DEMENTIA 101:
WHAT IS HAPPENING IN THE BRAIN?

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OBJECTIVES

• Terminology/Dementia Basics
• Most Common Types
  • Defining features
  • Neuro-anatomical/pathological underpinnings
  • Neuro-cognitive presentation
• Diagnostic Considerations
  • General
  • Neuropsychological
• Healthy Aging
COGNITIVE DOMAINS

• Attention
• Language
• Visuo-Spatial Function
• Memory
• Executive Function
DEMENTIA

- Umbrella term which captures a wide variety of conditions
- “…loss of cognitive functioning—thinking, remembering, and reasoning—and behavioral abilities to such an extent that it interferes with a person's daily life and activities…” NIH
- Typically occurs with advanced age
- Progressive
- Not normal aging
MEMORY ACROSS THE LIFESPAN

CVLT LD Male
CVLT LD Female
The continuum of Alzheimer's disease

- Aging
- MCI
- Dementia

Cognitive function vs. Years
Dementia by Pathology

**Tauopathy**
*Alzheimer's disease (AD)*
Pick’s disease
Corticobasal syndrome (CBS)
Progressive supranuclear palsy (PSP)
Argyrophilic grain disease (AGD)
*Frontotemporal dementia with parkinsonism linked to chromosome 17 (FTDP-17tau)*
Primary Progressive Aphasia with AOS

**Amyloidopathy**
*Alzheimer’s disease (AD)*
Posterior Cortical Atrophy (PCA)
*Logopenic Aphasia (LPA)*

**Synucleinopathy**
Parkinson’s disease (PD)
Dementia with Lewy bodies (DLB)
Multiple system atrophy (MSA)

**Polyglutamine**
Huntington’s disease (HD)

**TDP-43opathy**
Frontotemporal lobar degeneration with TDP-43-positive inclusions (FTLD-TDP)
  1. svPPA
  2. bvFTD
  3. aggPPA
  4. *Logopenic Aphasia (LPA)*
FTLD with motor neuron disease (FTLD-MND)
Hippocampal sclerosis (HS)
Amyotrophic lateral sclerosis (ALS)
*Frontotemporal dementia with parkinsonism linked to chromosome 17 (FTDP-17PGRN)*

**Prionopathy**
Creutzfeldt-Jakob disease (CJD)
Fatal familial insomnia (FFI)
Gerstmann-Straussler-Scheinker Syndrome (GSS)
ALZHEIMER’S DISEASE (AD)

- Far and away most common form of dementia
  - ~50%
- Gradual decline in mental abilities
  - Memory impairment
  - Course varies some, typically less aggressive
- Onset typically older age; 65+
  - Average onset ~75
  - ~50% meet criteria at 85
  - Early onset can occur (40s-50s), higher genetic component
  - Women > Men
AD PATHOLOGY

• Alois Alzheimer-1906
• Amyloid Plagues
  • outside cells
• Neurofibrillary tangles
  • inside cells
• Disrupt and eventually destroy neural networks in the CNS, breaking down communication
AD NEUROIMAGING

- Generalized cortical atrophy
- Medial temporal structures often most pronounced
  - Entorhinal Cortex
  - Hippocampus
- Supportive but not diagnostic
AD NEUROIMAGING

• Hippocampal Function
  • Memory *consolidation*
  • Essential in the formation of new memories
  • Declarative Memory
Figure 3-1: Coronal T1-weighted MRI slices with findings suggestive of Alzheimer disease (AD) pathology.
Patient with Alzheimer’s disease

Healthy control
COGNITIVE PROFILE OF AD

• Episodic memory
  • Impaired early in the course
  • Minimally benefit from retrieval cues
  • Errors in memory (intrusions)
  • Subtle decline in episodic memory often occurs prior to more obvious indicators of dysfunction
frontal lobe

somatomotor cortex

somatosensory cortex

parietal lobe

occipital lobe

temporal lobe

medulla oblongata

cerebellum

spinal cord
COGNITIVE PROFILE OF AD, CONT.

• Language
  • Semantic knowledge
    • Loss of *meaning* of words and general knowledge
    • AD patients often make superordinate errors in speech (e.g., naming a *bear* an *animal*, naming a *trout* a *fish*)
    • Breakdown in semantic networks
  • On cognitive testing, deficits in:
    • Naming
    • Verbal fluency
VASCULAR COGNITIVE IMPAIRMENT

- Cognitive impairment related to vascular factors
- Heterogenous syndrome/diverse etiology
- Three processes typically associated with VCI
  - Large artery infarctions
  - Small artery infarctions
  - Chronic subcortical ischemia
- Challenging to determine incidence rate
VASCULAR COGNITIVE FUNCTION

- Diverse Cognitively
- Large artery infarctions
  - Specific to the region (strategic infarct)
- Chronic ischemia
  - White matter pathology
  - “Subcortical syndrome”
  - Executive deficits with relatively mild memory difficulties
COGNITIVE PROFILES: VCI VS. AD

VCI
• Subcortical
• Prominent Executive Dysfunction
• Reduced attention
• Memory *Retrieval* Deficit

AD
• Cortical
• Prominent Memory Dysfunction
• ~Normal attention
• Memory *Consolidation* Deficit
VASCULAR POINTS TO CONSIDER

- Vascular events lead to dementia, but dementia does not always follow vascular events
  - Dementia often over-diagnosed if assessed within a year of stroke
- Controlling cardiovascular risk factors is encouraged for prevention
  - Research is mixed
- Overlap with AD pathology
Neurodegenerative burden

Alzheimer disease  Vascular dementia

Vascular cerebral lesion burden

VISWANATHAN A. NEUROLOGY (2009)
LEWY BODY DEMENTIA (LBD)

- 2nd most common form of dementia
- Approximately 10-20%
- Onset typically over 65
- Men = Women
- Course 6-12 years post symptom onset
LEWY BODY DEMENTIA

1. Cognitive impairment

2. Fluctuating Cognitive Course

3. Recurrent Hallucinations

4. Parkinsonism’s
LBD FEATURES

- Visual hallucinations
  - Fully formed/detailed/3-dimensional
  - Typically occur early in the course of the disease
  - Hallucinations can occur in AD, but typically much later
- Course fluctuations
  - A waxing/waning of alertness
  - Prominent confusion
  - Disorganized speech
LBD FEATURES, CONT.

