AN OVERVIEW OF FRONTOTEMPORAL DEMENTIA

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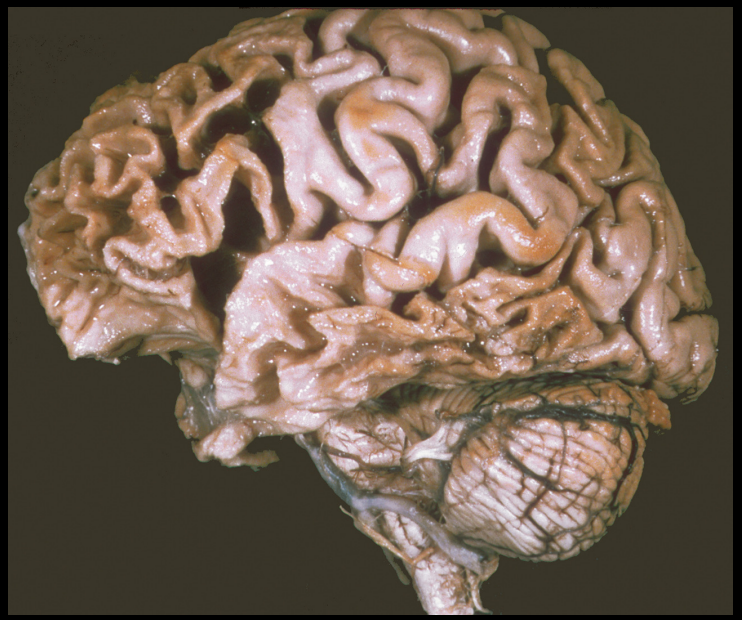
FTD: Demographics

- 3rd most common neurodegenerative dementia
  - 15% of all dementias
  - most common early onset dementia (50s-60s)
  - rare (fewer than 200,000 people with FTD in the US)
  - 7-10 year course
  - 20-30% familial



FTLD spectrum disorders

- behavioral variant (bvFTD)
- language variants (primary progressive aphasia / PPA)
  - semantic variant
  - nonfluent/agrammatic variant

- progressive supranuclear palsy (PSP)
- corticobasal syndrome (CBS / CBD)

bvFTD/PPA Diagnostic Criteria

- slowly progressive decline in behavior / cognition
  - social / executive / language dysfunction
  - most prominent feature, root cause of daily impairment
- not better accounted for by another medical / neurologic / psychiatric disorder
- clinical diagnosis ("possible")
  - supportive functional / structural imaging → "probable"
  - genetic mutation / expansion
  - FTLD histopathology
    - usually TDP43 or tau

  genetic mutation / expansion, FTLD histopathology → "definite"

Gorno-Tempini et al, *Neurology* 2011; Rascovsky et al, *Brain* 2011

Diagnostic Criteria: bvFTD (possible)

- Presence of persistent, recurrent symptoms (3)
  - disinhibition
    - social inappropriateness; loss of manners; impulsivity
  - apathy / inertia
  - loss of sympathy / empathy
    - diminished response to others; diminished social engagement
  - perseveration or compulsion
    - repetitive movements; complex rituals; speech stereotypy
  - hyperorality or dietary changes
    - Δ food preference; binge eat, tob, EtOH; oral exploration
  - neuropsychological profile
    - exec dysfunction with sparing of episodic mem and visuospat

Rascovsky et al, *Brain* 2011

Diagnostic Criteria: bvFTD (probable)

- meets criteria for possible bvFTD
- *progressive* behavioral decline
- functionally impaired due to cognitive / behavioral / social issues

