Neuropsychology Of Aging And Dementia

OUTLINE

1. Concepts of cognitive aging
2. Neurodegenerative dementia: a large-scale neurocognitive network disorder
3. Role of neuropsychology in diagnosis: assessment principles
4. Neuropsychological profiles of dementia: Amnestic, Aphasic, Visuospatial, Comportmental

HETEROGENEOUS PATHWAYS OF COGNITIVE AGING
A Race Against Time

1. Concepts of cognitive aging
2. Neurodegenerative dementia: a large-scale neurocognitive network disorder
3. Role of neuropsychology in diagnosis: assessment principles
4. Neuropsychological profiles of dementia: Amnestic, Aphasic, Visuospatial, Comportmental
DEMENTIA: A CLINICAL SYNDROME

• Progressive DECLINE from a prior level
• in one or more: memory, reasoning, language, visual processes, executive functions, social-interpersonal behaviors, comportment, personality
• that interferes with customary activities and social relationships, causes dependence, alienation
• Due to brain disease

WHAT CAUSES DEMENTIA?

- Irreversible
  - Neurodegenerative: NERVE CELL DEATH that is selective for cognitive networks
  - VASCULAR
    - Diffuse Lewy Body
    - Prion Diseases
    - Amyloid Plaques, Tau Tangles
    - Frontotemporal Lobar Degeneration
    - TDP-43 Proteinopathies
    - Others
  - Toxic Metabolic
    - FUS, other

Irreversible
Due to brain disease

- Reversible
  - There is evidence for mixed pathologies
  - Amyloid Plaques, Tau Tangles
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Irreversible
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TYPES OF NEUROPATHOLOGY DIAGNOSED AT BRAIN AUTOPSY THAT CAUSE CLINICAL DEMENTIA SYNDROMES

- Frontotemporal Lobar Degeneration
  - With TDP-43 Proteinopathy
  - With Tau Inclusions: e.g. Pick’s disease
  - With FUS Inclusions
- Plaques and Tangles: “Alzheimer’s Disease”
- NORMAL BRAIN TISSUE
- Cortical Lewy Body Disease

NORMAL BRAIN TISSUE

EARLY STAGE NEURODEGENERATIVE DISEASES CAUSE FOCAL COGNITIVE AND BEHAVIORAL DEFICITS WITHOUT WIDESPREAD IMPAIRMENT

PRE 1980 = LATE DETECTION
Neuropsychologically Widespread Deficits
Neuroanatomically Diffuse

LATE STAGE

POST 1980 = EARLY DETECTION
Neuropsychologically Circumscribed Deficits
Neuroanatomically Focal determined by Large-Scale Network connectivity

EARLY STAGE

POST 2011 = PRECLINICAL DETECTION, BIOMARKERS

3 LEVELS OF DEMENTIA CHARACTERIZATION

- CLINICAL SYNDROME - THE COGNITIVE AND BEHAVIORAL SYMPTOMS
- NEUROANATOMICAL SIGNATURE - REGIONS OF ATROPHY (MRI) AND/OR PHYSIOLOGICAL DYSFUNCTION (FDG-PET)
- NEUROPATHOLOGIC TISSUE DISEASE
  - CELLULAR AND MOLECULAR ABNORMALITIES FOUND AT POST MORTEM AUTOPSY

HOW ARE THE LEVELS RELATED?

PREDDS NEUROANATOMICAL NETWORK 1:1

PREDICTS PROBABILITIES OF NEUROPATHOLOGIC DISEASE

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PREDICTS NEUROPSYCHOLOGICAL PROFILE

