Age Associated Cognitive Decline and Mild Cognitive Impairment (MCI)

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Objectives

- Rationale for Neuropsychological Assessment
- Neuropsychological Evaluation in Growing Older
  - Age appropriate decline in cognitive function
  - ‘Abnormal’ aging
    - Dementias
    - Mild Cognitive Impairment
- Neuropsychology Crucial?
- Conclusions
- Future Directions

Rationale for Neuropsychological Assessment

- Aging and Brain disorders manifested by changes in cognitive and behavioral function
  - Dementia is decline in previously acquired cognitive and behavioral abilities which leads to deficits in ability to function
  - Mild Cognitive Impairment is ‘abnormal’ decline in cognitive function greater than expected for age.
- Neuropsychological assessment is only way to measure alterations in cognitive and behavioral function.
Normal Aging

- Extensive Data indicate aging is associated with cognitive decline

![Bar chart showing MMSE scores across different age groups.]

Normal Aging

- What, When and How Much cognitive decline occurs with aging varies:
  - Numerical ability/arithmetical and processing speed
    - beginning about age 25
  - Memory (Episodic or Declarative)
    - Late 30's or 40's perhaps as late as 50's to 60's
      - Seattle study found about age 53
  - Reasoning, verbal ability, and Visuoperceptual skills
    - Beginning in 50's and 60's
  - Word knowledge, vocabulary, word reading
    - Stable into late adulthood (70's+)
Longitudinal change in cognition with normal aging

Cognitive Changes in Normal Aging:
Simple Attention and Complex Attention
Attention: Simple Task

Attention / Processing Speed: Difficult Task
Cognitive Changes in Normal Aging
Language

Object naming:
Easy Item
Object Naming:
Difficult Item

Cognitive Changes in Normal Aging
Memory
Verbal Memory

- Bat
- Cannon
- Chair
- Floor
- Orange
- Mayor
- Bus
- Play
- Corner
- Salad
- Lever
- Square

Visual (non-verbal) memory
Cognitive Changes in Normal Aging: Visuoperceptual/Visual Reasoning

Visuospatial Perception: Spatial Perception

A COMpendium OF TeSTS AND ASSESSMENTS TECHNIQUES

Fig. 10–8 Judgment of Line Orientation (Benton, Hamsher, et al., 1983). Examples of double-line stimuli (a) to be matched to the multiple choices card below (b).
Cognitive Changes in Normal Aging: Reasoning

Verbal Reasoning

Easy
⊙ Wood and Coal

Hard
⊙ Platypus and Stork
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Cognitive Decline: Dementia and Mild Cognitive Impairment

- Extensive terms and research to defining where normal aging stops and pathology begins
  - Age-appropriate memory Impairment (AAMI)
  - Senility
  - Benign semnescent forgetfulness
  - Cognitive Impairment – No Dementia (Canada)
  - Mild Cognitive Disorder
  - Mild Cognitive Impairment (MCI)
  - Mild Neurocognitive Disorder
  - Questionable dementia
- Defining ‘Impairment’
Theoretical Progression from normal to dementia

From Petersen, 2003

Gross Pathology: Normal Coronal View
Gross Pathology: Alzheimer’s Disease

How to define where pathology begins?

Defining Impairment:
Dementia

- Dementia is broadly defined as a decline in cognitive function from a previous level of ability severe enough to interfere with work, school, social activities, etc. that is not due to delirium or encephalopathy
- DSM-IV TR defines dementia more specifically as requiring a deficit in memory and at least one other cognitive deficit
  - e.g., Aphasia, Agnosia, Apraxias, executive functions
  - AND
  - Impairment in ability to work, attend school, complete ADLs, etc.
- How to measure memory loss and cognitive or behavioral impairment
Identifying Cognitive Impairment

- Methods to define impairment in neuropsychological function for dx of dementia
  - Clinical interview with pt (and collateral source)
  - MMSE
  - Clinical Dementia Rating scale (CDR)
  - Neurologic/neurobehavioral exam
  - Clinical neuropsychological evaluation
- Structure of CNS does NOT allow for dx of dementia
  - MRI, CT, PET study can NOT identify cognitive impairment for dx of dementia

When is Impaired Actually Impaired

- Threshold for impairment can vary from diagnostician to diagnostician
- When is MMSE score impaired?
  - MMSE score 25/30?
  - MMSE score 23/30?
  - MMSE score 18/30?
- Neuropsychological criteria for defining impairment
  - < 16th percentile (<1.0 SD below average = possible impairment)
  - < 7th Percentile (<1.5 SD below average = MCI)
  - 2nd Percentile (<2.0 SD below average = dementia)
Neuropsychologic Profile of Dementias

