Diagnostic Procedures:
Cognitive and Psychological Tests, Neuroimaging

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Pretest
Question 1: Which study is the most specific in vivo reflection of amyloid-beta protein load?

1. PET using Pittsburgh compound B
2. PET using Philadelphia compound B
3. PET using deoxyglucose
4. CSF A-beta 42 measurement

Question 2: Which of these tests is most sensitive to frontal lobe damage?

1. Boston naming test
2. MMPI
3. Wechsler memory scale
4. Wisconsin card sorting test
5. Judgment of line orientation
Question 3: Simultanagnosia is usually seen in (or associated with):

1. Balint's syndrome
2. Anton's syndrome
3. FTLD
4. Lewy body dementia
5. Hemispatial neglect

Question 4: A patient can shave properly, but cannot show how to use a razor on command. What's the most likely cause?

1. Ideomotor apraxia
2. Kinetic apraxia
3. Ideational apraxia
4. Response inhibition
5. Inattention
Question 5: The classic PET pattern in AD shows hypometabolism in:

1. Bilateral parietal areas and precuneus
2. Bitemporal areas
3. Biparietal-occipital areas
4. Frontotemporal areas
5. Asymmetric, diffuse cortical
Where

What

Right: visuospatial

Left: language or symbolic
Division of Task Between the Two Hemispheres

- **Left Hemisphere**
  - Analytical and logical thinking
  - Language (except emotional prosody)
  - Expression of emotion

- **Right hemisphere**
  - Spatial abilities
  - Comprehension of complicated patterns & drawings
  - Perceiving emotion

Appreciation & expression of music?

Association Areas

- No precise definition
  - Areas that neither receive direct sensory information nor send direct fibers to subcortical motor nuclei

- All lobes contain association areas
- Integrate information
- Important for “higher mental function”
- Not centers for specific mental faculties
Lesions of Association Cortices

- Agnosias, apraxia, dyslexias, dysgraphias
  - Agnosia: failure of recognition that is not due to elementary sensory defects
  - Apraxia: loss of the ability to program the motor system to perform purposeful skilled movements
  - Dyslexia/dysgraphia: difficulty reading or writing with phonological/semantic/syntactical errors

Types of Agnosia

- Apperceptive agnosia
- Associative agnosia
- Auditory agnosia
  - Impaired capacity to recognize the meaning of non-speech sounds
- Color agnosia
  - Loss of the knowledge about the color of objects
- Tactile agnosia
  - Inability to name a palpated object, despite intact recognition
Apperceptive Agnosia

- Loss of ability to perceive an object when the object is present in an incomplete or unusual view
  - Fragmented letters, unusual views, silhouettes
- Lissauer’s 1st type of agnosia
Associative Agnosia

- Loss of the meaning of words or objects
- Verbal
  - What is a kite?
- Visual
  - Lissauer’s 2nd type of agnosia
  - Give the patient a comb and ask, “what is it?”
Test of Associative Agnosia

- Word-word or word-picture matching

- Carrot
- Egg plant
- Parsnip

- Have the patient point to objects as you list them

Types of Apraxia

- **Limb kinetic apraxia**
  - Fine movements are abnormal eg, pick up a coin

- **Ideomotor apraxia**
  - Spatial and temporal errors

- **Ideational apraxia**
  - Cannot sequence task
    - Different from conceptual apraxia (eg, hammering with a screwdriver)

- **Testing**
  - Transitive (screwdriver) maneuvers, intransitive maneuvers and imitating of hand postures
### Apraxias

<table>
<thead>
<tr>
<th>Limb apraxia type</th>
<th>Clinical features</th>
<th>Assessment tasks</th>
<th>Typical anatomical location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ideomotor</td>
<td>Gesture production errors</td>
<td>Gesture to command Gesture imitation Gesture comprehension Use of actual tool</td>
<td>Post. Left hemisphere Ant. Left hemisphere (comprehension spared)</td>
</tr>
<tr>
<td>Ideational</td>
<td>Impaired sequence of movements to perform task</td>
<td>Serial acts</td>
<td>Diffuse injury posterior hemispheres, bilateral or left</td>
</tr>
<tr>
<td>Conceptual/motor</td>
<td>Errors in tool selection, Content error in tool use</td>
<td>Gesture to command Tool-object matching Observation of tool use in natural environment</td>
<td>Diffuse injury posterior hemispheres, bilateral or left</td>
</tr>
</tbody>
</table>