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HOW ARE THE LEVELS RELATED?
**CLINICAL DEMENTIA SYNDROME**

<table>
<thead>
<tr>
<th>MAIN SYMPTOMS</th>
<th>NEUROANATOMY</th>
<th>NEUROPATH DIAGNOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMNESTIC DEMENTIA</td>
<td>Early: Amnesia; rapid forgetting, poor learning, poor recognition; apathy; Late: additional cognitive deficits; anosmia, executive</td>
<td>ATROPHY/ HYPOMETABOLISM</td>
</tr>
<tr>
<td>COMPORTMENTAL/ EXECUTIVE DEMENTIA</td>
<td>Early: Poor judgment, social disinhibition, executive dysfunction; Late: Language deficits, memory loss</td>
<td>ATROPHY/ HYPOMETABOLISM</td>
</tr>
<tr>
<td>LANGUAGE DEMENTIA</td>
<td>Early: Anosmia, comprehension deficits, writing, spelling; Late: behavioral symptoms</td>
<td>ATROPHY/ HYPOMETABOLISM</td>
</tr>
<tr>
<td>VISUOSPATIAL DEMENTIA</td>
<td>Early: Simultanagnosia, hemispatial neglect, Balint's syndrome; Late: Anosmia, memory loss</td>
<td>ATROPHY/ HYPOMETABOLISM</td>
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**WHAT ABOUT SCREENING?**

- Why spend so much time and effort in the neuropsychological evaluation?
- Why not have a screening test that the PCP can use during the Wellness Visit to identify those at risk or in early stages?

**DOES THE PCP HAVE THE TIME AND EXPERTISE FOR THIS?**

NOT FOR EARLY DETECTION

THEREFORE, NEUROPSYCHOLOGICAL ASSESSMENT IS ESSENTIAL FOR EARLY DETECTION AND RISK DETERMINATION

**INTERMEZZO**

Interpretation of performance (test scores) is influenced by:

- Race/ethnicity
- Educational level
- Quality of education
- Level of life achievement
- Prior medical history (TBI, brain tumor, stroke, )
- Prior history of early learning disability
- Psychiatric/behavioral factors
- Concurrent biological/psychological factors (e.g. sleep disorder, toxic/metabolic disorders, depression, anxiety)

**INTERMEZZO**

**Cognitive Test Is Not A Blood Test**
NEUROPSYCHOLOGICAL ASSESSMENT PROVIDES:
- The only objective marker of THE DEMENTIA SX
- Early detection - Preclinical? Subjective complaints?
- Magnitude of change and rate of decline
- Differential diagnosis
- Blueprint for management and patient/caregiver education

1. Is there change from a prior level of functioning?
ESTIMATED PRIOR ABILITY:
- IQ/Reading SCORES
- Level and quality of education
- Career/home/civic/social accomplishments
- Hobbies/recreation
- Usual emotional reactions
- Typical "character"

2. Is change interfering with routine activities of daily living? How?
ACTIVITIES OF DAILY LIVING QUESTIONNAIRE (ADL-Q)
Johnson, Barton, Rademaker, Rehkemper, Weintraub, ADAD, 2004

- Self-Care
- Employment/Recreation
- Household Care
- Travel
- Shopping/Money
- Communication

0 = Same as usual
1 = Some mild change
2 = More moderate change
3 = No longer able to do the activity due to cognitive change
9 = Item is not applicable or "don't know"

Mild=0-33%; Moderate=34-66%; Severe=>66%

3. What is the stage of dementia?
Mild, Moderate, Severe

STAGING TESTS:
- Montreal Cognitive Assessment
- MMSE
- Blessed Dementia Scale (BDS)

OBSERVER RATINGS:
- Clinical Dementia Rating (CDR)

STAGING DEMENTIA SEVERITY
Mild, Moderate, Severe

- Montreal Cognitive Assessment
  - Sensitive to mild impairment
  - Caveat: mixed findings in low education BUT recent study of short form useful in illiterate/lower education sample

- Mini Mental State Examination
  - Useful to track stages of dementia

http://www.mocatest.org/
Montreal Cognitive Assessment Memory Index Score (MoCA-MIS) as a Predictor of Conversion from Mild Cognitive Impairment to Alzheimer’s Disease
Parunyou Julayanont, MD, Melanie Brousseau, SWT, Howard Chertkow, MD, Natalie Phillips, PhD, and Ziad S. Nasreddine, MD, JAGS, 2014

Memory Index Score (0-15): 3x N free recall + 2x N cued recall + 1x N recognition

