Neurocognitive disorders Diagnostic Strategies

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Overview

Part 1: Basic Principles
- Cognitive decline
- Detecting cognitive decline

Part 2: Neurocognitive Disorders (NCD)
- Diagnostic criteria
- DSM-5 diagnostics

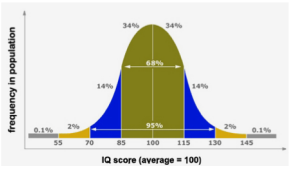
Part 3: Common NCD Etiologies
- Alzheimer's disease
- Vascular disease
- Lewy-body disease
- Frontotemporal degeneration

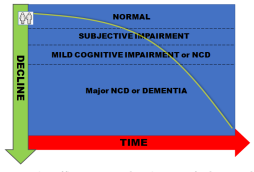
NORMAL AGING

- Cognitive abilities reach their peak when people are in their 30's and 40's
- Remain stable until late 50's and early 60's and then start to decline but only to a **SMALL DEGREE**
- Difficulties with
  - Attention
  - Processing speed
  - Working memory

Cognitive Impairment and Decline

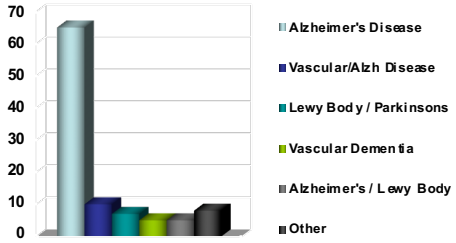
- **Cognitive impairment**: Poorer performance in neuropsychological domains than expected for age and education
- **Cognitive decline**: Reduced cognitive functioning from a previously higher level



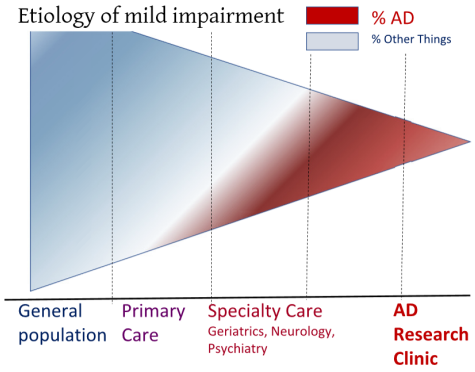


Public Domain Image http://hiqnews.megafoundation.org/Definition_of_IQ'.html

Common NCD Etiologies



Small et al. 1997, APA 1997, Morris 1994



Cognitive Function

- Heterogeneous cluster of mental functions
- **Neurocognitive Domains**: (APA 2013)
  - **Complex attention**: alertness, orientation, selection
  - **Executive function**: planning, inhibition, flexibility
  - **Learning and memory**: recognition, recall
  - **Language**: expression, comprehension
  - **Perceptual-motor function**: visual construction, motor abilities
  - **Social cognition**: recognition of emotions, social norms

EVALUATION AND DIAGNOSIS

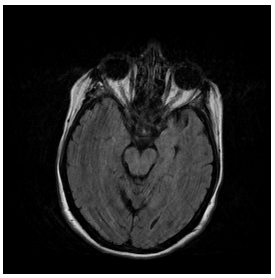
- Clinical presentation
- Medical history
- Physical examination
- Laboratory data
- Cognitive testing
- Imaging

Neuroimaging

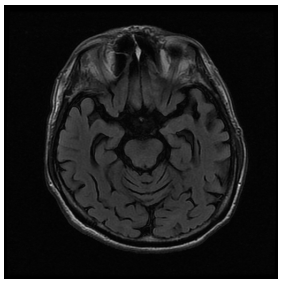
- What to look for:
  - General appearance of the brain
  - Look for ventricular enlargement
  - **Evaluate for vascular disease**
  - Look for specific **patterns of atrophy**