and

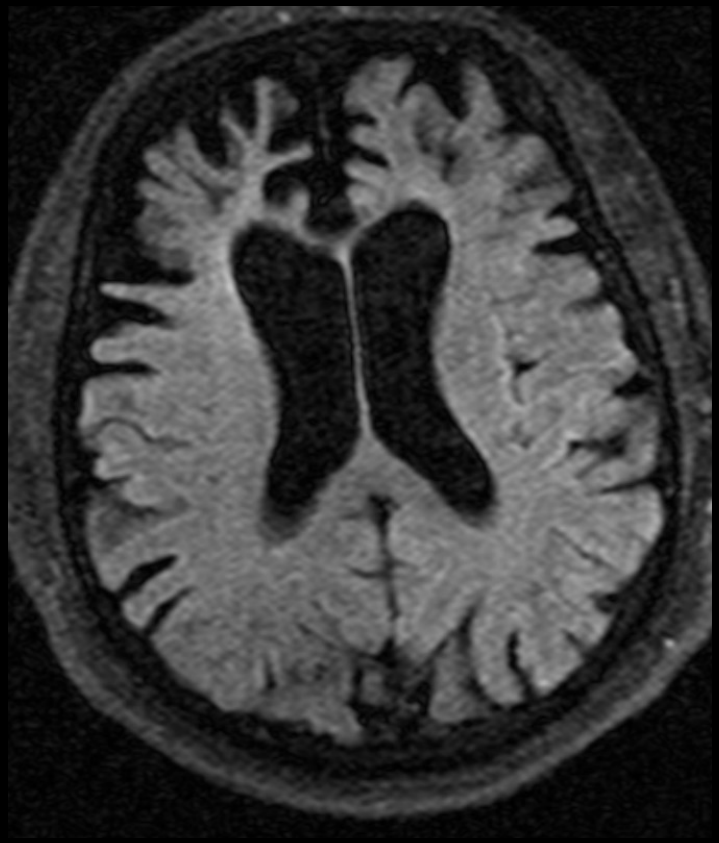
- supporting structural or functional imaging findings
  - frontal and/or anterior temporal atrophy
  - frontal and/or anterior temporal hypoperfusion/hypometab