Adapted from: Ochipa, In: Neurological Therapeutics

### Lesions of the Parietal Cortex

- **RIGHT lesion**
  - Disturbances in integration of personal and extrapersonal space
  - Hemispatial neglect
  - Constructional apraxia
  - Dressing apraxia
  - Anosognosia
    - Anton’s syndrome (+ cortical blindness)
  - Apperceptive agnosia

*B/L lesions: inability to grasp & manipulate objects*
Lesions of the Parietal Cortex

- LEFT lesion
  - Disorders of language
  - Body schema disturbances
    - Autopagnosia
  - Gerstmann syndrome (AG)
    - Finger agnosia
    - Acalculia
    - Right-left disorientation
    - Agraphia
  - Associative agnosia

Frontal Association Area

- Type: homotypic cortex
- Brodmann areas: 6, 8–12, 46, 47
- Function: integration of information on emotional & motivational state of the individual
- Projections: SMA, PMA, amygdala, hippocampus
- Input: MD, all cortices
Lesions of the Prefrontal Cortex

- Changes of mood & personality (orbitofrontal)
- Apathy, indifference, emotional leveling off (cingulate gyrus)
- Perseveration, utilization behavior
- Increased distractibility
- Motor hyperactivity
- Oculomotor impersistence
Frontal Cortex Area 6

- **Premotor Area**
  - Brodmann’s area—6 (lateral)
  - **Function**
    - Role in sensory guided movements and motor planning
    - Neurons activated in response to visual, auditory, somatosensory stimuli
  - **Dysfunction:** apraxia

- **Supplementary Motor Area**
  - Brodmann’s area—6 (medial)
  - **Function**
    - Participates in the advance planning of complex movements, particularly for movements involving both sides of the body
  - **Dysfunction:** apraxia

Frontal Eye Fields

- **Type:**
  - homotopic—unimodal
- **Function**
  - Responsible for voluntary conjugate movement of eyes independent of visual stimuli
- **Stimulation:**
  - Conjugate deviation of eyes to opposite side
- **Dysfunction:**
  - Defective scanning; gaze preference, oculomotor impersistence (not apraxia)
Auditory Cortex Lesions

- Unilateral lesion A1
  - Difficulty localizing sound

- Bilateral lesion of A1 (rare)
  - Cortical deafness

Auditory Association Area

- Type
  - Homotypic

- Brodmann
  - Area 20, 21, 22

- Connections
  - Superior temporal gyrus connected with auditory cortex
  - Middle/inferior temporal dominated by visual areas
  - In addition there are strong connections with limbic structures such as hippocampus and amygdala
Lesion: Temporal Association Cortex

- Superior
  - Auditory-oriented agnosia
    - Auditory agnosia
      - Impaired recognition of non-speech sounds
    - Pure word deafness
      - Impairment comprehension of spoken words with preserved ability to hear and recognize non-verbal sounds

- Inferior
  - Visual oriented agnosia, eg, prosopagnosia & topogragnosia

Lesion: Temporal Association Cortex

- Anterior temporal
  - Speech and language
    - Semantic language deficits (associative agnosia)
    - Connections with parietal association cortex

- Posterior temporal
  - Visual/auditory deficits
  - Densely connected with occipital association cortex
Visual Association Cortex

- **Peristriate area**
  - **Function:** complex visual processing including motion, form, and color
  - **Connections**
    - Contralateral peristriate area (18 and 19)
    - Frontal eye fields
    - Parietal heteromodal area
    - Temporal visual association areas

Visual Association Cortex

- **Middle and inferior temporal gyri**
  - **Function:** receives information from peristriate; visual contrast, size, shape, orientation, and movement
  - **Connections:**
    - Contralateral temporal visual association area
    - Frontal heteromodal region
    - Posterior heteromodal region
    - Paralimbic and limbic areas of temporal lobe
Visual Association Cortex Dysfunction: Peristriate Area (18, 19)

