Neurocognitive Disorders: Cognition and Aging

Anne Vanderbilt, MSN, CNS, CNP
Clinical Nurse Specialist
Nursing Education and Professional Practice
Geriatrics
Cleveland Clinic
• 58 year old woman presents to clinic with chief complaint of memory loss.

• She reports having difficulty remembering appointments, forgetting names and misplacing things.

• She complains of difficulty concentrating.

• This has been occurring gradually for the past 3-4 months but has been worse the past 1 month.

• She is very worried because her mother had Alzheimer’s disease when she was in her 80’s.

• What more information do you want to know?
Ms. A

• PMH: HTN, Hyperlipidemia

• PSH: Cesarean delivery x 2

• Medications:
  – Amlodipine 5mg daily
  – Simvasatin 20mg daily
  – Zoloft 50mg daily
  – Tylenol PM - prn

• SH: married with 2 teenage children, drinks 1-2 glasses of wine / day, does not smoke, no drugs, reports a lot of stress in her life right now

• VS 152/84, HR 82 R, R 20  Weight 92 kg, 171 cm

• Physical Exam is Normal
Objectives

- Describe age related changes in cognition
- Define mild cognitive impairment
- Discuss types of dementia
- State strategies to preserve cognition function as we age
What is Normal Aging?

“You can only perceive real beauty in a person as they get older” Anouk Aimee

- Highly individualized
- Biological vs. chronological age
- Effect of exercise and lifestyle

Source: Microsoft clip art
Normal Age Related Changes

Senior citizen bond:
I still haven't found what I'm lookin' for.

In fact... I can't remember what I came in here for in the first place...

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Age related structural changes - Neurology

- Reduced brain size
- Reduced nerve cells
- Decreased cerebral blood flow
- Slower nerve conduction velocity resulting in slower reflexes and delayed response to stimuli

Source: radiology assistant. Alzheimer Centre and Image Analysis Centre, Vrije Universiteit Medical Center, Amsterdam and the Rijnland Hospital, Leiderdorp, The Netherlands
Age Related Cognitive Changes

• Personality is unchanged
  – But may be expressed more openly

• Intelligence is unchanged
  – Crystallized intelligence
    – Ability to use skills, knowledge, and experience
  – Fluid intelligence or fluid reasoning
    – Capacity to think logically and solve problems in novel situations
    – Independent of acquired knowledge

• Early phases of learning are more difficult

• Working memory is reduced
Conditions that Affect Cognition OTHER than Dementia

• Depression and Stress
• Sleep deprivation
• Alcohol and substances abuse
• Head Injury
• Stroke
• Vitamin Deficiency – B12, folate
• Hypothyroidism
• Infection; ie Tertiary syphilis, HIV
• Delirium
• MEDICATIONS: anticholinergics, antihistamines, benzodiazepines, muscle relaxants, hypnotics and opioids
Mild Cognitive Impairment (MCI)

- National Institute of Aging and Alzheimer’s Association Criteria 2011
- Must meet all 4 criteria

1. Concern regarding a change in cognition
   - Concern may be from patient, family or clinician

2. Impairment in one or more cognitive domain
   - usually episodic memory
   - decline in performance over time

3. INTACT level of functional abilities

4. NO DEMENTIA
More on Mild Cognitive Impairment

• Some cognitive decline is measurable on advanced tests such as the Montreal Cognitive Assessment (MOCA)

• Some difficulty with complex tasks found at work

• Often need to write more things down and / or work at a slower pace
Does MCI progress to Dementia?