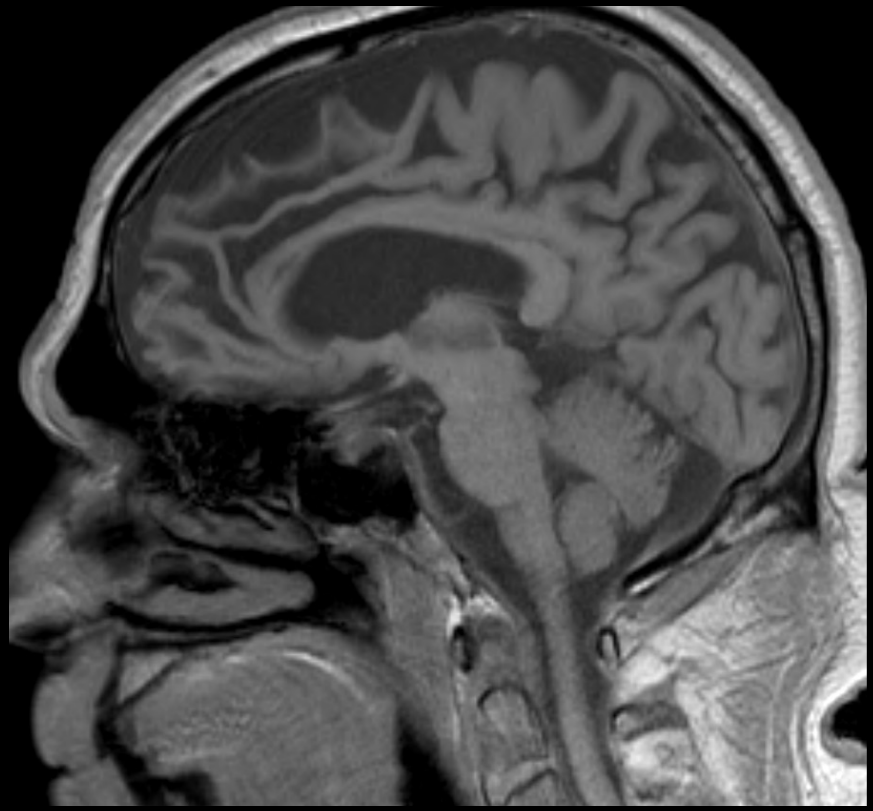
exclusionary

- biomarker evidence of Alzheimer's disease

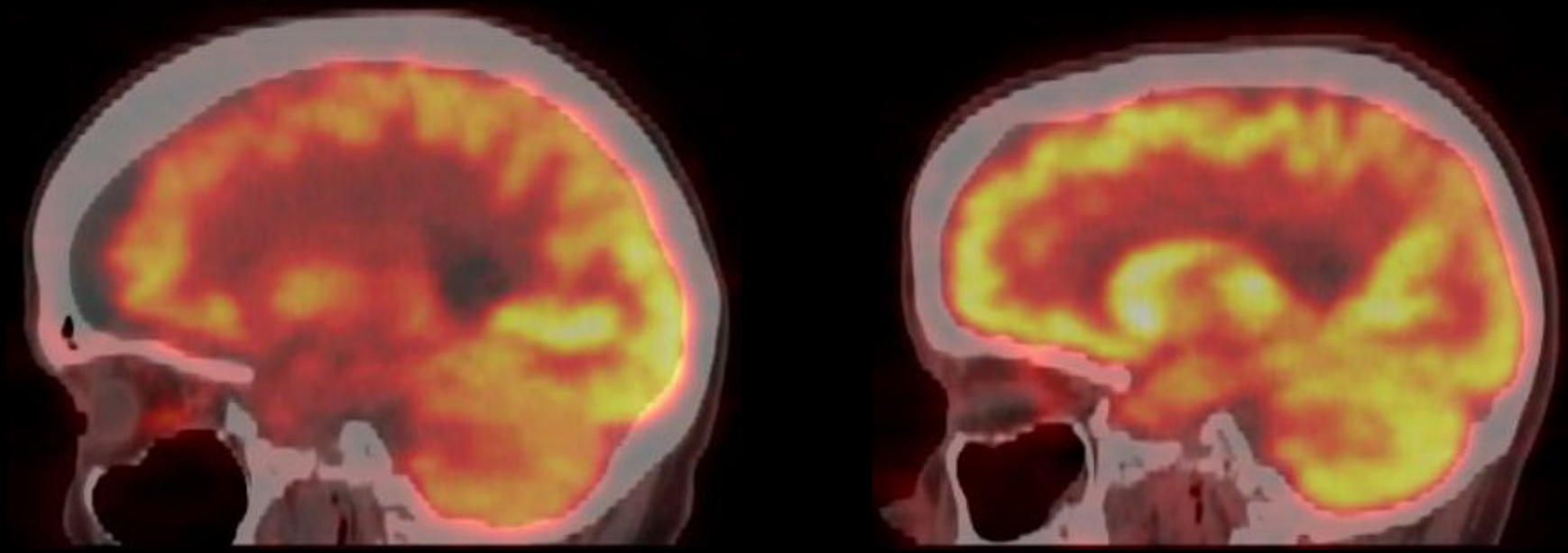
Rascovsky et al, *Brain* 2011

Imaging: bvFTD





Functional brain imaging: FTD vs AD



Diagnostic Criteria: PPA

- Core criteria:
  - most prominent feature is difficulty with language
  - language impairment is the principal cause of impaired daily living activities
  - aphasia is the most prominent deficit at symptom onset and for initial disease phases

- Exclusionary criteria:
  - another non-degenerative neurologic, psychiatric, or medical process better accounts for the clinical symptoms
  - prominent initial episodic memory, visual memory, or visuoperceptual impairment
  - prominent initial behavioral disturbance

Gorno-Tempini et al, *Neurology* 2011

Diagnostic Criteria: svPPA