- **Stimulation**
  - Experience of color, light, shadow, outline, and movement

- **Lesion**
  - Selective peristriate lesions: deficits of depth perception, distance judgment, spatial orientation, hue discrimination

Visual Association Cortex Dysfunction: Temporal Association Area

- **Lesion**
  - Deficits of pattern recognition
  - Deficits in what things are
    - Topographagnosia
      - Agnosia for directions
      - Agnosia for building recognition
    - Prosopagnosia
  - Deficit of color recognition (achromatopsia)
    - Different from color agnosia and color anomia
  - Motion blindness
Visual Association Areas

- **Occipito-parietal**
  - Interfere with peristriate outflow to parietal heteromodal areas where visual-somatosensory interactions occur
  - Examples:
    - Balints syndrome (bilateral parieto-occipital lesion)

- **Occipito-temporal**
  - Damage input from peristriate areas to temporal visual association areas and their outflow toward language areas and limbic structures
  - Examples:
    - Alexia
    - Pattern discrimination difficulties
    - Visual agnosias (prosopagnosia; achromatopsia)
Balint’s Syndrome

- **Location:**
  - Bilateral parieto-occipital regions

- **Characteristics**
  - Optic apraxia
  - Optic ataxia
  - Simultanagnosia

**Optic apraxia:** inability to direct gaze voluntarily toward a new stimulus in peripheral vision

**Optic ataxia:** deficit in reaching for or pointing to an object visually

Frontal Lobe Syndromes

- Bilateral limb apraxia (L premotor)
- Akinetic mutism (SMA)
- Motor speech apraxia (operculum)
- Nonfluent aphasia (L)
- Abulia (prefrontal)
- Behavioral disinhibition (orbitofrontal)
Temporal Lobe Syndromes

- Pure word deafness (bilateral auditory)
- Fluent aphasia
- Achromatopsia
- Visual agnosia
- Prosopagnosia
- Alexia

Parietal Lobe Syndromes

- Topognosis, barognosis, agraphesthesia
- Astereognosis
- Gerstmann’s (left-acalculia, agraphia, R/L disorientation, finger agnosia
- Ocular apraxia (bilateral PTO)
- Balint’s syndrome
Occipital Lobe Syndromes

- Visual field deficits
- Cortical blindness
- Anton’s syndrome

Mental Status Examination

- Attention
- Mood
- Memory
- Language
- Visuospatial relationships
- Executive (reasoning, judgment, decision making, comportment)
Mental Status Examination

- Diffuse
  - Arousal
  - Attention
  - Mood and motivation

- Focal
  - Language
  - Visuospatial
  - Explicit memory

Attention

- Inattention can degrade all other mental state functions
- Inattention defining feature of acute confusional state (delirium)
- **Diffuse** brain dysfunction (toxic encephalopathy)
- **Frontal** lobe dysfunction (frontotemporal dementia)
**Depression**

- Patient complains of memory problem
- Relatives concerned about depression
- Vegetative symptoms, anxiety
- Subacute onset, symptoms follow a traumatic event
- History of depression common
- Orientation intact
- Concentration impaired
- Variable results on mental status testing
- Poor effort on testing
- Aphasia and apraxia absent

**Dementia**

- Patient minimizes memory problems
- Relatives concerned about memory
- No or few symptoms of depression
- Insidious onset of cognitive symptoms
- History of depression less common
- Orientation impaired
- Recent memory impaired
- Consistent results on mental status testing
- Good effort on testing
- Aphasia and apraxia present
Mini-Mental State Exam

MMSE

MMSE

- Scoring:
  - 24–30 uncertain cognitive impairment
  - 18–23 mild to moderate cognitive impairment
  - 0–17 severe cognitive impairment

<table>
<thead>
<tr>
<th>Age</th>
<th>60-64</th>
<th>65-69</th>
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<td>27</td>
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<td>29</td>
<td>29</td>
<td>28</td>
<td>28</td>
<td>27</td>
<td>27</td>
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</table>