• Probably but not always

• Rate of progression from MCI to Alzheimer’s Disease
  – 6 to 25% per year
  (American Academy of neurology – AAN - 2001)

• Some studies suggest 80% conversion in 6 yrs

• Some evidence that MCI is Pre- Dementia
Myths vs. Facts about Dementia

• Memory loss is a natural part of aging

• Alzheimer’s disease is more common in women

• Inability to maintain attention and changing level of consciousness is a symptom of dementia

• Diabetes is a risk factor for dementia

• There are more than 10 types of dementia
Dementia Defined

- Umbrella term describing symptoms
- A “syndrome” of impaired cognition caused by brain dysfunction (loss of intellectual capacity)
- A progressive cognitive decline that occurs in a normal state of consciousness and in the absence of other acute or subacute disorders

Source: radiology assistant.
Dementia (DSM-IV) Complex Medical Syndrome

- Memory impairment
- One or more of the following cognitive disturbances:
  (a) aphasia (language disturbance)
  (b) apraxia (impaired ability to carry out motor activities)
  (c) agnosia (failure to recognize or identify objects)
  (d) disturbance in executive functioning (i.e., planning, organizing, sequencing, abstracting)
- Significant impairment in functioning and a significant decline from a previous level
- Deficits do not occur exclusively during the course of a delirium
DSM 5 – Criteria for Neurocognitive Disorders

Mild or Major

- No longer use the term “Dementia”
- Memory loss is no longer a requirement for diagnosis

1. Cognitive decline from a previous level of performance in one or more of domains
2. Deficits in testing or equivalent clinical evaluation
3. The cognitive deficits are sufficient to interfere with independence
4. The cognitive deficits do not occur exclusively in the context of a delirium.
5. The cognitive deficits are not primarily attributable to another mental disorder
Background of Dementia

• Primarily a disease of late life
  > 65: 10%
  > 85: 60%

• Many types
  – Alzheimer’s
  – Vascular
  – Lewy Body
  – Frontotemporal
  – Normal pressure hydrocephalus
  – Mixed

• Estimated that 1/2 people with dementia are undiagnosed

• Primary reason for institutionalization
Types of Dementias

- Alzheimer’s disease 50-80%
- Vascular dementia 10-15%
- Dementia with Lewy Bodies
- Frontotemporal Dementias 10 %
- Normal Pressure Hydrocephalus (NPH)
- Mixed Dementia
Alzheimer’s Disease (AD)

- Most common form in the elderly
- 5.4 million in the U.S.
- Beta-amyloid protein plaques build up between neurons
- Tau proteins build up
  - Inside the cells and cause neurofibrillary tangles
- Begins in the hippocampus (memory center)
- Gradually moves to other areas of the brain
- Decreased acetylcholine
- Impaired glucose metabolism
- Slow progressive disease
  - Average is 8 to 10 years but may be much longer

http://www.alz.org/braintour/plaques_tangles.asp
Recent Research / Diagnosis

• Biomarkers in Cerebrospinal fluid
  – Amyloid 42 (A42) detected

• PET scan with radiotracer PDG detects glucose uptake

• Functional MRI

Source: radiology assistant. Alzheimer Centre and Image Analysis Centre, Vrije Universiteit Medical Center, Amsterdam and the Rijnland Hospital, Leiderdorp, The Netherlands
New Criteria and Guidelines 2011

• National Institute on Aging (NIA) and the Alzheimer’s Association

• Three stages of Alzheimer’s Disease
  1. Preclinical disease
  2. MCI due to AD
  3. Alzheimer’s DEMENTIA

• Role of Imaging and biomarkers under investigation
  – Not used routinely for clinical practice
Early Onset Alzheimer’s Dementia

“The Great American Love Goddess.”

• < 1 % of cases

• Onset of cognitive symptoms < 65 – usually much earlier

• Presenile genes PS1, PS2

• More rapid course of decline

Source: classicmoviepeople.com
Alzheimer’s Risks Factors

• Age (over 65)
• Female gender
• African American (2x) or Hispanic (1.5x)
• APOE 4 allele (lipoprotein gene)  
  – May be a factor in 20-25%
• Low education
• Depression
• History of head injury
• Heart disease
• Diabetes
  \[ \text{Vascular Disease} \]
• Smoking
Vascular Dementia

• Impairment of blood flow to parts of the brain
  – Multi-infarct
  – TIA

• Symptoms similar to Alzheimer’s
  – Memory loss less pronounced
  – Decision making more affected