Two cases

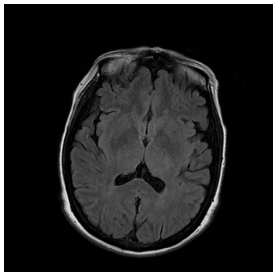
62 yo with h/o schizoaffective d/o and cognitive decline

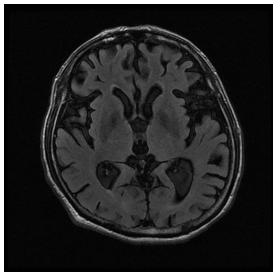


70 yo with psychosis and cognitive decline

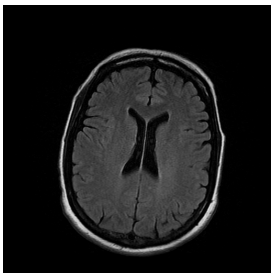


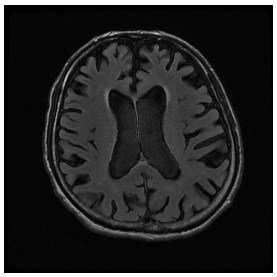
Two cases



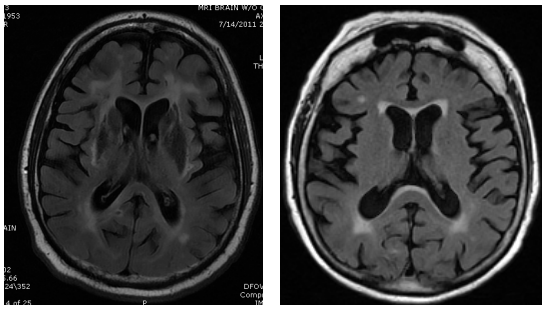


Two cases



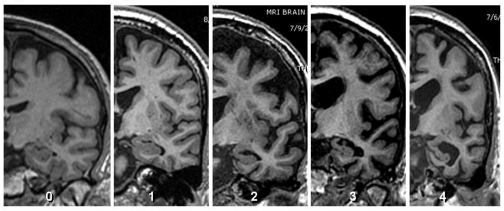


MRI - Vascular disease



Patterns of atrophy on MRI

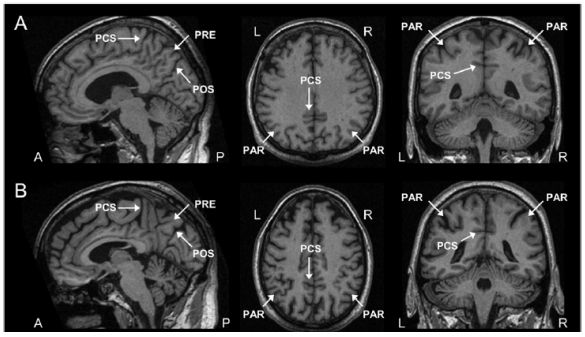
- Figure 1. Visual Rating Scale



Images of five degrees of atrophy in Hippocampus and Entorhinal cortex according to Visual Rating Scale where 0 = no atrophy, 1 = minimal atrophy, 2 = mild atrophy, 3 = moderate atrophy and 4 = severe atrophy.

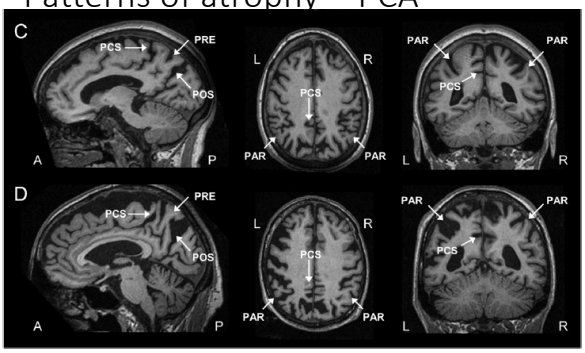
Varon et al. Int J Geriatr Psychiatry. 2015