Language Screen Exam

1. Spoken Language Comprehension
2. Reading Comprehension
3. Naming
4. Repetition
5. Narrative picture description
6. Writing

(picture good also for neglect, simultanagnosia)
Aphasia Syndromes

<table>
<thead>
<tr>
<th>Type</th>
<th>Fluency</th>
<th>Repetition</th>
<th>Comprehen.</th>
<th>Naming</th>
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<tbody>
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<td>Non-Fl</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Broca’s</td>
<td>Non-Fl</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Transcort. motor</td>
<td>Non-Fl</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Transcort. Sensory</td>
<td>Fluent</td>
<td>-</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Wernicke’s</td>
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<td>+</td>
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<tr>
<td>Conduction</td>
<td>Fluent</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Anomic</td>
<td>Fluent</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
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</table>

+ impaired; - relatively preserved

Assessment of Behavior

- Cognitive
  - Intelligence
  - Academic skill
  - Language
  - Visual spatial
  - Attention
  - Memory
  - Executive functions

- Noncognitive
  - Alertness
  - Comportment/demeanor
  - Speech
  - Mood
  - Personality
  - Effort/motivation
  - Frustration tolerance
Important Point #1:
Diagnosis of Cognitive Impairment Does Not Imply Etiology

- CI can be caused by many things:
  - Head injury
  - Cerebrovascular disease
  - Toxic/metabolic disorder
  - Depression/psychiatric disorders
  - Degenerative disease

Cognitive Impairment in the Elderly

- Transient vs. persistent
- Ambiguous
- Delirium
- Depression
- TGA
- Syncope
- Dementia
- Boundary condition
- Reversible vs. non-reversible
- NPH
- Infection
- Toxic
- Metabolic
- Static vs. degenerative
- AD
- LBD
- Vascular
- Korsakoff’s
- FTD
- Head Injury
Important Point #2:
Aspects of Cognition Change with Demographics

<table>
<thead>
<tr>
<th>Trial</th>
<th>Word Recalled</th>
<th>Age35</th>
<th>Age65</th>
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<tbody>
<tr>
<td>Trial 1</td>
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<td>12</td>
<td>9</td>
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<td>Trial 2</td>
<td>7</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>Trial 3</td>
<td>9</td>
<td>11</td>
<td>9</td>
</tr>
<tr>
<td>Trial 4</td>
<td>11</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>Trial 5</td>
<td>13</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>30' Delay</td>
<td>15</td>
<td>15</td>
<td>15</td>
</tr>
</tbody>
</table>

Important Point #3:
Cognitive domains are not a unitary (eg, memory)

- Short-term vs. long-term
- Episodic vs. semantic
- Anterograde vs. retrograde
- Recent vs. remote
- Encoding vs. retention vs. retrieval
- Declarative vs. nondeclarative
Short- vs. Long-term Memory

- **Short-term Memory**
  - Limited capacity
  - Information can only last up to a few minutes
  - Lost or replaced if attention is focused elsewhere
  - May be maintained through active rehearsal

- **Long-term Memory**
  - Large capacity
  - Potential to hold information indefinitely
  - Maintained even after intervals in which attention is focused elsewhere
  - No need for active rehearsal

Episodic vs. Semantic Memory

- **Episodic memory**
  - Information acquired at a particular time and place
  - Recall dependent upon time and place of learning
  - Examples:
    - What did you have for breakfast this morning?
    - What did you do on your last trip out of town?

- **Semantic memory**
  - Refers to general facts and knowledge
  - Recall not linked to any specific temporal/spatial context
  - Examples:
    - What is ‘breakfast’?
    - What is the capital of Texas?
Declarative vs. Nondeclarative

- **Declarative memory**
  - Acquisition of facts, experiences, and information about events
  - Memory expressed through conscious declaration
  - Examples:
    - Episodic memories
    - Semantic memories

- **Nondeclarative memory**
  - Acquisition of skills, conditioned responses, and predispositions to act
  - Memory expressed through doing
  - Examples:
    - Riding a bicycle
    - Classical conditioning
    - Priming