• May have step-like progression symptoms instead of slow progressive decline

• ‘PURE’ vascular dementia is uncommon – 10-15%

• MIXED vascular dementia is VERY common

Source: Alzheimer’s Association
Dementia with Lewy Bodies

- Lewy bodies deposits in areas of the brain
- Presents with impairment in attention and alertness
- Usually visual hallucinations in early stages
- Muscle rigidity and tremors similar to Parkinson’s disease
- Younger patients
- Faster course of disease
Frontotemporal Dementia (FTD)

ie primary progressive aphasia, Pick’s disease and progressive supranuclear palsy

• Younger age onset typically 45 – 65 yo
  – more common than AD in the younger population

• Prominent behaviors
  – Personal neglect, disinhibition, hyperorality

• Speech disorders
  – Aphasia and echolalia

• Rapid decline
Normal Pressure Hydrocephalus (NPH)

Clinical Triad

1. Gait apraxia (**paramount symptom**)  
2. Urinary incontinence  
3. Confusion

- **Neuroimage**  
  - Pronounced ventricular enlargement
- **Clinical improvement with shunt**
- **No reliability predicting shunt effects**

*Source: hydrocephalus association*
Mixed Dementia

- Vascular: 9%
- Alzheimer Disease: 47%
- Lewy Body: 2%
- Frontotemporal: 5%

Chertkow H CMAJ 2008;178:316-321
How to make a Diagnosis? True or False

• AD can only truly be diagnosed by autopsy
• CT scan or MRI can identify dementia
• PET scan or fMRI should be ordered routinely for diagnosis of dementia
• Neuropsych testing should be ordered routinely for diagnosis of dementia
• Alzheimers Disease can be diagnosed accurately by history and exclusion of other pathologies
Guidelines for Diagnosis


• American Geriatric Society – 2010

• History: Always obtain from family or other caregiver:
  – Progression of symptoms
  – Head injury
  – Alcohol or other substance use
  – Depression

• Comprehensive physical and neurologic examination

• Assess functional status – ADL and IADL

• Evaluate mental status for attention, immediate and delayed recall, remote memory, executive function, depression.
  – Mini-Cog, Minimental status exam. Montreal Cognitive Assessment
  – Number of animals named in 1 minute
    – 18 is average; less than 10 markedly abnormal, MMSE,
  – Geriatric Depression Scale, PHQ – 9
Cognitive Assessment

Part of comprehensive mental status examination including

• Orientation
• Attention and concentration
• Memory
• Judgment
• Executive control functions
• Speech and language
• Presence of delusions, hallucinations
• Mood and affect
Mini-Cognitive Assessment Instrument (Mini-Cog)

Step 1. Ask the patient to repeat three unrelated words, such as “ball,” “dog,” and “television.”

Step 2. Ask the patient to draw a simple clock set to 10 minutes after eleven o’clock (11:10). A correct response is a drawing of a circle with all of the numbers placed in approximately the correct positions, with the hands pointing to the 11 and 2.

Step 3. Ask the patient to recall the three words from Step 1. One point is given for each item that is recalled correctly.

**Interpretation**

<table>
<thead>
<tr>
<th>Number of items correctly recalled</th>
<th>Clock drawing test result</th>
<th>Interpretation of screen for dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal</td>
<td>Positive</td>
</tr>
<tr>
<td>0</td>
<td>Abnormal</td>
<td>Positive</td>
</tr>
<tr>
<td>1</td>
<td>Normal</td>
<td>Negative</td>
</tr>
<tr>
<td>1</td>
<td>Abnormal</td>
<td>Positive</td>
</tr>
<tr>
<td>2</td>
<td>Normal</td>
<td>Negative</td>
</tr>
<tr>
<td>2</td>
<td>Abnormal</td>
<td>Positive</td>
</tr>
<tr>
<td>3</td>
<td>Normal</td>
<td>Negative</td>
</tr>
<tr>
<td>3</td>
<td>Abnormal</td>
<td>Negative</td>
</tr>
</tbody>
</table>
Clock Draw Test