- Core criteria (2):
  - impaired confrontation naming
  - impaired single word comprehension

- Supporting features (3):
  - impaired object knowledge (esp low freq)
  - surface dyslexia / dysgraphia
  - spared repetition
  - spared grammar and motor speech production

Gorno-Tempini et al, *Neurology* 2011

Diagnostic Criteria: nfvPPA

- Core criteria (1):
  - agrammatism
  - speech apraxia

- Supporting features (2):
  - impaired comprehension of syntactically complex sentences
  - spared single-word comprehension
  - spared object knowledge

Gorno-Tempini et al, *Neurology* 2011

Diagnostic Criteria: PPA (probable)

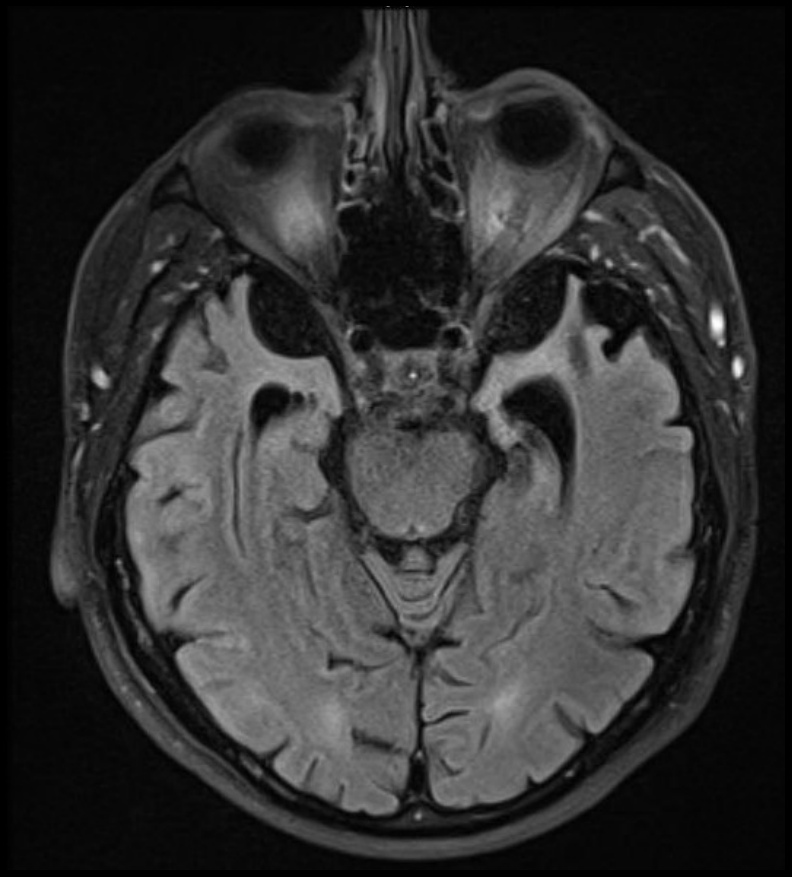
- clinical diagnosis of a PPA variant
  - initial prominent, isolated, progressive language impairment
  - ADLs only affected by language issues