Encoding vs. Retention vs. Retrieval

- **Encoding**—the process by which information is transferred from STM→LTM

- **Retention**—the process by which stored information is maintained in a usable/searchable representation

- **Retrieval**—the process by which stored memories are brought back into conscious awareness
Memory Profiles

Memory Dysfunction in AD

- Preserved
  - Short-term memory
  - Semantic memories
  - Remote retrograde memories

- Impaired
  - Long-term memory
  - Episodic memories
  - Recent retrograde memories
Important Point #4:
If you can’t Mental Status Exam ‘em we can’t Auditory Verbal Learning Test ‘em

- Delirium
- Psychosis
- Non English speaker
- Sensory impaired

Neuropsychological Testing

- Wakefulness/arousal/attentional matrix
  - Concentration: span/vigilance/working memory
    - Digit span, PASAT, cont. performance tests…
  - Perseverance
    - Word list generation, serial recitation tests
  - Resistance to interference and response inhibition
    - Trail A-B, Stroop test, go-no-go procedure…

- Mood
  - MMPI, BDI, HDRS
Diagnostic Procedures

Trail B

Stroop

red blue orange purple
orange blue green red
blue purple green red
orange blue red green
purple orange red blue
green red blue purple
orange blue red green
green purple orange red
Diagnostic Procedures

Token Test

- Memory
  - Wechsler, verbal, visual and auditory learning tests…
- Language
  - Boston naming, aphasia battery, reading/spelling, Token test
- Calculation
- Perceptual tasks
  - Facial recognition, visual organization, space perception, judgment of line orientation…
- Constructional tasks
  - Rey-Osterrieth figure, cube construction, clock drawing…
Rey-Osterrieth Complex Figure

Visual Spatial Construction
Visual Spatial Construction

Visual Spatial Construction
Visual Spatial Construction

Clock Drawing
Clock Drawing

Baseline

One-year later

- Spatial distribution of attention
  - Bilat. stimuli, target cancellation, blindfolded exploration…

- Paralinguistic aspects of communication
  - Identification facial affect, discrimination/production affective prosody…

- Reasoning and abstractions
  - Wisconsin sort card, advance matrices, WAIS III…

- Planning and sequencing
  - Maze test, Tower of London…
Wisconsin Card Sort Test

Correct

Incorrect

“Non-shift” trial

“Shift” trial

“Inevitable-error” trial

Shape dimension

Color dimension

Dimensional change

Wisconsin Card Sort Test

1

2

3

4
Diagnostic Procedures

WAIS-III

Full-Scale IQ (FSIQ)

Verbal IQ (VIQ)

- Verbal Comprehension Index (VCI)
  - Vocabulary
  - Similarities
  - Information
  - Comprehension

- Working Memory Index (VMI)
  - Arithmetic
  - Digit Span
  - Letter-Number Sequencing

Performance IQ (PIQ)

- Perceptual Organization Index (POI)
  - Picture Completion
  - Block Design
  - Matrix Reasoning

- Processing Speed Index (PSI)
  - Digit Symbol-Coding
  - Symbol Search

Conceptual Sorting

airplane  BUTTERFLY  EAGLE

streetcar  SHARK  train
Diagnostic Procedures

- Air/Fly vs. Ground/Don’t Fly
- Animals/Living vs. Vehicles/Inanimate
- Compound vs. Simple Words
- Upper Case vs. Lower Case
- White vs. Black Lettering
- Blue vs. Pink Background
- Pattern vs. Solid Fill
- Large vs. Small Shapes
- Rounded vs. Angled Shapes

Tower of London

Initial Position vs. Goal Position
Tower of London

Tower of London
Brain Systems as Memory Systems: Encoding Nondeclarative Memories

- Basal ganglia
  - Motor skill learning
  - Priming
- Cerebellum
  - Motor skill learning
  - Classical conditioning
- Amygdala
  - Conditioned fear
  - Emotional modulation of memory

Brain Systems as Memory Systems: Retrieval

- Retrieval of previously learned information is reliant upon the integrity of:
  - White matter
  - Frontal-subcortical nuclei (basal ganglia)
The Normal Curve