Normal Score 10

Mild Cognitive Impairment
(Numbers error and placement of hands)
Score 8

Moderate Cognitive Impairment
Score 4

Severe Cognitive Impairment
Score 2

Source: Journal of American Board of Family Medicine 2003

Sunderland, 1989  
UB  74
## PHQ-9

**PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)**

Over the last 2 weeks, how often have you been bothered by any of the following problems? (Use *✓* to indicate your answer)

<table>
<thead>
<tr>
<th></th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Little interest or pleasure in doing things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Feeling down, depressed, or hopeless</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. Trouble falling or staying asleep, or sleeping too much</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. Feeling tired or having little energy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. Poor appetite or overeating</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7. Trouble concentrating on things, such as reading the newspaper or watching television</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>9. Thoughts that you would be better off dead or of hurting yourself in some way</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

**For office coding:**

0 + 0 + 0 + 0 = Total Score: __________

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

<table>
<thead>
<tr>
<th>Not difficult at all</th>
<th>Somewhat difficult</th>
<th>Very difficult</th>
<th>Extremely difficult</th>
</tr>
</thead>
<tbody>
<tr>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>

Developed by Drs. Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke and colleagues, with an educational grant from Pfizer Inc. No permission required to reproduce, translate, display or distribute.
More Advanced Test

• Cognition

1. Folstein Mini-Mental Status

2. Montreal Cognitive Assessment
   www.mocatest.org/pdf_files/test/MoCA-Test-English_7_1.pdf

3. St Louis University Mental Status Assessment
   medschool.slu.edu/agingsuccessfully/pdfsurveys/slumsexam_05.pdf
Labs and Imaging

• Labs
  – CBC, THS, B12, folate, serum calcium, liver and kidney function tests, electrolytes

• Serologic test for syphilis (selectively)

• Glucose and HIV for patients at risk

• Non-Contrast CT or MRI

• Likelihood of detecting structural lesions is increased with
  – Onset age <60 years
  – Focal (unexplained) neurologic signs or symptoms
  – Abrupt onset or rapid decline (weeks to months)
  – Predisposing conditions (eg, metastatic cancer or anticoagulants)

• Neuroimaging may detect the 5% of patients with clinically significant structural lesions that would otherwise be missed

• FDG-PET scans approved by Medicare for atypical presentation of course of AD in which frontotemporal dementia diagnosis is suspected
# Functional Assessment

<table>
<thead>
<tr>
<th>Activities of daily living (ADL)</th>
<th>Instrumental activities of daily living (IADL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Bathing</td>
<td>• Telephone</td>
</tr>
<tr>
<td>• Dressing</td>
<td>• Shopping</td>
</tr>
<tr>
<td>• Transferring</td>
<td>• Food prep</td>
</tr>
<tr>
<td>• Eating</td>
<td>• Housekeeping</td>
</tr>
<tr>
<td>• Toileting</td>
<td>• Laundry</td>
</tr>
<tr>
<td>• Continence</td>
<td>• Transportation</td>
</tr>
<tr>
<td></td>
<td>• Medications</td>
</tr>
<tr>
<td></td>
<td>• Finances</td>
</tr>
</tbody>
</table>
Behavior Assessment

All behavior has meaning and is used to communicate or express unmet needs and/or difficulty managing stress

- Restlessness
- Anxiety
- Irritability
- Anger outbursts
- Verbal and physical aggression
- Wandering
- Repetitive vocalizations
- Hoarding, rummaging
- Delusions
- Hallucinations
Ms. A

- 58 yo woman presents to clinic with chief complaint of memory loss.
- She reports having difficulty remembering appointments, forgetting names and misplacing things.
- She complains of difficulty concentrating.
- This has been occurring gradually for the past 3-4 months but has been worse the past 1 month.
- She is very worried because her mother had Alzheimer’s disease when she was in her 80’s.