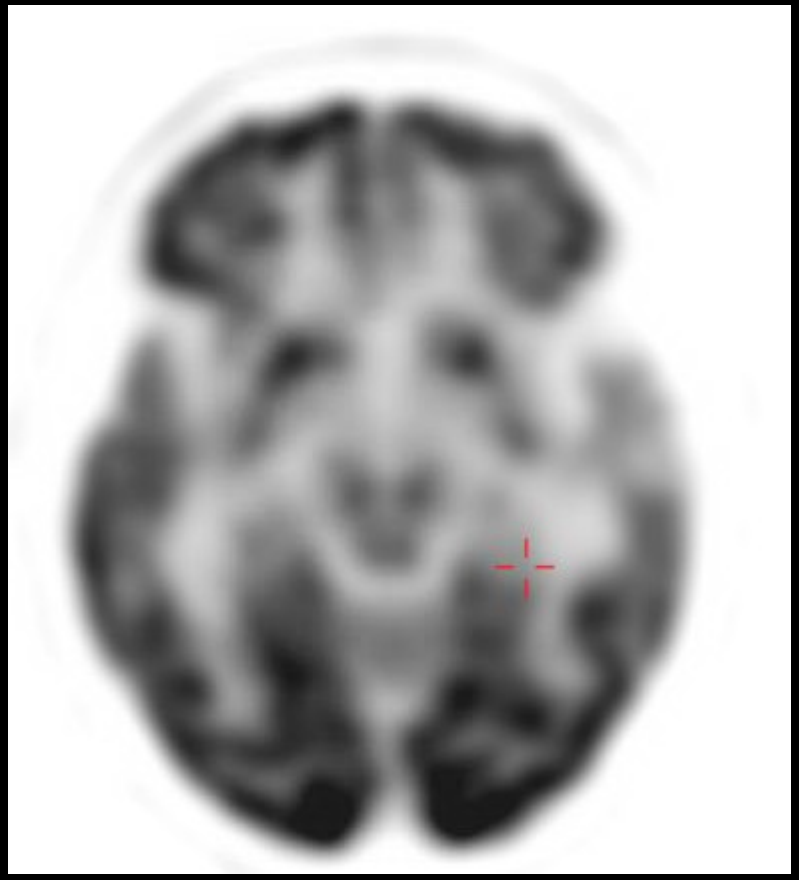
and

- supporting structural/functional imaging findings
  - svPPA: anterior temporal lobe
    - typically TDP43 neuropathology
  - nfvPPA: L posterior fronto-insular cortex
    - typically tau neuropathology

