AGING, MEMORY, AND THE BRAIN

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NORMAL AGING AND THE BRAIN

- Reduced brain weight and volume
- Fewer neurons
- Widening of sulci (grooves)
- Enlargement of the ventricular system

NORMAL AGING AND THE BRAIN

- Decreased number of proteins
- Decreased enzyme levels (DA & NE)
- Decreased number of receptors (DA, NE, and Ach)
- Sensory changes

AGING AND MEMORY

STABLE MEMORY FUNCTIONS IN AGING

- Remote memory
- Crystallized abilities
- Recall of verbal information
- Remembering “gist” / themes
- Simple Attention

AGE-SENSITIVE MEMORY FUNCTIONS

- New Learning (particularly if exceeds working memory span)
- Rapid Learning
- Recall of nonverbal information
- Remembering details
- Material requiring manipulation or multitasking

MEMORY DYSFUNCTION IN ALZHEIMER'S DISEASE

- Impaired encoding
- Rapid forgetting
- Recency Recall
- Intrusions during recall
- Impaired Recognition

MEMORY IN OLD AGE VERSUS AD

- Despite overlap, each displays a distinct pattern in memory performance
- Qualitative features assist discrimination
- Findings suggest different underlying processes; not a continuum

MILD COGNITIVE IMPAIRMENT (MCI)

- Memory disturbance in absence of other cognitive deficits or frank dementia
- Performance on formal memory testing that falls below normal (WMS)
- May = early phase of Alzheimer's (10% / yr)

ALZHEIMER'S DISEASE

ALZHEIMER'S DISEASE IN TEXAS

- 280,964 people with AD in Texas alone
- Prevalence - 10% increase with each decade over 65
- Population is aging
  - Over 85, 2M in 1900, 20M in 1997, 30-40M in 2030
- In 2025, -> 97% increase -> 1/2M

IMPACT OF ALZHEIMER'S DISEASE ON SOCIETAL COSTS

- Some studies report that Alzheimer's disease costs $100 billion in the United States annually
- A cost of $35,000 per patient per year
- Alzheimer's patients/families spend >$200,000 over the remainder of the patient's life
- 10% to 30% of nursing home residents have Alzheimer's disease

DIAGNOSTIC CRITERIA FOR ALZHEIMER'S DISEASE

- Development of multiple cognitive deficits manifested by both
  - Memory impairment
  - One (or more) of the following cognitive disturbances: aphasia; apraxia; agnosia; disturbance in executive functioning
- Significant impairment in social or occupational functioning, representing a significant decline from a previous level of functioning
- Gradual onset and progressive cognitive decline

DIAGNOSTIC CRITERIA FOR ALZHEIMER'S DISEASE (cont)

- Cognitive deficits are NOT due to any of the following:
  - Other central nervous system conditions that cause progressive deficits in memory and cognition
  - Systemic conditions that are known to cause dementia
  - Substance-induced conditions
- Deficits not occurring exclusively during the course of a delirium
- Disturbance not better accounted for by another Axis I disorder

THE 5 A'S OF ALZHEIMER'S DISEASE

- Amnesia
- Agnosia
- Aphasia
- Apraxia
- Abstraction

SYMPTOMS OF ALZHEIMER'S DISEASE

- Gradual memory loss
- Decline in ability to perform routine tasks
- Disorientation
- Poor judgment
- Language ("empty speech")
- Apathy/poor motivation

MEMORY LOSS IN ALZHEIMER'S DISEASE

- "Memory leads the way"
- Memory worst and first
- More problems with new (recent) info than with old (remote)

DIAGNOSIS OF ALZHEIMER'S DISEASE

- IMPORTANT - IT'S TREATABLE!
  - reversible conditions (depression, thyroid, B12)
  - cholinesterase inhibitors
  - other: NSAIDS, estrogen, chol Rx, BP Rx, stroke Rx
- IMPORTANT - Rx is not only treatment
- What is most important in diagnosing AD?