The Normal Curve & IQ Scores
Clinicoradiologic Pearls: 
Age and Atrophy

- Atrophy of the cerebral cortex, hippocampi, and cerebellum clearly evolves with age
- One must not overinterpret atrophy in individuals over 80 years of age
- One must not underinterpret atrophy in individuals less than 65 years of age

Clinicoradiologic Pearls: 
Coronal vs. Axial MR Images for Focal Atrophy

- Coronal images often depict hippocampal and temporal cortical atrophy better than axial images
- Axial images often depict focal frontal, parietal, or occipital cortical atrophy slightly better than coronal images
- Both coronal and axial images provide useful radiologic data in patients with degenerative dementing illnesses
Vocabulary

- **Single photon emission computed tomography (SPECT)**
  - Uses a radioactive metabolite to measure cerebral perfusion
    - Usually uses technetium-99 based agents
  
<table>
<thead>
<tr>
<th>Dataset:</th>
<th>Functional &gt; structural</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strengths:</td>
<td>Reasonably accessible functional imaging tool, longer half-life metabolite</td>
</tr>
<tr>
<td>Weaknesses:</td>
<td>Poor resolution limits application, ionizing radiation</td>
</tr>
</tbody>
</table>

- **Positron emission tomography (PET)**
  - Uses a radioactive isotope to measure cerebral metabolism
    - Usually, 18-fluorodeoxyglucose (18FDG), but others such as 18-fluorodopa may be used

<table>
<thead>
<tr>
<th>Dataset:</th>
<th>Functional &gt; structural</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strengths:</td>
<td>Higher spatial resolution than SPECT</td>
</tr>
<tr>
<td>Weaknesses:</td>
<td>Logistics and cost (short metabolite half-life, need for on-site cyclotron), ionizing radiation</td>
</tr>
</tbody>
</table>
FDG-PET in Cognitive Impairment/Dementia—Normal

Amnestic Mild Cognitive Impairment
Mild Cognitive Impairment

MCI, then DLB, then autopsy-proven LBD

Mild Cognitive Impairment to Alzheimer’s Disease

Age 83

Age 86
MRI Changes from MCI to AD

Clinically Normal

MRI Changes from MCI to AD

MCI
Clinicoradiologic Pearls:
MRI Changes from MCI to AD

- Usually there is observable progressive hippocampal atrophy in the transition from MCI to AD by visualizing MR images.
- Hippocampal volumetric measurements do decrease in the transition from MCI to AD.
- Hippocampal atrophy in MCI patients predicts conversion to AD.
- Again, lack of hippocampal atrophy makes one question another etiology (e.g., LBD), but this is not a consistent association.
Clinicoradiologic Pearls: MRI Changes in Mild to Severe AD

- Cerebral cortical and hippocampal atrophy progresses as the severity of dementia increases.
- The atrophy tends to be symmetric, although there are some patients with strikingly focal or asymmetric hippocampal and/or cerebral cortical atrophy.
- The degree of hippocampal atrophy is often more pronounced than the degree of cortical atrophy.

PET in AD

Reiman et al, NEJM 1996
PET in AD

- General findings of AD:
  - Temporoparietal hypoperfusion on SPECT
  - Temporoparietal and posterior cingulate hypometabolism on PET
- Posterior cingulate, parietal cortex, temporal cortex, and prefrontal cortex metabolism is consistently reduced in AD and ApoE4 homozygotes
PIB binds specifically to fibrillar beta-amyloid (Aβ) deposits, and is a sensitive marker for Aβ pathology in cognitively normal older individuals and patients MCI and AD.

From: Rabinovici and Jagust. Behav Neurol. 2009; 21(1): 117-128

Amyloid Angiopathy

T1 + Gad  FLAIR  GRE
Clinicoradiologic Pearls
Amyloid Angiopathy

- The principle component of neuritic plaques is $A\beta_{42}$; that of amyloid angiopathy is $A\beta_{40}$
- Amyloid angiopathy (AA) often accompanies Alzheimer’s disease (AD), but AA can occur in the absence of dementia and AD can occur in the absence of AA
- Microhemorrhages associated with AA are best seen with the GRE sequence on MRI

Lewy Body Dementia
Clinicoradiologic Pearls: MRI Findings in Lewy Body Dementia

- In “pure” Lewy body dementia (LBD), also known as Dementia with Lewy bodies (DLB), there is usually no or only mild cerebral cortical and hippocampal atrophy.