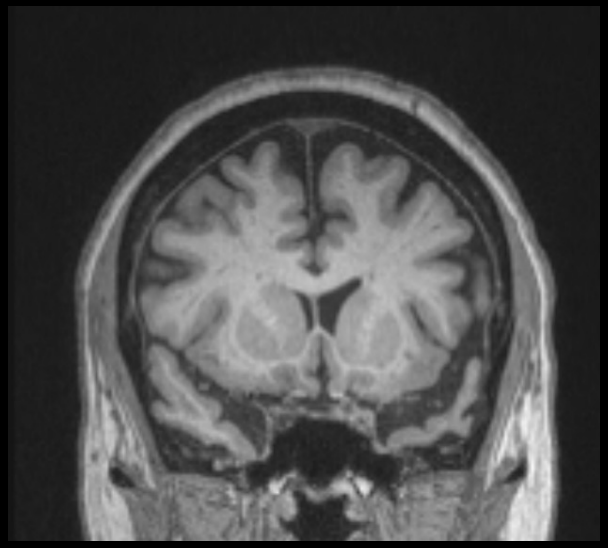
Gorno-Tempini et al, *Neurology* 2011

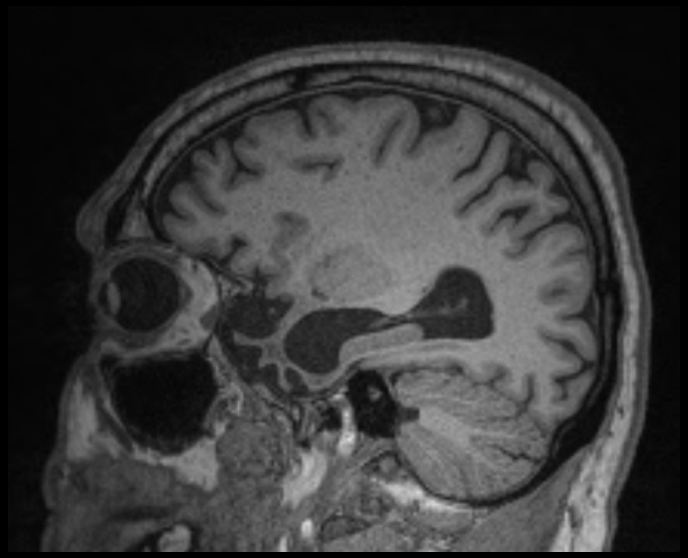
Imaging: svPPA

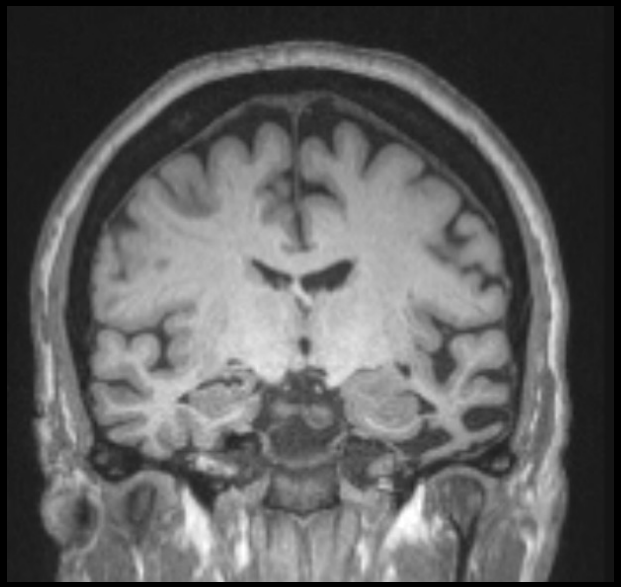


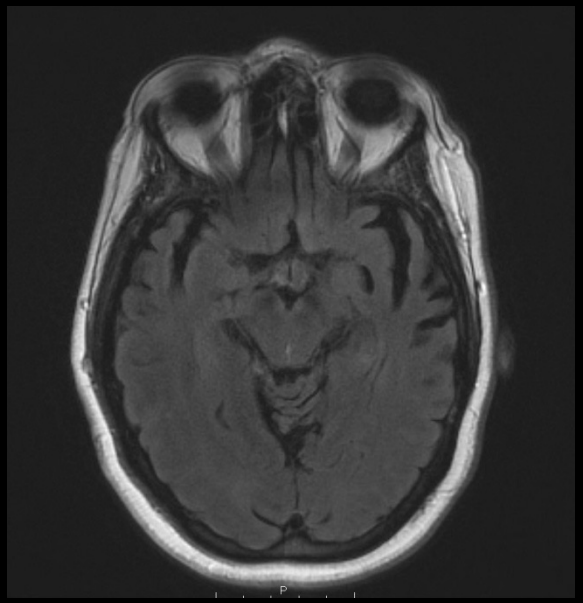


Imaging: svPPA

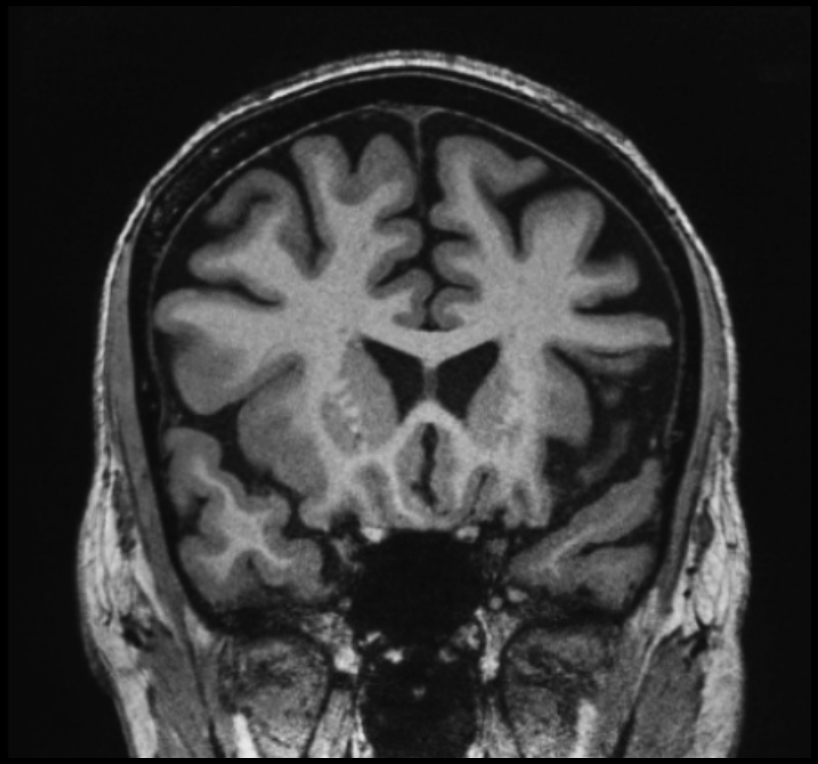