Patterns of atrophy - PCA



Lehmann, M. 2011

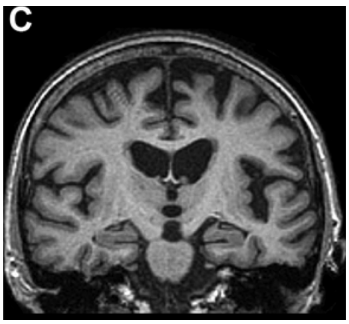
Patterns of atrophy - PCA



Lehmann, M. 2011

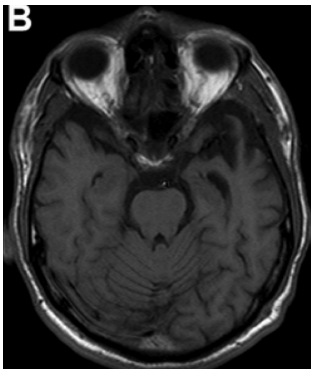
FTD

- **Nonfluent agrammatical form**
- Imaging:

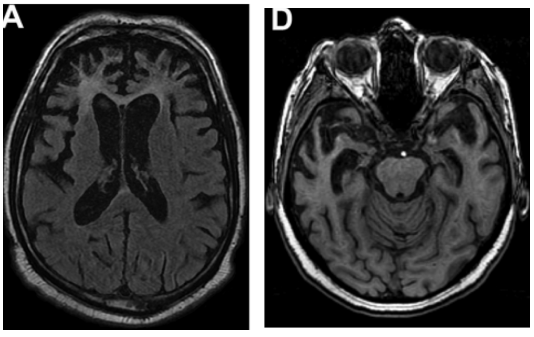


FTD

- **Semantic form**
- Imaging:



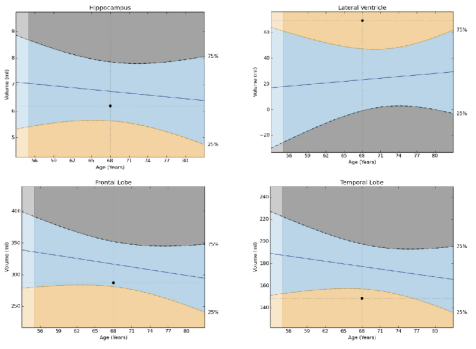
FTD – Behavioral variant



ORDER

- MRI Brain w/o contrast.
- Indication: Cognitive decline
  - Include **thin coronal slices** using SPGR or similar sequence to evaluate for specific **patterns of atrophy.**
  - Please provide volumetric analysis if **Neuroreader** or similar software available.

MRI Brain – may include volumetric readings



MRI Brain

Neuroreader™

Report

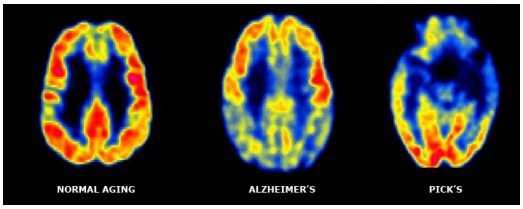
Conclusion

All structures with a percentile lower than 25% and a percentile over 75% for all ventricles and CSF (orange font):
-Left Ventral Diencephalon (24.65%)
-Temporal Lobe (17.04%)
-Right Temporal Lobe (17.10%)
-Left Temporal Lobe (19.73%)

-Lateral Ventricle (90.22%)
-Right Lateral Ventricle (88.13%)
-Left Lateral Ventricle (90.96%)

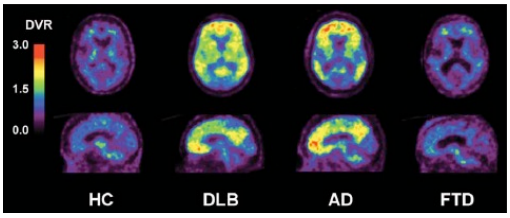
DIAGNOSIS

- Neuroimaging
  - FDG - PET
    - Better at separating AD from other dementias
    - Sensitivity and Specificity up to 86%