- Movement symptoms similar to PD but less severe
  - Slow gait/shuffling/poor balance
  - Increased fall risk
  - Flat affect
  - Resting tremor not as common as PD
LBD RELATED FACTORS

- REM Sleep Disorder
  - Dream re-enactment which occurs during REM cycle
    - Vocalizations
    - Complex and purposeful motor behaviors
  - Associated with early Lewy Body pathology

- Psychiatric factors
  - Visual hallucinations can be disruptive
FIGURE 4: Comparison of brain perfusion SPECT images for AD and DLB.
LBD PATHOLOGY

• Lewy bodies
  • Protein deposits in nerve cells
  • Disrupts connections between nerve cells
• Same pathology as Parkinson’s Disease
  • Deep brain structures with PD
• Cortical Lewy bodies related to cognitive/neuropsychiatric symptoms
• Individuals with PD can develop dementia (Parkinson’s Dementia)
• AD pathology
LBD COGNITION

- Visual/visuo-spatial function
  - Markedly impaired early
- Attention
  - Impaired early, particularly complex/sustained aspects
- Executive Difficulties
  - Impaired early
- Memory
  - Similar to AD, but often not to the same degree
- Global impairment as disease progresses
FRONTOTEMPORAL DEMENTIA (FTD)

• Typically represents progressive behavioral change or aphasia
• Emerges most often in the 50s-60s
• Men = Women
• Progress more rapidly than AD
• Can be quite complex diagnostically
FTD–BEHAVIORAL VARIANT

- Most common of the FTDs
- Progressive change in personality and behavior
- Breakdown of behavioral inhibition
  - Impulsive/inappropriate
  - Reduced sympathy/socially disconnected
- Markedly reduced insight
- Personality change often initially thought to represent psychiatric condition
FTD LANGUAGE VARIANTS

• Progressive Aphasia
  • Changes in language, may be slow/hesitant or exhibit stuttering
  • May make grammatical errors in speech (e.g., leaving out words)

• Semantic
  • Loss of meaning for words
  • May use more generalized words (e.g., pass me the “thing”)

• With disease progression, conditions become more similar (Behavioral + Language Variants)
FTD
IMAGING/PATHOLOGY

- Imaging
  - Behavioral Variant
    - Focal/symmetric of the frontal lobes
  - Language Variants
    - Asymmetric atrophy (L > R)
    - Temporal lobes-Semantic
    - Frontal lobes-Non-fluent

- Pathology
  - FTLD-tau, FTLD-TDP, and FTLD-FUS
Progressive Aphasia
- Slow changes in language, may be slow/hesitant or exhibit stuttering
- May make grammatical errors in speech (e.g., leaving out words)

Semantic
- Loss of meaning for words
- May use more generalized words (e.g., pass me the “thing”)
FTD COGNITIVE PRESENTATION

• Behavioral Variant
  • Executive dysfunction (difficulty with planning/complex decision making)
  • Typically intact memory abilities
  • In general, cognitive testing less helpful in diagnosis, often based on behavioral presentation

• Language Variants
  • Impairment in speech production
DIAGNOSTIC METHODS

• Medications
• Lab rule outs:
  • B12
  • Thyroid
  • Folate
• Sleep difficulties
  • OSA
• Cognitive Screening
• Neuroimaging
NEUROPSYCHOLOGICAL ASSESSMENT

• Quantify potential impairment
• Identify strengths/weaknesses
• Potential limitations (functional & decision making)
• Explore psychiatric factors
• Diagnostic clarity
• Establish a baseline of cognitive status
COGNITIVE DOMAINS

- Attention
- Language
- Visuo-Spatial Function
- Memory
- Executive Function
- Mood
- ADLs
NEURO-COGNITIVE PROFILE: AMNESTIC MCI

A-MCI

Normal
Mild
Moderate
Severe

Mood  Att  Lang  VP  Mem  EF  ADLs
NEURO-COGNITIVE PROFILE: ALZHEIMER’S DEMENTIA

Mood  Att  Lang  VP  Mem  EF  ADLs

Normal

Mild

Moderate

Severe
NEURO-COGNITIVE PROFILE: VASCULAR IMPAIRMENT

VCI

Normal

Mild

Moderate

Severe

Mood  Att  Lang  VP  Mem  EF  ADLs
HEALTHY AGING

• Intellectual Activity
  • Increases mental stimulation
  • Hobbies (e.g., taking a course, playing games, reading/writing)

• Social Activity
  • Stay socially involved
  • Get involved (e.g., groups, volunteering, church)
HEALTHY AGING, CONT.

- **Exercise**
  - Robust body of research highlighting the positive benefits
  - As effective as some anti-depressants
  - Increases multiple neurotransmitters

- **Sleep**
  - Sleep difficulties may be associated with an increased risk for AD
  - 5% increase in beta-amyloid following one night of sleep deprivation
QUESTIONS?