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.

68% in 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.

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

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.

18th largest economy in the world exceeding the market values of companies such as Apple and Google.

Dementia: US$ 818 billion
Apple: $742 billion
Google: $368 billion

(source: Forbes 2015 ranking)

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

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

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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
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 Disease, 2010 to 2050

<table>
<thead>
<tr>
<th>Age Group</th>
<th>2010</th>
<th>2020</th>
<th>2030</th>
<th>2040</th>
<th>2050</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ages 65-74</td>
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<tr>
<td>Ages 75-84</td>
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<tr>
<td>Ages 85+</td>
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DEMENTIA, HEALTHCARE & ECONOMIC BURDEN

• $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  

• 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
**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

<table>
<thead>
<tr>
<th>Condition</th>
<th>With Alzheimer’s or other dementias</th>
<th>Without Alzheimer’s or other dementias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure</td>
<td>804</td>
<td>753</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>791</td>
<td>590</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>772</td>
<td>576</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>727</td>
<td>475</td>
</tr>
<tr>
<td>Stroke</td>
<td>716</td>
<td>550</td>
</tr>
<tr>
<td>Diabetes</td>
<td>678</td>
<td>386</td>
</tr>
<tr>
<td>Cancer</td>
<td>682</td>
<td>392</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medical Condition by Alzheimer’s/Dementia (A/D) Status</th>
<th>Total Medicare Payments</th>
<th>Hospital Care</th>
<th>Physician Care</th>
<th>Skilled Nursing Facility Care</th>
<th>Home Health Care</th>
<th>Hospice Care</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Coronary artery disease</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>With A/D</td>
<td>$26,223</td>
<td>$9,753</td>
<td>$2,199</td>
<td>$4,386</td>
<td>$2,343</td>
<td>$3,092</td>
</tr>
<tr>
<td>Without A/D</td>
<td>16,366</td>
<td>5,556</td>
<td>1,565</td>
<td>1,410</td>
<td>971</td>
<td>374</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>With A/D</td>
<td>25,385</td>
<td>7,472</td>
<td>2,154</td>
<td>4,242</td>
<td>2,267</td>
<td>2,590</td>
</tr>
<tr>
<td>Without A/D</td>
<td>14,014</td>
<td>4,681</td>
<td>1,380</td>
<td>1,225</td>
<td>844</td>
<td>255</td>
</tr>
<tr>
<td><strong>Congestive heart failure</strong></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>With A/D</td>
<td>28,773</td>
<td>8,825</td>
<td>2,310</td>
<td>4,794</td>
<td>2,455</td>
<td>3,452</td>
</tr>
<tr>
<td>Without A/D</td>
<td>24,412</td>
<td>8,960</td>
<td>2,075</td>
<td>2,596</td>
<td>1,742</td>
<td>807</td>
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<tr>
<td><strong>Chronic kidney disease</strong></td>
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<td></td>
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<td></td>
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<tr>
<td>With A/D</td>
<td>28,002</td>
<td>8,457</td>
<td>2,255</td>
<td>4,666</td>
<td>2,319</td>
<td>3,075</td>
</tr>
<tr>
<td>Without A/D</td>
<td>20,077</td>
<td>6,989</td>
<td>1,779</td>
<td>1,883</td>
<td>1,201</td>
<td>473</td>
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<tr>
<td><strong>Chronic obstructive pulmonary disease</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With A/D</td>
<td>27,797</td>
<td>8,481</td>
<td>2,283</td>
<td>4,624</td>
<td>2,399</td>
<td>3,189</td>
</tr>
<tr>
<td>Without A/D</td>
<td>18,962</td>
<td>6,792</td>
<td>1,725</td>
<td>1,749</td>
<td>1,201</td>
<td>602</td>
</tr>
<tr>
<td><strong>Stroke</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With A/D</td>
<td>26,608</td>
<td>7,751</td>
<td>2,177</td>
<td>4,564</td>
<td>2,254</td>
<td>3,199</td>
</tr>
<tr>
<td>Without A/D</td>
<td>19,169</td>
<td>6,305</td>
<td>1,753</td>
<td>2,294</td>
<td>1,455</td>
<td>605</td>
</tr>
<tr>
<td><strong>Cancer</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With A/D</td>
<td>25,207</td>
<td>7,352</td>
<td>2,109</td>
<td>3,934</td>
<td>2,074</td>
<td>2,862</td>
</tr>
<tr>
<td>Without A/D</td>
<td>15,987</td>
<td>4,833</td>
<td>1,447</td>
<td>1,050</td>
<td>692</td>
<td>484</td>
</tr>
</tbody>
</table>

*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.  

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
  o Memory
  o Executive function
  o 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):
  o Short-term (or working) memory (<1 min)
  o Long-term (lifetime) memory
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)

Sensory Store

Short Term Store (STM)

Long Term Store (LTM)

Attention

Rehearsal

Transfer

Retrieval

Information lost (forgetting)
Normal Aging, continued

• As people age, they retain their ability to perform basic ADL without needing assistance (Galvin, 2012; Gold, 2012).
  - Inability to perform IADL typically precedes inability to perform basic ADL (Galvin, 2012).
  - 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

- Vocabulary: +20% for 50 YO, +20% for 80 YO
- Mental Math: -20% for 50 YO, -20% for 80 YO
- Verbal Fluency: -40% for 50 YO, -40% for 80 YO
Normal Aging: Cognitive Changes

20 YO

- Auditory Attention
- Working Memory
- Picture Ordering

50 YO

80 YO

+20%

-20%

-40%

-60%
Normal Aging: Cognitive Changes

- Selective Attention: -60% (50 YO), -60% (80 YO)
- Mental Flexibility: -40% (50 YO), -60% (80 YO)
- Visual Construction: -20% (50 YO), -40% (80 YO)
Normal Aging: Memory Changes

- 50 YO
- 80 YO

-20% to +20%

20 YO

Story Recall

Picture Recall

List Memory
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

The graph illustrates the mean T-scores for various cognitive abilities across different age groups:

- Inductive reasoning
- Spatial orientation
- Perceptual speed
- Numeric ability
- Verbal ability
- Verbal memory

The x-axis represents age, ranging from 25 to 81 years, while the y-axis represents mean T-scores, ranging from 35 to 60.
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 lifestyle
- 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 \( N = 2 \)

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)

• 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
Sociocultural Determinants

• Culturally appropriate definitions of normality and functionality

• Acculturation (Trimble, 2000)


• Socioeconomic status

  • Rural versus urban AI/AN (Jervis & Manson, 2002)

• Linguistic and cultural translation

• Education and task familiarity
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%
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

![Graphs showing cognitive performance and neuropathology scores for different stages and conditions.]

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Distinguishing Normal from Pathological Aging

Cognitive Function

- No Symptoms
- MCI
- Dementia

gradual accumulation of neuropathology
Treatment Targets

Presymptomatic / MCI

Cognitive Function

Years

Presymptomatic

gradual accumulation of neuropathology

decrease neuropathology

MCI

Dementia

Presymptomatic / MCI
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)
Thank you for your attention!
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