- **So-called 'cortical' dementias**
  - Memory loss (impaired recall without benefit of recognition cues) with other cortical findings such as agnosias, aphasias, and/or apraxias.
  - Prototype is Dementia of Alzheimer’s type

- **So-called 'subcortical' dementias**
  - Slowed processing speed, with deficits in attention, memory (poor spontaneous retrieval but intact recognition), visuospatial skills, and executive functions (initiation, planning, behavioral apathy).
  - Prototype is Vascular dementia or Parkinson’s disease dementia

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Alzheimer’s Disease

- **Early deficits**
  - Early and profound impairment in memory
  - Deficient consolidation and rapid forgetting
    - Retention rate over 20-30 minutes < 50 %
  - Attention/working memory intact
  - Social withdraw (common early)
  - Verbal fluency (semantic < phonemic) and dysnomia
  - Visuoconstructional apraxia
  - Executive function (impulsivity, indifference, poor insight)

- **Later stage deficits**
  - IQ, attention, behavioral apathy, agitation, delusions
Vascular Dementia

- Early deficits
  - Memory impaired
    - Poor spontaneous recall, but recognition intact
  - Attention (divided attention/working memory)
  - Visuoperceptual/Visuoconstructional apraxia
  - Executive function (reasoning, sequencing, apathy)
  - Verbal fluency (semantic > phonemic)
  - Social withdraw, depression
  - Focal neurological deficits
- Later stage deficits
  - IQ, agitation, delusions

Lewy Body Dementia

- Early deficits
  - Early and profound impairment in Attention
    - Immediate memory/working memory impaired
  - Visuoperceptual/Visuoconstructional apraxia
  - Executive function (reasoning, sequencing, poor insight)
  - Fluctuating mental status, visual hallucinations
  - Memory not severely impaired
- Later deficits
  - Memory, IQ, language/speech, agitation, delusions
Frontotemporal Dementia

- Early deficits (considerable variability)
  - Executive function (impulsivity, reasoning, sequencing, apathy, disinhibition, poor insight)
  - Behavioral/Mood (Early and profound changes)
  - Attention (divided attention/working memory)
  - Verbal fluency (phonemic < semantic) naming deficits
    - Primary progressive aphasias have early and profound language deficits
  - Memory (mild deficits only)

- Later deficits
  - Memory, IQ, visuoperceptual, agitation, echolalia, mutism, stimulus bound behaviors

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Mild Cognitive Impairment (MCI)

- Term to describe Pts with cognitive impairment, but do NOT meet diagnostic criteria for dementia
- Peterson et al. (Mayo Clinic) defined MCI as:
  - Subjective memory complaint
  - Objective memory deficit compared to age-matched peers (1.5 or more standard deviations below average)
  - Otherwise cognitively intact
  - Otherwise intact daily functioning
    - Patient may use adaptations for memory loss
  - Not demented

Who Cares? Why MCI is Important

- Earliest cut-point distinguishing normal aging from abnormal aging
  - Controversy
    - Unique disease entity? OR
    - Prodromal state representing initial stages of disease?
- MCI increases risk to develop dementia
  - Annual progression of healthy community living older adults (aged 55+) to dementia is about 1-2 % per year
  - Annual progression from MCI to dementia is 10-15%
- MCI first clinical point to initiate treatment?
Theoretical benefit for various rates of early detection

From Petersen, 2003

Advances: Diagnostic Criteria

- Dropped need for subjective memory complaint
- Different measures and cut-offs
  - Original required only one measure within a domain to be $\leq -1.5$ SD below peers
    - (e.g., if one of 2 memory scores $\leq -1.5$ SD = MCI)
  - ‘comprehensive’ require 2 (or more) measures within a domain to be $\leq -1.0$ SD below peers
  - ‘liberal’ require only one score fall $\leq -1.0$ SD below peers
  - ‘conservative’ requires 2 (or +) measures within a domain $\leq -1.5$ SD below peers
Advances: Diagnostic Subtypes

- Single Domain MCI
  - Amnestic MCI (aMCI-s)
    - The “original” with memory ≤ -1.5 SD below demographically-matched peers.
  - Non-amnestic MCI (naMCI-s)
    - Non-memory domain (e.g., language, attention, etc.) ≤ -1.5 SD below peers.