DIAGNOSTIC WORK-UP FOR DEMENTIA

- Diagnostic Interview
- Exam, including Neurologic and Mental Status exam
- Labs(CBC,chemistries,LFTs,TSH,RPR/MHA-TP,Vit B12,cholesterol)
- Neuroimaging
- Neuropsychological evaluation
- Language evaluation, LP, genetics - specialist referral

NEUROBEHAVIORAL HISTORY AND EXAM

- Attention
- Visuospatial
- Language
- Memory
- Executive Functions
- Personality/Behavior

STAGES OF ALZHEIMER'S DISEASE

- Stage I (1-3 y) - poor recent memory, may get lost, empty speech, apathetic
- Stage II - (2-10 y) poor recent and remote memory, gets lost easily, empty speech, poor comprehension, agitation, delusions
- Stage III - very poor thinking, repeats words, limb rigidity, incontinence

PATHOPHYSIOLOGIC MECHANISMS IN ALZHEIMER'S DISEASE

- Cholinergic mechanisms
- Neuritic plaques
  - Beta-amyloid
- Neurofibrillary tangles
- Free-radical mechanisms
- Inflammatory mechanisms
- Cholesterol/statins?

TREATMENT OF ALZHEIMER'S DISEASE

- Cholinesterase inhibitors
- Vitamin E
- Hormone replacement
- NSAIDS
- Herbal
- "Amyloid Vaccine"?!, "ACE" inhibitors
- Antidepressants/other psychiatric
- Behavior/environment modification

CHOLINESTERASE INHIBITORS:

- Approved for use in mild-moderate AD (MMSE ~10-26)
- GI side effects
- Expected outcome of therapy - to SLOW decline
- ADL's, Behavior, Cognition improved up to 2 yrs vs. placebo

VITAMIN E

- Disease-modifying agent
- Benefits proven in double-blind study (Sano et al., 1997)
- Vitamin E 1000 International Units BID
- Blood thinner

ESTROGEN REPLACEMENT THERAPY

- **Retrospective studies have shown decreased risk of AD**
- **Prospective study (Mulnard et al., 2000) showed no benefit in women with AD**
- **BUT, possible preventive** effect still under study

ANTI-INFLAMMATORY MEDICATIONS

- Retrospective study (Stewart et al., 1997) showed decreased risk with NSAIDS (but not aspirin)
- Prospective study of COX-2 inhibitors ongoing
- Caution: bleeding risk

GINGKO BILOBA

- Blood thinner
- Benefit unproven - $15M study
- 120-240 mg daily

"AMYLOID VACCINE"

- Mouse model of AD
- Plaques could be prevented or reversed in mice injected with amyloid (Schenk et al., July 1999)
- Human safety trials ongoing in UK

AMYLOID CLEAVAGE ENZYME INHIBITORS

- Amyloid precursor protein
  - –cleaved at different sites by different enzymes
  - –-> long or short forms of amyloid
- Longer amyloid is “sticky” -> plaques

BEHAVIOR-MODIFYING MEDICATIONS

- 70-90% of patients with dementia
- Multiple medications can treat these symptoms
- Behavior/environment modification

HUMAN ADULT BRAIN CAN CREATE NEW CELLS

- TRUE
- or
- FALSE?

WHAT'S SO SPECIAL ABOUT THE BRAIN?

- SPECIALIZATION (DIFFERENTIATION)
- 100 BILLION NEURONS
- 60-100 TRILLION SYNAPSES (connections)

THE REASON FOR RECESS

- Stimulating evironment
- Running wheel
- Stress
- Depression

RESOURCES FOR TEACHERS

- http://lshome.utsa.edu/programs/Neurobiology/nlca/NLCA.htm
  - Society for Neurosci & NABT
- http://www.sfn.org/cnl/
  - Society for Neuroscience

RESOURCES FOR TEACHERS II

- http://www.aan.com/public/lessonplans/
- http://faculty.washington.edu/chudler/neurok.html
- http://faculty.washington.edu/chudler/experi.html