Frontotemporal Dementia (FTD)
Compare and contrast with Alzheimer disease

- Most common cause of dementia by far -70%
- More common with advancing age
  \[ \geq 65 \text{ YO} \rightarrow 7\% \]
  \[ \geq 85 \text{ YO} \rightarrow 30-47\% \]
- Insidious onset, slowly progressive course
- Earliest manifestation usually STM (short term memory loss)
• Other **early** cognitive deficits
  – Executive function (abstract thinking, planning, organizing)
  – Language (forget words, verbal expression, comprehension of reading)

• **Middle-to-late stage manifestations**
  – Gait instability / falls
  – Incontinence
  – BPSD (Behavioral and Psychological Symptoms of Dementia)
  – Personality changes
  – At best, modest / temporary improvement with CEI (cholinesterase inhibitors)
FTD

• Pathologically / clinically heterogeneous disorder with focal degeneration of frontal and/or temporal lobes

• Onset typically late 50’s- early 60’s; mean age 58
  – Onset 20-80; unusual < 40 or > 75

• Earliest manifestations
  – Personality changes / social behavior changes (behavior variant)
  – Language deficits

• Slowly progressive to more global dementia

• Some with extrapyramidal or motor symptoms

• 1/3 with FH
• Pick disease → behavioral variant with Pick bodies (intracellular inclusions)
• Other terms
  – Frontal lobe dementia
  – Frontal lobe degeneration
  – Frontotemporal lobar degeneration
  – Pick complex
FTD Subtypes

- Behavioral variant (BV)
- Progressive Nonfluent Aphasia (PNFA)
- Semantic Dementia (SD) → progressive fluent aphasia
- Motor Syndromes
  - Motor Neuron Disease (MND)
  - Corticobasilar Degeneration (CBD)
  - Progressive Supranuclear Palsy (PSP)
Clinical manifestations:

• Progressive Δ in personality / social behavior OR
• Progressive aphasia
• Ultimately a global dementia
• More rapid progression than AD; shorter with motor neuron variant
  – Four- eight years
Behavioral Variant

• Most common presentation of FTD
• Personality \( \Delta \)
  – Apathy \( \rightarrow \) withdrawal; \( \downarrow \) spontaneity; abulia
  – Social disinhibition / impulsivity / \( \uparrow \) sentimentality / violent aggression
• Lack insight
  – All by two years
  – Lack of concern
• Loss of social awareness
  – Offensive remarks; inappropriate behavior
  – Hygiene; inappropriate elimination
  – Antisocial acts; criminal acts
  – Inappropriate sexual comments; \( \downarrow \) libido
• Stereotypical or ritual behaviors
  - Same foods
  - Catch-phrase
  - Hoarding
  - Counting
  - Pacing
• Eating pattern Δ’s
  - overeat; binge
  - ETOH
  - Hyperorality
• Emotional blunting / loss of empathy
  - Self- centered
  - Difficulty recognizing others’ emotional expression
• Mental rigidity
  – Inflexible routines
  – Inability to adapt to new situations
  – Inability to see others’ point of view
• Deficits modulating attention
  – Distractibility
  – Perseverative behavior
  – Utilization behavior
• Collateral history is imperative
• Cognitive function relatively intact early (MMSE)
  – With progression → impaired executive function, problem-solving, attention
  – Memory and visuospatial skills less severe
• Subtype with impaired executive function and subtle behavioral Δ’s initially
• Altered speech
  – Aspontaneity - echolalia
  – Paucity of speech - perseveration
  – ↑’d, often pressured, speech
  – Stereotypy - mutism
• Progressive Nonfluent Aphasia

• Anomia is initial manifestation
  - Word-finding; object naming
• Progressively dysfluent speech
  - Simplification; circumlocution; phonemic paraphasia
• Ultimately, difficulty with comprehension; may become mute
• Restricted to expressive language for few- several; years global dementia later
• Some develop behavioral manifestations or motor neuron disease
• MRI – left perisylvian atrophy
Semantic Dementia (temporal variant)

• Initially a progressive speech disturbance
  – Impaired comprehension; anomia; semantic parapahsias
  – Normal fluency → effortless speech lacking meaning & information
  – Normal repetition
• Incomplete awareness, particularly impaired comprehension
• Dyslexia / dysgraphia
• Read and write phonetically
• Verbal fluency tests
  – category fluency > letter fluency
• MRI- temporal atrophy, L > R; more anteriorly than AD
• Visual object recognition impairment affects long-term memory
• Episodic memory (autobiographical) is relatively preserved
• Less commonly R temporal lobe deficits
  – recognizing faces / voices
• Behavioral problems usually within few years
Motor Syndromes

- Motor Neuron Disease (MND)
- Corticobasal Degeneration (CBD)
- Progressive Supranuclear Palsy (PSP)
Motor Neuron disease (MND)

- Precede or follow dementia, usually behavioral variant
- 50 % with MND have / develop dementia
- Progressive atrophy / flaccidity / fasciculation's of predominantly bulbar muscles and UE’s
- UMN signs less prominent
- Clinical features of both FTD-MND usually within two years
- Course more rapidly progressive
- MRI- bifrontal atrophy
Corticobasal degeneration (CBD)

- Asymmetric rigidity / apraxia
- Alien limb syndrome
- Dystonia
- Impaired joint position, 2-point discrimination, agraphesthesia
- Mirror movements
- Gait impairment and supranuclear gaze palsy spread to other side
- Cognitive impairment develops in most
- MRI- asymmetric atrophy of frontoparietal, basal ganglia and/or cerebral peduncles
Progressive Supranuclear Palsy (PSP)

- Supranuclear vertical gaze palsy
- Axial dystonia
- Bradykinesia
- Rigidity
- Falls
- Most with dementia and overlap with behavioral variant FTD
- MRI- symmetric atrophy of superior cerebellar peduncle and midbrain
Differential Dx

• Of BV – FTD
  – Psychiatric disorder → bipolar; OCD; depression
    • Major psychoses uncommon in BV-FTD (delusions, hallucinations)
  – AD
    • Younger onset; prominent behavioral sx without significant amnesia
  – DLBD
    • Early visual hallucinations
  – Structural frontal lobe disease → MRI
    • CVA, tumor, abscess
BV-FTD (99% sensitive / 80-85% specific)

- Abnormal social conduct
- Eating disorders
- Stereotyped behavior
- Apathy
- Absent memory / visuospatial deficits
Differential Dx of progressive aphasia

- Most with progressive aphasia consistent with PNFA or SD have FTD at autopsy
- AD → 1/3 of PNFA or SD had AD
- VD
- Primary brain tumor → MRI
- DLBD → ~ 15% with progressive aphasia have DLBD
• Neuropsychological testing for diagnosis is limited
• FTD > AD
  – ↓ performance on executive function and social cognition
  – ↑ performance on memory and visuospatial function
Treatment of FTD

• No FDA- approved tx
• Neurochemical basis for FTD is unknown
• Abnormalities in serotonin and dopamine
  – not cholinergic
• SSRI’s
  – disinhibition; impulsivity; repetitive behavior; eating disorders; sexual disinhibition
• Trazodone
  – agitation; aggression; depression; eating disorder
Treatment of FTD

• Atypical antipsychotics (olanzapine, quetiapine, aripiprazole)
  – agitation
  – particularly vulnerable to EPS; use as last resort
  – quetiapine with less D2 antagonism

• Stimulants (Methylphenidate, dextroamphetamine)
  – $\uparrow$ DA & NE
  – apathy; disinhibition
  – may cause delirium