Alzheimer's Disease Biomarkers

- **IMAGING**
  - Amyloid imaging techniques



Vascular NCD

- **Common features**: cognitive deficits match sites of vascular damage (often complex attention, executive function)
- **Pathophysiology**: vascular injury (e.g., ischemic stroke, hemorrhage, small vessel disease)
- **Progression**: variable age of onset and survival; insidious, step-wise, or rapid progression based on nature of injuries
- **Often comorbid with Alzheimer's disease**

Vascular NCD

Multi-infarct dementia (cortical vascular dementia)
Small vessel dementia (subcortical vascular dementia)
Strategic infarct dementia
Hypoperfusion dementia
Haemorrhagic dementia
Hereditary vascular dementia (CADASIL)
Alzheimer's disease with cardiovascular disease

Table 1: Subtypes of vascular dementia

O'Brien JT et al. Lancet 2015

Vascular NCD

- **Second most common etiology of major NCD (~20%)**
- **Population Prevalence**: (APA 2013)
  - Age 65: 0.5-1%
  - Age 80: 16%
- **Prevalence by Neuropathology Series**: (APA 2013)
  - Age 70: 13%
  - Age 90: 44.6%
- **Within 3 months of stroke**: 20-30% NCD diagnosis

Alzheimer's Disease

- **Common features**: impairments in memory, learning early; language, executive and social cognitive function later
- **Pathophysiology**: accumulation of amyloid plaques, neurofibrillary tangles and loss of synapses and neurons
- **Progression**: onset typically in 70-80s; steady and gradual progression; survival 6-12 years (avg. 10 years)

Lewy-Body Disease

- **Common features**:
  - Primary: fluctuating cognition (e.g., inattention), visual disturbances, spontaneous parkinsonism
  - Secondary: sleep disturbance, sensitivity to antipsychotic agents
- **Pathophysiology**: cortical presence of *Lewy bodies*
- **Progression**: typical onset ~70s; cognitive features before motor features; duration of survival 5-7 years

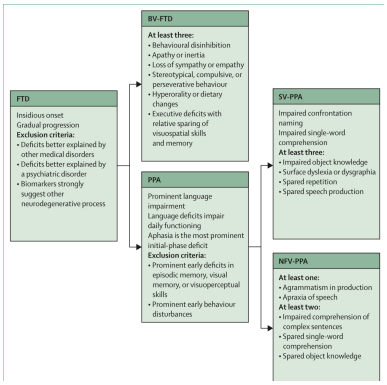
Lewy-Body Disease

- **Second most common neurodegenerative etiology of NCD (2-30% of cases; average report ~10-20%)**
- In post-mortem brain biopsy, Lewy bodies found in 20-35% of individuals with dementia
- **Population Prevalence**: 0.1-5% of individuals >65 years
- M:F ratio = 1.5:1

Frontotemporal Degeneration

- **Common features**:
  - Behavioral Variant: disinhibition, apathy, loss of empathy, perseverative/stereotyped behavior, dietary changes
  - Language Variant: decline in speech production, word finding, object naming, grammar, or word comprehension
- **Pathophysiology**: preferential degeneration of frontal and temporal neural networks
- **Progression**: typical onset ~50s; more rapid progression; duration of survival 6-10 years after symptoms, 3-4 years after diagnosis

FTD



Bang J et al. Lancet 2015

FTD Spectrum

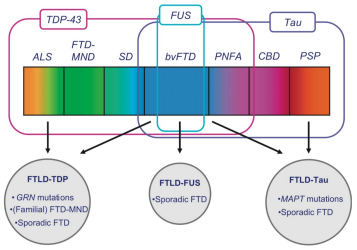


Figure 2 Clinical, genetic and pathological spectrum of frontotemporal lobar degeneration.

Seelaar H et al. JNNP 2011

Questions?