- In “common” LBD, in which Alzheimer’s pathology is present in addition to limbic +/- cortical Lewy bodies, atrophy in the hippocampi and cerebral cortex looks similar to that seen in AD.

- Some patients with DLB have generalized ventricular enlargement, which must be distinguished from that seen in NPH.

PET in Lewy Body Dementia: SPECT or PET in Lewy Body Dementia

- Occipital +/- parietal hypoperfusion/hypometabolism most consistent finding based on the literature.

- PET may be over-rated in the setting of mild dementia associated with DLB. In other words, don’t use PET to confirm or negate the diagnosis when the clinical features are typical of DLB.
Frontotemporal Dementia: Progressive MR Changes

Initial Evaluation  2 yrs later  2 yrs later

PET in Frontotemporal Dementia
PET in Frontotemporal Dementia

- Frontal and/or temporal hypometabolism is highly suggestive of FTD
- PET is often quite helpful in confirming FTD or distinguishing FTD from AD.

Progressive Nonfluent Aphasia/Apraxia of Speech
Progressive Fluent Aphasia/Semantic Dementia

Clinicoradiologic Pearls: MRI Findings in Progressive Fluent Aphasia/Semantic Dementia

- The focal deficits in this syndrome suggest cortical dysfunction which is maximal in the dominant hemisphere
- Almost all patients have severe anomia associated with focal atrophy of the left anterior inferolateral temporal cortex (Brodmann’s area 38)
- Despite normal or only mildly impaired verbal memory functioning, the left hippocampus can vary from normal in size to markedly atrophic
PET in Semantic Dementia

Corticobasal Syndrome:
Moderate
Corticobasal Syndrome:
Moderate

Clinicoradiologic Pearls:
MRI Findings in Corticobasal Syndrome
- The focal or asymmetric deficits in this syndrome suggest cortical dysfunction which is maximal in the posterior frontal (areas 4, 6) and/or parietal (areas 3, 1, 2, 5, 7, 40) regions
- The MRI findings can vary from entirely normal to striking focal/asymmetric atrophy. Atrophy can extend well beyond the frontoparietal cortex
- Some patients have increased T2 signal in subcortical white matter adjacent to maximally-affected cortical region, which presumably reflects gliosis and/or spongiosis
PET in CBS

The focal or asymmetric hypometabolism tends to be maximal in these structures (and are variable from pt to pt):

- Supplementary motor area
- Posterior frontal
- Anterior parietal
Posterior Cortical Atrophy
Progressive MR Changes

1/99
59 yr

7/00
60 yr

PET in PCA
Vascular Dementia
Binswanger’s Disease

Autopsy confirmed Binswanger’s (+AD, and LBD)
Clinicoradiologic Pearls: MRI Findings in Vascular Dementia

- The differentiation of benign leukoaraiosis from true vascular changes causing cognitive dysfunction is still being defined. Many older individuals will have mild to moderate patchy and/or confluent white matter changes on MRI, which may or may not be clinically significant.

- Binswanger’s disease refers to a subcortical arteriopathy that is also still being defined. Most patients have cognitive impairment, gait impairment, and urinary incontinence (sound familiar?)

- Cognitive decline/dementia developing after 1 or more cerebral infarcts are the defining features of vascular dementia.

Normal Pressure Hydrocephalus

Note periventricular T2 signal changes suggestive of transependymal flow; Flow rate: 19.8 ml/min (nl 2–18)
Normal Pressure Hydrocephalus

Note accentuation of flow void in cerebral aqueduct (arrows)

Clinicoradiologic Pearls:
MRI Findings in Normal Pressure Hydrocephalus (NPH)

- Most NPH patients have ventricular enlargement, and one or more of the following: cognitive impairment, gait impairment, and urinary incontinence; this is presumed due to the “stretching” of axons traversing the periventricular regions

- Not all patients with NPH will benefit from shunting
Clinicoradiologic Pearls:
MRI Findings in Normal Pressure Hydrocephalus (NPH)

- The accentuated flow void in the aqueduct suggests decreased compliance, and thus elevated aqueductal flow rate.