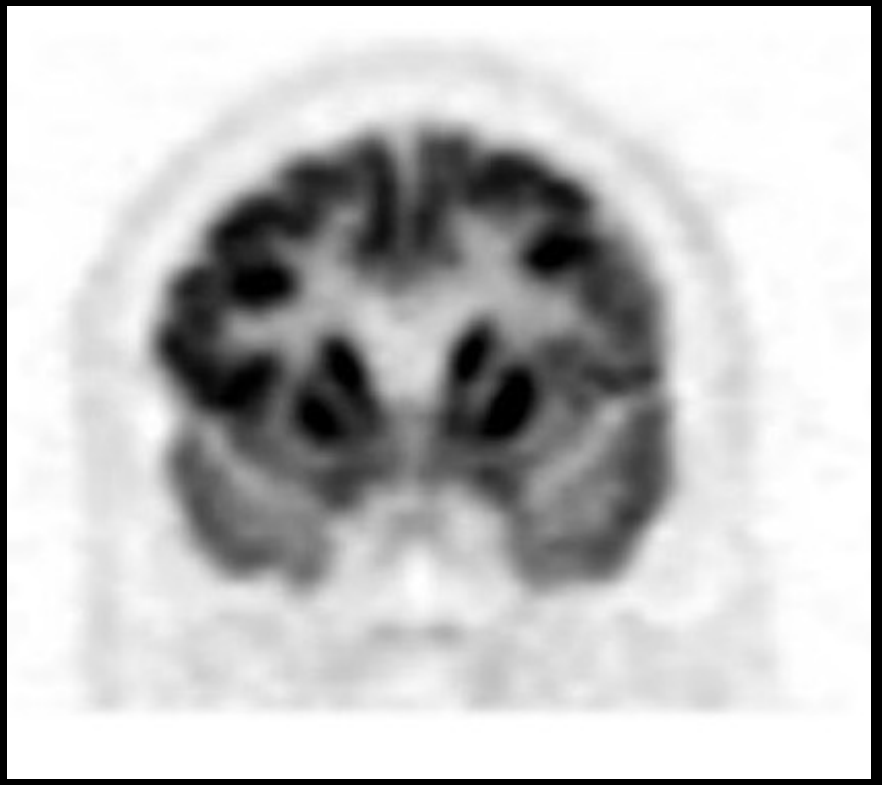






Imaging: nfvPPA



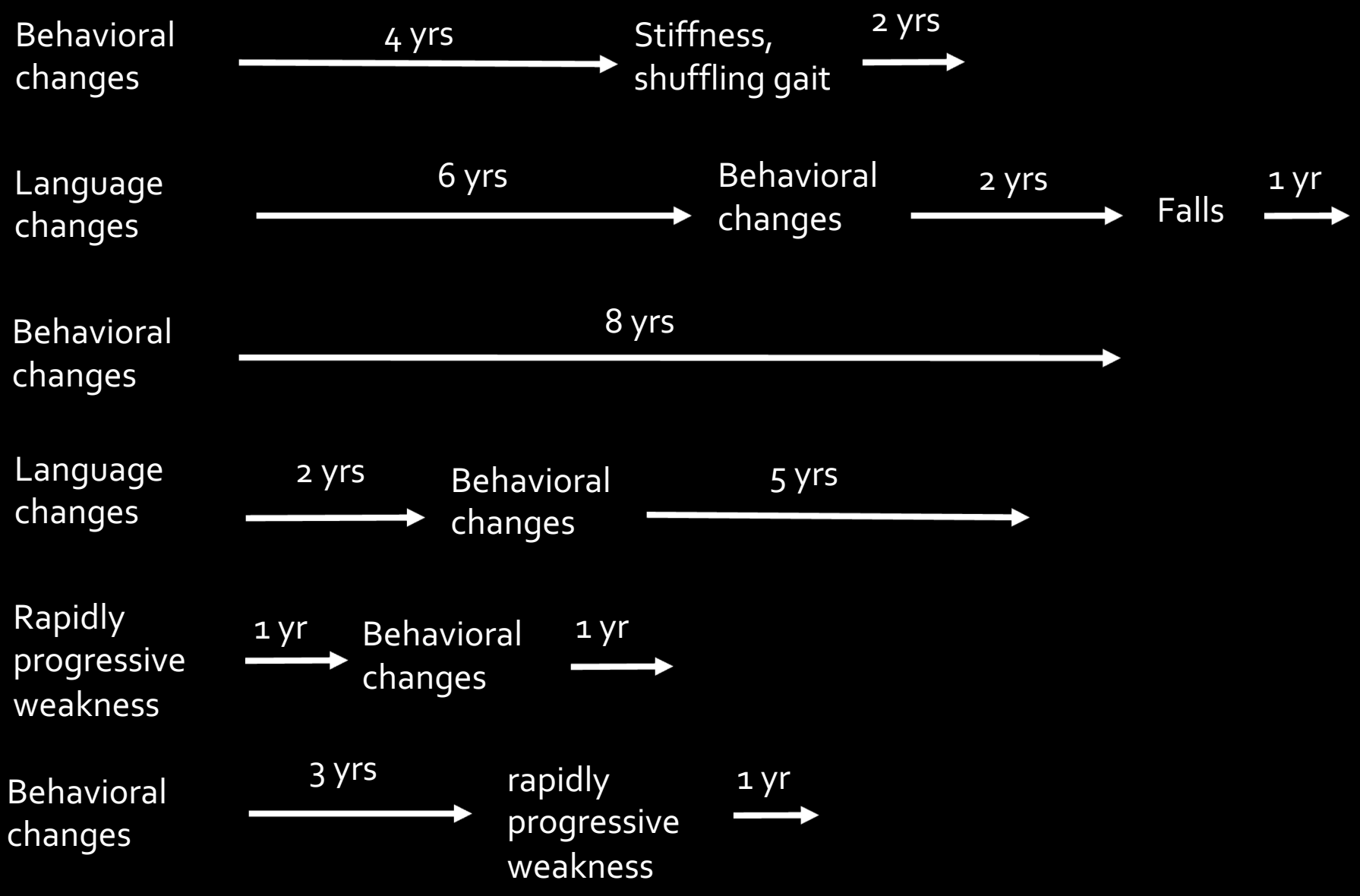


Progression Over Time

- cognitive changes
  - behavior ↔ language; memory
- motor changes
  - Parkinsonism, restriction of eye movements, motor neuron disease (MND)