Executive Index Score (0-13): Trails + clock + digits FB + letter A + serial 7’s + letter fluency + abstraction

Attention/Concentration Index Score (0-18): Letter A + serial 7’s + digit span FB + sentence repetition + word list immediate trials total

Language Index Score (0-6): Naming + sentence repetition + letter fluency

Visuospatial Index Score (0-6): cube + clock + naming

Orientation Index Score (0-6): day, date, month, year, location, city

ANNUALIZED PERCENT CHANGE IN MMSE SCORE VS ACTIVITIES OF DAILY LIVING SCORE

Change Scores
-5.0 -4.0 -3.0 -2.0 -1.0 0.0 1.0 2.0 3.0

MMSE PENALIZES PATIENTS WITH PPA DUE TO ITS EMPHASIS ON VERBAL SKILLS
Osher et al, 2007

CLINICAL DEMENTIA RATING (CDR) – MORRIS, ET AL, 1999

YIELDS: STANDARD SUM OF BOXES SCORE
STANDARD GLOBAL SCORE (weighted towards memory)
Morris et al, 1993

Progressive Aphasia Severity Scale- PASS

4. What domain(s) is the most salient?
Neuropsychological Assessment

OUTLINE KEY ISSUES
WORK, HOME, SAFETY, SOCIAL

What is the functional impact of Neuropsychological and Behavioral Deficits?

NEUROPSYCHOLOGICAL PROFILE
DIFFERENTIAL DIAGNOSIS
Clinical Dementia Syndrome
Presumed Large-Scale Network
Possible Causes (Etiologies)

RECOMMENDATIONS
Take into account key deficits
Resources for care
Supportive counseling/education
Planning for the future

Sapolsky et al, Neurology, 2010
In late stages of dementia, all domains are affected; profiles cannot be discerned.

Early Profile of Progressive Visuospatial Dysfunction
Aka Posterior Cortical Atrophy

Principles Of Assessment

- Select “pure” measures
- Tailor tests appropriate for patient
- Cover all domains, but be brief
- Identify PRIMARY DOMAIN Of Deficit
- Identify “Secondary” symptoms - word list memory test failed due to aphasia
- Types of Measures: Computerized, Paper-and-Pencil

DEMENTIA OF THE ALZHEIMER TYPE (AMNESTIC)
DRILLED WORD SPAN MEMORY TEST

<table>
<thead>
<tr>
<th>Word</th>
<th>Learning Trials</th>
<th>Delayed Recall</th>
<th>Recognition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apple</td>
<td>✓</td>
<td>✓</td>
<td>×</td>
</tr>
<tr>
<td>Shoe</td>
<td>✓</td>
<td>✓</td>
<td>×</td>
</tr>
<tr>
<td>Horse</td>
<td>✓</td>
<td>✓</td>
<td>×</td>
</tr>
<tr>
<td>Truck</td>
<td>✓</td>
<td>✓</td>
<td>×</td>
</tr>
<tr>
<td>Window</td>
<td>✓</td>
<td>✓</td>
<td>×</td>
</tr>
<tr>
<td>Dress</td>
<td>✓</td>
<td>✓</td>
<td>×</td>
</tr>
<tr>
<td>Park</td>
<td>✓</td>
<td>✓</td>
<td>×</td>
</tr>
<tr>
<td>Truck</td>
<td>✓</td>
<td>✓</td>
<td>×</td>
</tr>
<tr>
<td>Machine</td>
<td>✓</td>
<td>✓</td>
<td>×</td>
</tr>
<tr>
<td>Elbow</td>
<td>✓</td>
<td>✓</td>
<td>×</td>
</tr>
</tbody>
</table>

Case 1

- 81 yo male, retired M.D.; insidious onset, progressive, 4y
  - Presenting SX: forgetfulness
  - PMH: CAD, allergies, asthma
  - CT unremarkable

Neuropsychological profile:
Amnesia

Impact on ADL: repetitive, losing belongings, forgets events
- Dementia? Yes
- Memory abn? Yes
- Other abn? Executive
- Profile: Progressive Amnesia+
- Clinical dementia DX: Dementia of the Alzheimer type
- Path: AD
Case 2

