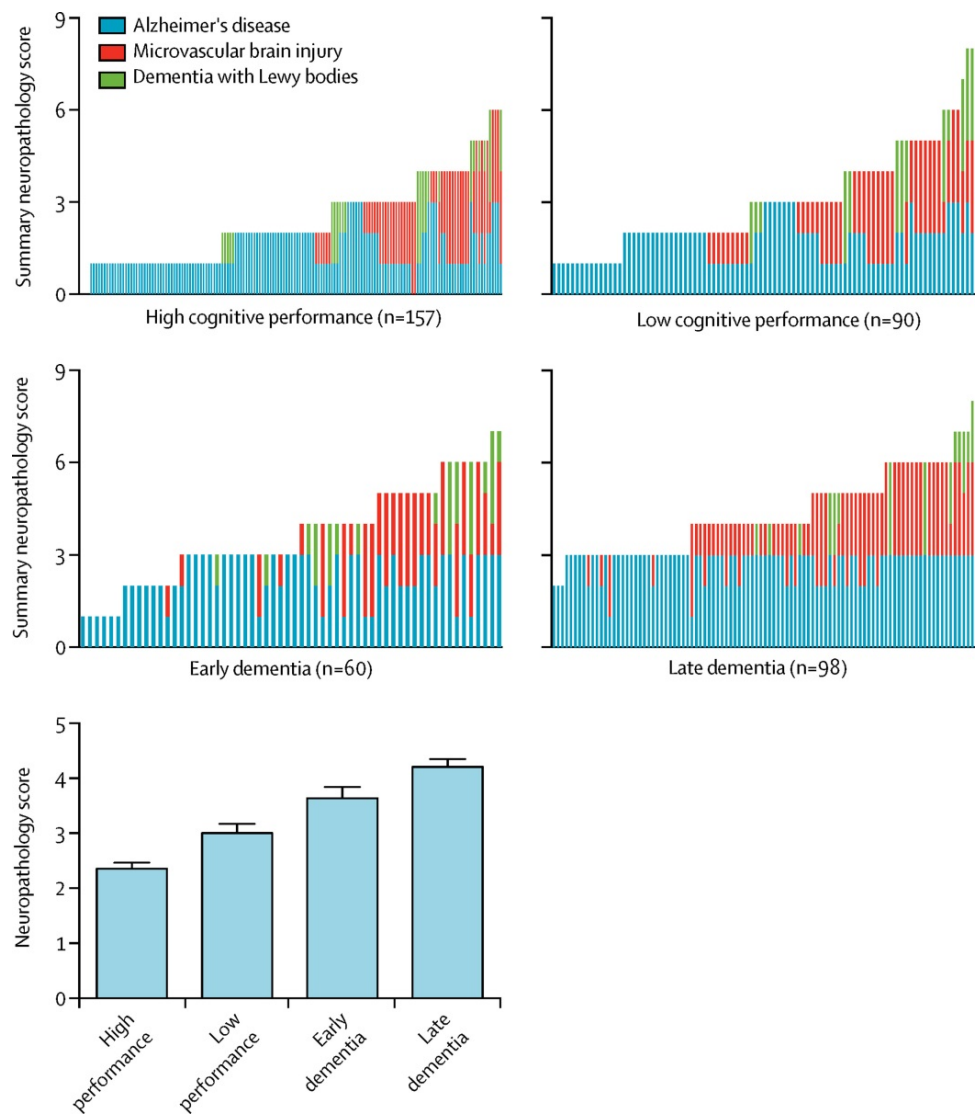
Distinguishing Normal from Pathological Aging
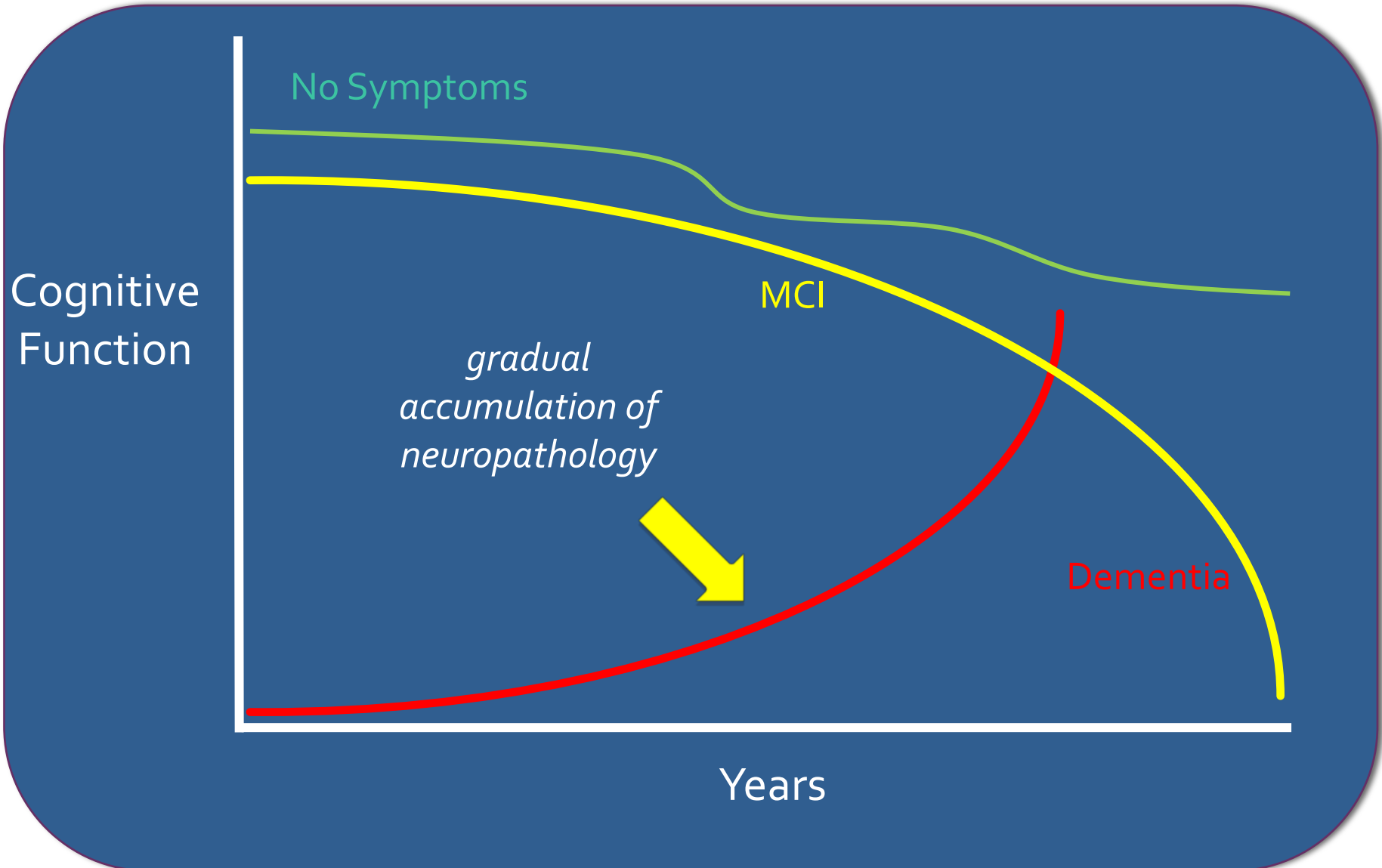
Treatment Targets

Encouraging Developments

- Critical need for culturally appropriate and ecologically meaningful measures

- Critical need for specific normative data

- Trends toward alternative approaches to interpret cognitive data (Schretlen et al)

- Viability of virtual/telemedicine neuropsychological assessment in AIAN populations (Wadsworth et al., 2016)

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Thank you for your attention!

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