- Multiple Domain MCI
  - Multidomain amnestic MCI (aMCI-m)
    - Memory + another domain ≤ 1.5 SD below peers
  - Multidomain nonamnestic MCI (naMCI-m)
    - 2 or more nonmemory domain < -1.5 SD below peers

Why MCI Subtype Important?
Predict Different Dementias?

- Each dementia may have distinct MCI:
  - aMCI-s ⇒ AD
  - aMCI-m ⇒ AD or Vacular dementia (VaD)
  - naMCI-s ⇒ FTD or Lewy Body dementia (DLB)
  - naMCI-m ⇒ VaD or DLB

- Early data:
  - MCI subtypes not consistent conversion to distinct dementias, BUT
    - aMCI-s and multiple domain MCI greater risk for AD
Progression of Aging

- **Healthy**
  - 273 (70%) \(\Rightarrow\) healthy
  - 34 (9%) \(\Rightarrow\) naMCI
  - 9 (2%) \(\Rightarrow\) aMCI
  - 49 (13%) \(\Rightarrow\) AD
  - 25 (6%) \(\Rightarrow\) mortality

- **Amnestic MCI**
  - Healthy = 15%
  - Dementia = 49%

- **Non-amnestic MCI**
  - Healthy = 24%
  - Dementia = 27%

Progression Rate:
MCI to _________

- **Dementia**
  - Annual conversion rates
    - Low = 2 % per year
    - High = 31 % per year
    - Mean = 10-15 % per year

- **Cognitively Healthy** (revert to healthy status)
  - Study period (1.7 to 6 years)
    - Low = 15 %
    - High = 44 %
  - Annual conversion rate
    - Mean = 8-11 % per year
Conversion Rate: MCI subtypes

Dementia
- aMCI-m=60%
- naMCI-m=60%
- naMCI-s=31.3%

Cognitively Healthy
- naMCI-s=26.3%
- naMCI-m=0%

MCI and Dementia: Risks and Protective Factors

- Progression to Dementia less likely if
  - Non-amnestic MCI-single domain (naMCI-s)
  - Minimal cerebrovascular disease
    - No stroke, diabetes, heart disease, smoking, HTN, hyperlipidemia
  - Mild to moderate ETOH intake
  - Exercise
  - High “cognitive reserve”
    - May account for lack of association between severity of brain pathology and clinical symptoms
    - High academic achievement, premorbid IQ, occupational attainment, leisure activities
  - No psychiatric symptoms (anxiety, amotivation, or depression)
When to Refer for Neuropsychologic Evaluation?

- Assessment of neuropsychological function crucial for diagnosis and management of dementias and MCI
  - However, assessment sensitivity and specificity needs vary depending upon issue
    - To distinguish patient neuropsychological function as normal or grossly abnormal, clinical neuropsychologic eval. **NOT** needed.

Neuropsychology Crucial?

- Detailed neuropsychologic eval assists:
  - Differential diagnosis
    - Dementia vs. pseudodementia
    - Differential diagnosis of dementias
    - Identify subtypes of MCI
      - Amnestic MCI versus non-amnestic MCI
  - Treatment planning
    - Allow early detection to start treatment
      - Different dementia/MCI subtypes may = different tx
    - Monitor treatment effectiveness of cognitive deficits
    - Determining care needs (placement)
  - Determining competency/functional capacity
Distinguishing normal aging from abnormal is complex

- Inter-individual variations in normal aging
  - Cognitive progression within neuropsychological domains occurs at different rates
    - Processing speed and reaction time decline first
    - Language (word knowledge, reading) most resilient
  - Cognitive progression likely affected by numerous biological and environmental variables

- Intra-individual variability in cognitive functions important to consider
  - 30% of individuals will have a score < 5th %ile on comprehensive neuropsychological evaluation.

- Criteria used to distinguish normal aging from abnormal aging better identified
  - Common standard is MCI

MCI useful diagnosis

- Often used criteria to Diagnose MCI
  - Score on neuropsychological measure < -1.5 SD below the mean of healthy peers

- Increases likelihood of progression dementia
  - 10-15% progress from MCI to dementia per year

- Subtypes of MCI proposed
  - Amnestic MCI (single or multiple domain)
  - Non-amnestic MCI (single or multiple domain)

- MCI represents early clinical point to start treatment
  - Increase exposure/power of any intervention?
Questions

Cognitive function varies within individuals

- Percent of healthy individuals with at least one memory score < 5th %ile
Defining Cognitive Impairment: Dementias

