POWER OF POSITIVE AGING

NEUROPLASTICITY AND THE AGING BRAIN
Worlds First Senior Moment
• Loss of memory is a normal part of aging
• The brain can form new connections throughout life
• We can predict which individuals with memory complaints will progress to Alzheimer’s disease dementia
THERE WILL BE A LOT OF AGING BRAINS

• By 2029, 20% of population over 65

• 65 y/o will live, on average, 20 more years

• Effect of 10-25% reduction in 7 risk factors may prevent up to 500,000 cases of AD
IS MEMORY LOSS A NORMAL PART OF AGING
MEMORY

• Multiple sub-systems:
  ➢ **Episodic** (personally relevant events/episodes)
  ➢ **Working** (manipulate learned info)
  ➢ **Semantic** (knowledge of facts, meaning of words)
  ➢ **Procedural** (performance of skills)
• Can run independently
MEMORY PROCESS

Immediate Memory

1. encoding

Short Term Memory

2. storage

Long Term Memory

3. Retrieval
WHAT'S NORMAL, WHAT'S NOT?

Cognitive Function

Normal Aging

Years
NORMAL COGNITIVE AGING

- Slowing of central processing
- Mild changes in memory
- Other cognitive abilities relatively preserved
NORMAL AGING: COGNITIVE CHANGES

Vocabulary
Mental Math
Verbal Fluency

-60%
-40%
-20%
+20%

20 YO

50 YO
80 YO
NORMAL AGING: COGNITIVE CHANGES

20 YO

Selective Attention

Mental Flexibility

Visual-Construction

50 YO

80 YO

+20%

-20%

-40%

-60%
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?
MEMORY CAN WORSEN DUE TO:

- Stress/anxiety/depression
- Overly tired/ sleep deprivation
- Medications (hypnotics, narcotics, anti-cholinergics, anti-histamines)
- Medical conditions (thyroid, sleep apnea, vitamin deficiencies, etc.)
- Alcohol, drugs
- Neurodegenerative disease
PHYSIOLOGY OF BRAIN AGING
DOES AGING CAUSE LOSS OF BRAIN CELLS?

Yes, but not overwhelming

- 20 y/o -- 20 billion cells
- 90 y/o -- 10% less
- 0.5-1% volume loss/ year
SYNAPSES WITH AGING

• Synapses are connections between cells

• Age related loss of synaptic density

• Programmed loss of neurons and synapses in early development – may be same with aging
+ AGING CHANGES

- Cortical myelin increase into 7th decade
- Dendritic branching can continue
- Axonal sprouting
NEUROPLASTICITY
WHAT IS IT?

• Processes that result in stability or compensation for age or disease related changes
• Include:
  • Neurogenesis (new cells)
  • Synaptogenesis (new connections between cells)
  • Dendritic arborization (improved reserve)
NEUROGENESIS

- Adult hippocampal neurogenesis
  Neural stem cells
  Requires appropriate microenvironment
  Important for cognitive and emotional regulation
REMODELING

- Synaptic function
- Dendritic branching
- Axonal Sprouting

Fig. 1 – Two possible patterns of age-related alterations in cortical pyramidal cells. The normal mature neuron (A) may show regressive dendritic changes characterized by loss of basilar dendritic branches and eventual loss of the entire dendritic tree (D, E, F). Other neurons (B, C) may show progressive increase in dendritic branching. Drawing based on Golgi impregnations.
NEUROPLASTICITY STRATEGIES

- Lifestyle
- Exercise
- Diet
- Cognitive
- Stress reduction
- Pharmacologic
PHYTOCHEMICALS

- Cucumin
- Resveratrol
- Ginkgo biloba
- Coconut Oil
- Marijuana

- Antioxidant
- Anti-inflammatory
- Improved metabolism
CURCUMIN

- Derived from turmeric (curuma longa)
- Used as food preservative and spice
- Prevalence of AD 4 X less in India
- May be anti-amyloid, anti-oxidant, anti-inflammatory
CURCUMIN

- Hard to absorb
- Has many chemicals in it
- Human trials have yet to show benefit
RESVERATROL

- Found in grapes, red wine and berries
- Wine consumption may reduce risk of AD
- Neuroprotective properties
- Trial in AD was negative
GINKGO BILOBA

- Ginkgo tree found in Korea, Japan, China
- Tree can live for 1000 years
- Usually contains 24% flavonoids, 6% terpenoids – dose 120-240 mg a day
- Negative studies in AD and normal aging
COCONUT OIL

- Caprylic acid comes from coconut oil
- Medium chain fatty acid
- Converted to ketones which brain can use for energy
- No studies to show effectiveness
- Medical food (Axona) similar idea
POLY UNSATURATED FATTY ACIDS

- Omega 3 Fatty Acids/ DHA
- Fundamental to CNS function
- Mainly from fish
- Epidemiology studies suggest cognitive benefit (but not all)
- AD trial negative
MARIJUANA

- Contains cannabinoids
- Brain has cannabinoid receptors
- May be neuroprotective, ↓ inflammation
- May improve appetite, agitation, sleep
- But... study results inconsistent
  - small numbers tested
  - short period of time
MARIJUANA

- Quality and potency of drug not assured
- Correct dose unclear
- THC may not be all bad but needs standardization
- *We need more reliable studies*
NORMAL “FORGETFULNESS” VS. ALZHEIMER’S DISEASE
ALZHEIMER’S DISEASE EXISTS ON A CONTINUUM FROM NO/MINIMAL SYMPTOMS TO DEMENTIA

- No Symptoms
- Mild Cognitive Symptoms
- Increasing Cognitive Dysfunction; Increasing Neurodegeneration
- Dementia

Time

(© JL Cummings, 2008)
The Original Amyloid Cascade Hypothesis

Alzheimer’s is the cumulative product of a series of pathological events that may begin with the deposition of beta-amyloid in the brain.
WHAT’S NORMAL, WHAT’S NOT?

Cognitive Function

No Symptoms

MCI

gradual accumulation of neuropathology

Dementia

Years
DEMENTIA

- Decline in memory and other cognitive functions
- Impairs social or occupational function
- Absence of delirium
- Dementia ≠ Alzheimer’s
PREDEMENTIA AD (AMNESTIC MCI) PATIENTS WITH AD-TYPE AMYLOID PROGRESS TO ALZHEIMER’S DEMENTIA

Number progressing to AD

Time (months)

Normal amyloid level
Pathological amyloid level

Hansson et al, Lancet Neurol 2006; 5: 228–234
AMYLOID IMAGING:
RISK FACTORS FOR ALZHEIMER’S

• Age
• Genetics
• Cardiovascular factors
• But....there may be protective factors:
  • Exercise
  • Education
  • Social engagement
• Diet
QUIZ

• Loss of memory is a normal part of aging
• The brain can form new connections throughout life
• We can predict which individuals with memory complaints will progress to Alzheimer’s disease dementia
SUMMARY

• Cognitive function can remain at a high level throughout life

• Brain can remodel itself throughout life

• Many interventions may promote neuroplasticity
  Difficult to measure neuroplasticity in humans

• Lifestyle interventions have important role and combined could have significant impact