- 46 yo, woman, PhD, nurse; insidious onset, progressive, 2 y
- Presenting SX: word-finding difficulty; agrammatic speech, writing
- Impact on ADL: Only activities dependent on language; otherwise, completely independent
- MRI: Non specific bifrontal atrophy, L>R; Auditory EPs- abn, L temporal
- PMH: breast cancer
- FH: learning disabilities (spelling, writing)

Percent Change in Test Scores Over 2 Years

Non Language Tests

Language and Related Tests

Dementia? YES
Memory impaired? NO
Other cog/beh deficits? Language
Neurocognitive Profile Agrammatic Aphasia
Neuroanatomy L Perisylvian
Clinical Dementia DX Primary Progressive Aphasia
Presumed Cause? FTLD (tau)

The Multilingual Naming Test (MINT)

"candle" "parachute"
"wig" "axle"

Multilingual Naming Test (MINT)

http://www.alz.washington.edu/WEB/forms_uds.html
https://flintbox.com/publicproject/19927/
Case 3

- 61 yo man, professional landscaper
- Insidious onset, progressive, 8 y
- Reported Sx: Trouble "seeing"
- PMH: none
- CT, MRI, EEG normal
- Dementia? Yes
- Memory abn? No
- Other abn? Yes
- Profile: Progressive Visuospatial Dysfunction (aka PCA)
- Anatomy: Parietal; temporoparietal
- Suspected Pathology: AD vs LBD

<table>
<thead>
<tr>
<th>Domain / Tests</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADL</td>
<td>Mattis DRS Total</td>
</tr>
<tr>
<td>ATTENTION</td>
<td>Mattis DRS ATT</td>
</tr>
<tr>
<td>DRS INITIATION</td>
<td>Mattis DRS INIT</td>
</tr>
<tr>
<td>LANGUAGE</td>
<td>Speech</td>
</tr>
<tr>
<td>BNT</td>
<td>Verbal fluency</td>
</tr>
<tr>
<td>Calculations</td>
<td></td>
</tr>
<tr>
<td>VISUOSPATIAL</td>
<td>DRS Constructions</td>
</tr>
<tr>
<td>MEMORY</td>
<td>DRS Memory</td>
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From Weintraub and Mesulam, 2003

Visual-Verbal Test (Feldman & Drasgow, 1959)

Case 4

- 61 yo woman, assembly line worker
- Insidious onset progressive, 2 y
- Presenting Sx: "Dwelling" on her birth mother, inattentive, "bizarre" uncharacteristic behavior
- PMH: none
- FH: Mother
- CT, EEG normal
- Memory abn? No
- Other ABN? Yes
- Profile: Executive/Comportment
- Anatomy: Frontotemporal
- Pathology: FTLD

Visual-Verbal Test (Feldman & Drasgow, 1959)
Referrals for Neuropsychological Examination

1. MMSE is normal in an individual with complaints. GET A BASELINE
2. Is there cognitive decline beyond age/personal best?
3. Are there character changes without explanation?
4. What is the rate of decline?
5. What level of care is needed?
6. Is treatment having an effect?

7. Are cognitive/behavioral changes under age 65 signs of young onset dementia?
8. Can delirium be differentiated from dementia?
9. Is the patient safe/able to live alone? To drive?
10. What can the patient/family do to address cognitive/behavioral symptoms?

NORTHWESTERN CARE PATHWAYS PROGRAM FOR DEMENTIA (CARE-D)™: TRANSLATIONAL NEUROPSYCHOLOGICAL RESEARCH

- Memory
- Behavior/Action
- Language
- Visuospatial

ADL Problems to target:
- Word finding
- Reading
- Writing
- Language comprehension
- Spelling

ADL Problems to target:
- Poor judgment
- Social disorganization
- Loss of empathy
- Impulsivity

ADL Problems to target:
- Misplacing
- Personal belongings
- Trouble finding
- Judgment distance
- Bumping into furniture

MORHARDT ET AL, 2016

THE END