- PMH: HTN, Hyperlipidemia
- PSH: Cesarean delivery x 2
- Medications:
  - Amlodipine 5mg daily
  - Simvasatin 20mg daily
  - Zoloft 50mg daily
  - Tylenol PM - prn
- Social history
  - Married with 2 teenage children, drinks 1-2 glasses of wine / day, does not smoke, no drugs, reports a lot of stress in her life right now
- VS 152/84, HR 82 R, R 20
- Weight 92 kg, 171 cm
- Physical Exam is normal
Delirium vs. Dementia
Delirium (DSM IV)

1. Disturbed consciousness
2. Change in cognition or perception (not dementia)
3. Acute onset; fluctuation
4. Physiological consequence of medical condition

Source: Cleveland Clinic Center for Geriatric Medicine
**Delirium Clinical Presentation**

<table>
<thead>
<tr>
<th>Onset shortly after admission to hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hyperactive</strong></td>
</tr>
<tr>
<td>• Increased psychomotor activity</td>
</tr>
<tr>
<td>• Rapid speech</td>
</tr>
<tr>
<td>• Irritability</td>
</tr>
<tr>
<td>• Restlessness</td>
</tr>
<tr>
<td>• Paranoia</td>
</tr>
</tbody>
</table>

*Variable, unpredictable course and may persist for several weeks after discharge*
Delirium: Precipitating Factors

Surgical: Type surgery; Intra-operative blood loss; post-op anemia
Medical: Severity illness; restraints; psychotropic drug(s); > 3 medications; bladder catheter; iatrogenic event

Predisposing Factors
- Old
- Sensory impaired
- Cognitive impaired
- Malnourished
- Dehydration
- Depression
- Prior delirium

Protective Factors
- Young
- Healthy
- High functional Status

## Differentiate Delirium vs. Dementia

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Delirium</th>
<th>Dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Short, rapid, hours/days</td>
<td>Insidious and gradual</td>
</tr>
<tr>
<td>Presentation</td>
<td>Disoriented, fluctuating moods</td>
<td>Vague symptoms, loss of intellect, agitated, aggressive</td>
</tr>
<tr>
<td>Course</td>
<td>Hours, weeks, or longer</td>
<td>Slow and continuous</td>
</tr>
<tr>
<td>Sleep/Wake</td>
<td>Worse at night in darkness and on awakening, insomnia</td>
<td>Worse in evening; “sundowning”, reversed sleep</td>
</tr>
<tr>
<td>Duration</td>
<td>Hours to &lt; month</td>
<td>Month to years</td>
</tr>
<tr>
<td>Affect</td>
<td>Labile variable; fear/panic, euphoria, disturbed</td>
<td>Easily distracted, inappropriate anxiety, labile to apathy</td>
</tr>
</tbody>
</table>
## Differentiate Delirium vs. Dementia

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Delirium</th>
<th>Dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Judgment</strong></td>
<td>Impaired; difficulty separating facts and hallucinations</td>
<td>Impaired, bad/inappropriate decisions, denies problems</td>
</tr>
<tr>
<td><strong>Psychotic symptoms</strong></td>
<td>Delusions</td>
<td>Misperceives people and events as threatening; late delusions, hallucinations</td>
</tr>
<tr>
<td><strong>Level of Consciousness</strong></td>
<td>Disturbed</td>
<td>Intact</td>
</tr>
<tr>
<td><strong>Recent Memory</strong></td>
<td>Impaired, but remote memory is intact</td>
<td>Short term memory deficit in early course, progresses to long-term deficits, confabulation, perseveration</td>
</tr>
</tbody>
</table>
Depression in Older Adults

- Most common emotional disorder
- Mild to severe forms
- Symptoms
  - Depressed mood
  - Associated psychological symptoms
  - Somatic manifestations
  - Suicidal thoughts or attempts
  - Psychotic symptoms
1. Depressed, sad, or irritable mood
2. Diminished pleasure in people/activities
3. Feelings of worthlessness, self reproach, excessive guilt
4. Difficulty thinking or diminished concentration
5. Suicidal thinking or attempts
6. Fatigue and loss of energy
7. Changes in appetite & weight
8. Disturbed sleep
9. Psychomotor agitation or retardation
Depression and Cognitive Impairment

• Common Together

• Cause and effect unknown

• “Pseudodementia”
  – Major depression misdiagnosed as dementia
  – slow to answer questions
  – Many non-responses
  – “I don’t know” responses