The MRI-aqueductal flow protocol (or NPH aqueductal flow protocol) is helpful in deciding in whom you recommend VP shunting, but response to therapeutic tap more informative than MRI. However, shunting should NOT be based purely on flow rate.

Prion Disease

Autopsy revealed CJD
Prion Disease

FLAIR

DWI

143

8/01 11/01 5/01

144

5/01 8/01 11/01
Prion Disease

**Clinicoradiologic Pearls:**

**MRI Findings in Prion Disease**

- Increased signal (NOT ENHANCEMENT) in the cortical ribbon, or basal ganglia, are the most consistent findings on FLAIR or diffusion-weighted images (DWI) MR scans in patients with CJD.

- Some patients with autopsy-proven CJD have had entirely normal MRI scans.

- DWI is more sensitive than FLAIR in CJD.

- FLAIR or DWI may allow determination of efficacy of potential agents for treatment of CJD.
Nonvasculitic Autoimmune Inflammatory Meningoencephalitis (NAIM)

- “Hashimoto’s encephalopathy”
- Sjögren's-associated encephalopathy
- Neuropsychiatric lupus or “lupus cerebritis”
Nonvasculitic Autoimmune Inflammatory Meningoencephalitis (NAIM)

Clinicoradiologic Pearls: MRI Findings in NAIM

- Diffusely increased signal in the white matter, or meningeal enhancement, are the 2 most frequent findings in NAIM

- Most patients with NAIM have entirely normal MRI studies
Limbic Encephalitis

65M
9/1/00
+
symptoms

65M
9/11/00
↓
symptoms

CSF in Cognitive Disorders

- Mainly done to differentiate degenerative from other (potentially treatable) etiologies: inflammatory, infectious, neoplastic etc.
- Neuron specific enolase and protein 14-3-3: high levels indicate accelerated neuronal death. Thus are high in trauma, stroke, encephalitis AND in CJD, occasionally steroid responsive encephalopathies and even rapidly progressive AD
Biomarkers for MCI/AD

- No CSF analyte was associated with functional decline in AD
- Among controls, p-tau181 concentration was the most sensitive to functional decline, whereas in MCI it was Aβ42 concentration.
- Across all diagnostic groups, persons with a combination of tau and Aβ42 abnormalities exhibited the fastest rate of functional decline.
- p-tau181 levels reflect neurofibrillary tangle formation and the density of tangles correlates better with cognitive decline and dementia than plaque load

Posttest

*(repeat of pretest questions)*
Question 1: Which study is the most specific in vivo reflection of amyloid-beta protein load?
1. PET using Pittsburgh compound B
2. PET using Philadelphia compound B
3. PET using deoxyglucose
4. CSF A-beta 42 measurement

Question 2: Which of these tests is most sensitive to frontal lobe damage?
1. Boston naming test
2. MMPI
3. Wechsler memory scale
4. Wisconsin card sorting test
5. Judgment of line orientation
Question 3: Simultanagnosia is usually seen in (or associated with):

1. Balint's syndrome
2. Anton's syndrome
3. FTLD
4. Lewy body dementia
5. Hemispatial neglect

Question 4: A patient can shave properly, but cannot show how to use a razor on command. What's the most likely cause?

1. Ideomotor apraxia
2. Kinetic apraxia
3. Ideational apraxia
4. Response inhibition
5. Inattention
Question 5: The classic PET pattern in AD shows hypometabolism in:

1. Bilateral parietal areas and precuneus
2. Bitemporal areas
3. Biparietal-occipital areas
4. Frontotemporal areas
5. Asymmetric, diffuse cortical

Answer Key

- Question 1: 1
- Question 2: 4
- Question 3: 5
- Question 4: 1
- Question 5: 1
Questions and Answers