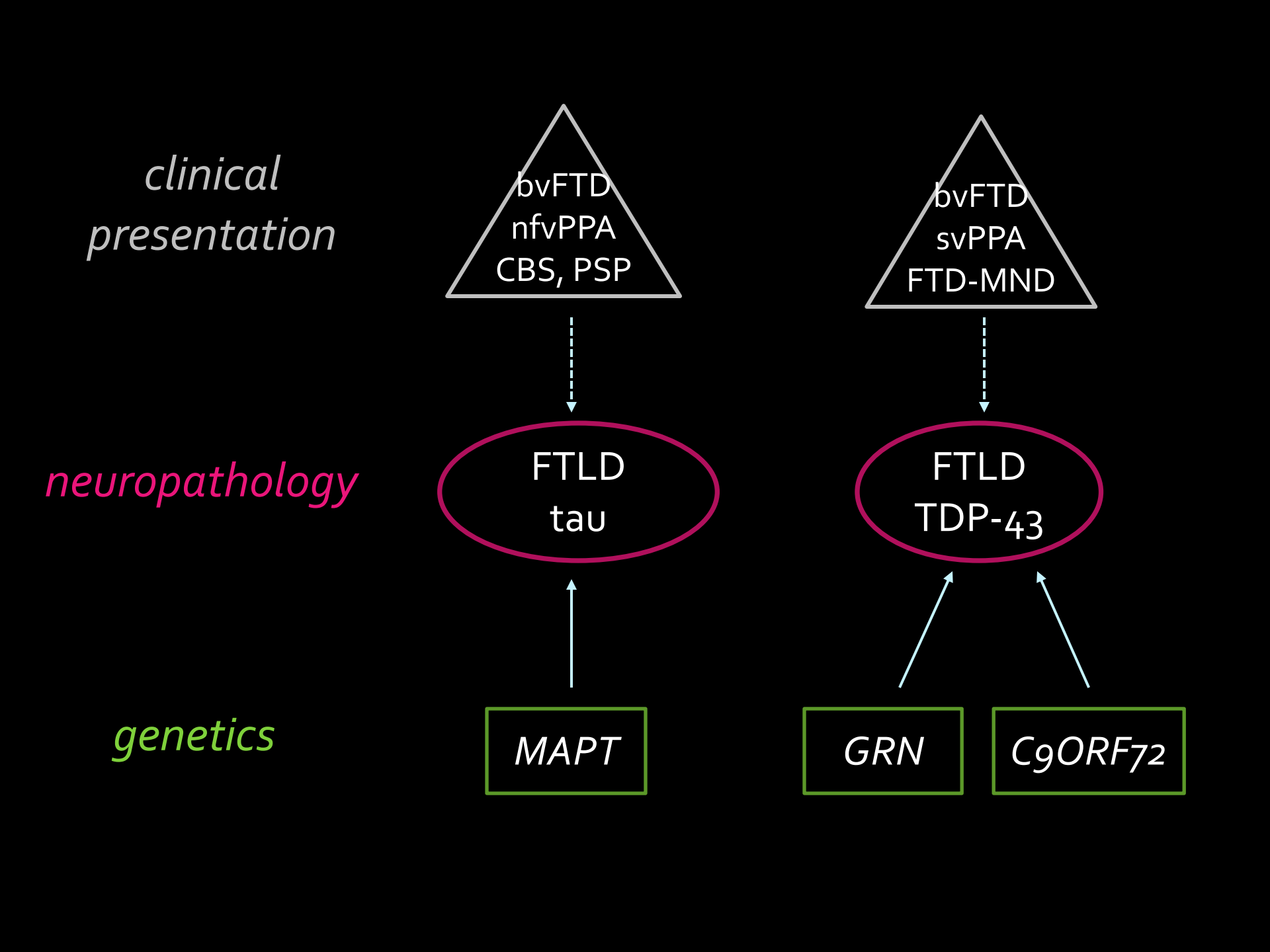
- survival is 2-20+ years after diagnosis
  - average is 7-8 years
  - depends in part on how early the diagnosis is made
  - shortest: FTD-MND / longest: svPPA

Variable Time Course of Symptoms



FTD Genetics

- 3 major genes
  - *C9orf72*
  - *GRN*
  - *MAPT*
- autosomal dominant; nearly 100% penetrant
  - variable age of onset and symptomatology
- the majority of FTD (70-80%) is not due to a single gene variant
- identifying a FTD gene variant also identifies the neuropathology subtype (e.g., tau or TDP-43)


clinical presentation
bvFTD
nfvPPA
CBS, PSP
bvFTD
svPPA
FTD-MND
neuropathology
FTLD
tau
FTLD
TDP-43
genetics
MAPT
GRN
C9ORF72

Treatment

- disease modifying medication (slow / stop / reverse)
  - none currently, except for MND
- symptomatic medications
  - nothing is yet proven
  - typically avoid Alzheimer's medications
  - antidepressants / mood stabilizers: SSRIs, valproate
  - antipsychotics
  - stimulants?
- non-pharmacologic treatment
  - SLP (cog rehab, LSVT, AAC, swallow eval), PT, OT

Compensatory strategies: Behavioral

- household responsibilities
  - break down tasks into manageable steps
  - activity templates
  - daily schedule for activities, chores
- set up routines with a companion
  - non-family member can initiate activities
  - structured environment can be beneficial
- roaming
  - medical alert bracelet, pocket cards

Compensatory strategies: Communication

- slow down
  - more time to think of words, organize thoughts
  - more time to process what is being said
- eliminate distractors
  - one-on-one conversation typically better
- provide multimodal prompts
  - partner asks multiple choice or yes/no questions
  - use gestures, facial expression, visual aids (pic/word)

Online & Local Resources

- Association for Frontotemporal Degeneration
  - www.theAFTD.org
- Rare Dementia Support
  - www.raredementiasupport.org
- FTD Talk
  - www.ftdtalk.org
- CurePSP
  - www.psp.org
- UW Speech & Hearing Sciences Clinic
  - sphsc.washington.org/clinic