- Neuropsychological deficits should follow known neuropathological disease patterns
  - Distinguish pseudodementia from dementias
- Neuropsychological deficits vary between dementias
  - AD has more profound memory deficits than Frontotemporal dementia
- Within a dementia syndrome, considerable inter-individual variability
  - One pt with AD may exhibit more language dysfunction while another may exhibit more visuospatial deficits

Normal Aging

- Average MMSE score by age
Parkinson’s Disease Dementia

- Early deficits
  - Information processing/Psychomotor speed
  - Executive function (reasoning, sequencing, apathy, disinhibition)
  - Attention (divided attention/working memory)
  - Visuoperceptual/visuoconstructional
  - Verbal fluency (phonemic < semantic) and naming deficits. Hypophonia, micrographia, dysarthria.
  - Memory (poor spontaneous recall, intact recognition)

- Later deficits
  - Memory, IQ, attention (basic)

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Historical Overview of Neuropsychology

- Origins of Neuropsychology
  - Relationship to Behavioral Neurology
    - Functional Anatomical Correlation
    - Cortical Localization/Lateralization
  - Relationship to Psychology
    - Normative comparisons
    - Quantifying Brain Functions
Neuropsychological Evaluation: Fundamentals

- Assessment of Brain-Behavior Relationships
  - Identify and quantify presence (or absence) of neuropsychological deficits

- Assumptions for Evaluation
  - Brain dysfunction affects behavior
  - Behavior changes can be associated with particular brain processes/areas/neurological syndromes
  - Assessment can be reliable
  - Assessment can be valid
  - Assessment affects diagnosis/treatment

Brain Organization

- Output
- Organization
- Verbal Skills
- Non-verbal skills
- Learning and memory
- Attention and concentration
- Senses

Baker GA. personal communication, 2008
Neuropsychological Evaluation

Methods

- MMSE
- Clinical observations
  - Neurological exam
- Self-report
- Collateral (spouse) report
- Neuropsychologic Eval.
  - Intelligence
  - Attention/Processing Speed
  - Language
  - Memory
  - Visuoperceptual
  - Abstraction/Problem solving
  - Personality/Behavior

Neuropsychology Crucial?

(continued)

- Detailed neuropsychologic assessment assist in:
  - Early detection allow for early start of treatment
  - Identification of MCI subtype may lead to different treatment
    - Progression of amnestic MCI to dementia higher
    - Progression of non-amnestic MCI to dementia low
Temporal Detection of Mild Cognitive Impairment

From Petersen, 2003

Clinical Neuropsychological Evaluation: Benefits

- Neuropsychologic (cognitive and behavior) is:
  - Systematically measured across multiple domains
    - Memory, language, attention/executive, visuoperceptual, mood
  - Assessed using reliable and validated tools:
    - Score obtained in Seattle same as Tampa
  - Referenced (compared against):
    - Healthy demographically matched peers
    - Individual level based on premorbid expectations
  - Threshold for impairment can be adjusted for individual needs
  - Research vs. clinical vs. medicolegal

From Petersen, 2003
Diagnostic Value of Neuropsychological Evaluations

- Define severity/type of cognitive impairment/dementia
- Distinguish Dementia from pseudodementia
- Differential diagnosis of dementias
- Diagnose Mild Cognitive Impairment
- Identify pts needs for accommodation/adaptations
- Identify pts at risk to live alone, drive, make decisions, etc.
- Evaluate for effectiveness of therapies or to track progression of disease
- Predict mortality
  - Individuals with greater intra-individual variability in cognitive function at greater risk for death (Shipley et al. 2006; MacDonald et al. in press)
  - Simple and choice reaction time mean & variability
  - Verbal memory

Severity/Type of Cognitive Impairment

- Neuropsychological evaluation can quantify cognitive deficits AND strengths
  - Describe severity (mild vs. profound) of deficits
  - Describe cognitive and behavioral strengths
- Neuropsychological deficits vary between dementias
  - AD has more profound memory deficits than Frontotemporal dementia
- Variable clinical presentation within a dementia disease (e.g., inter-individual variability)
  - One pt with AD may exhibit more language dysfunction while another may exhibit more visuospatial deficits
When ‘impaired’ is not impaired: Depression/pseudodementia

- Neuropsychological evaluation effective at distinguishing dementia from pseudodementia
  - Performance within and across neuropsychological profile not consistent with functional neuroanatomy or known neuropsychological pathology
    - Patients with dementia tend to provide false positive errors on memory tests
    - Patients with pseudodementia give more false negatives ("I don’t know.")
    - Fluctuation of scores within a neuropsychological domain
    - Failure on symptom validity tests/tests of task engagement
      - Passed by individuals with mild/moderate dementia