• Depression may also be mistaken for hypoactive delirium

Source: At home personal care
Does the Type of Dementia Really Matter?
Consequences

• Patients with dementia have difficulty
  – Identifying changes in health status
  – Describing symptoms of co-morbid conditions
  – Asking clearly for pain relief
  – Comprehending instructions
  – Following directions for self care and safety

• Are more vulnerable to stress when making transitions in care
Truth vs. Myth - Treatment

• Nemanda
  – Newest drug to treat AD reverses the damage done to the brain

• High doses of Vitamin E
  – Has shown to be beneficial to people with dementia

• Estrogen
  – Recommended for postmenopausal women to prevent development of AD

• NSAIDs
  – Have been shown to be effective in slowing the progression of dementia
Treatment - Pharmacology

- Cholinesterase Inhibitors
- Tacrine (Cognex)- Off market in USA
- Donepezil (Aricept)
- Rivastigmine (Exelon)
- Galantamine (Razadyne)

- Memantine (Nemanda)
Alternative Treatments

- Phosphatidylserine
- Coral calcium
- Tramiprosate
- Coenzyme Q10
- Ginkgo biloba
- Huperzine A
- Omega-3 fatty acids
- Medical foods - Caprylic acid / Axona

Source: alzheimer’s association
Alternative Treatments

- Phosphatidylserine
- Coral calcium
- Tramiprosate
- Coenzyme Q10
- Ginkgo biloba
- Huperzine A
- Omega-3 fatty acids
- Medical foods - Caprylic acid/ Axona

Source: alzheimer’s association
Nonpharmacological Interventions

- Regular physical exercise
- Mental stimulating activity
- Socialization
- Diet
  - High in antioxidants
  - Mediterranean
Mr. B

• 68 yo man brought to office by family for concerns about behavior change, angry and irritable alternating with periods of pronounced apathy, repetitiveness, misplacing things, poor judgement, poor behavioral control, gradual onset over 4 years

• PMH
  – HTN, OA

• Medications
  – Lisinopril, HCTZ

• Social history
  – Rare ETOH, no smoking or illicit drugs
  – Physically active
  – 12 years education
Evaluation

• MMSE 22 / 30
  – Deficits in ST memory and executive function

• MOCA 13 / 30
  – CT scan - mild atrophy and small amount of white matter changes

• What next?
PREVENTION
Healthy is Brain Healthy

• Healthy brain initiative
• Diet
• Exercise
• No smoking
• Avoid alcohol
• Manage cholesterol
• Manage diabetes
Cognitive Reserve – Education – Mentally Stimulating Activity

- People with fewer years of education are at higher risk for Alzheimer’s and other dementias
- More years of education builds a “cognitive reserve” that enables individuals to better compensate
- Cognitive reserve hypothesis - education increases the connections between neurons
- Learn a new language
- Learn to play on instrument
- Benefit of mentally stimulating computer games
  - Luminosity
Mental Exercises / Neurobotics

• Lifetime of complex mental activities decreased the risk of dementia by 50%
  — Reading
  — Socially active
  — Inquisitive
  — Avoiding routine

• It’s never too late to start exercising the brain
Mind Exercise

• Which of the following two words are most opposite in meaning?
  – Irrational, pleasing, privy, wise, perceptible

• Which of the following two words are closest in meaning?
  – Change, stereotype, delete, pigeonhole, identify
Mind Exercise

• Which of the following two words are most opposite in meaning?
  — *Irrational*, pleasing, privy, *wise*, perceptible

• Which of the following two words are closest in meaning?
  — Change, *stereotype*, delete, *pigeonhole*, identify
Future Directions

• More to come
  – Role of imaging and biomarkers on diagnosis

• Vaccination

• Use of inhaled Insulin

• Lifestyle
  – Diet, mental and physical activity
Healthy Aging

- ngm.nationalgeographic.com/ngm/0511/sights_n_sounds/index.html
Cleveland Clinic

Every life deserves world class care.