PRIMARY PROGRESSIVE APHASIA (PPA)

- PPA is characterized by an insidious onset and gradual progression of aphasia (language impairment)
  - Common signs of aphasia:
    - Difficulty with word finding and comprehension, using words incorrectly, difficulty constructing sentences accurately/in the right order
  - It is characterized by isolated language deficits during early stages of the disease
  - In later stages, language remains the most affected, but other areas may also decline
- PPA occurs when the language-dominant hemisphere is the principal target of degeneration
  - Almost all right-handers and the majority of left-handers display left hemisphere dominance for language
    - Broca’s area located in the inferior frontal gyrus, is important for language fluency, grammatical structure
    - Wernicke’s area located in the temporoparietal junction/anterior parietal lobe is important in linking words to their meaning/language comprehension
    - ***Both Wernicke’s and Broca’s area are generally found in the left hemisphere, but not always***
  - Most PPA cases are due to frontotemporal degeneration (FTD) or Alzheimer’s disease (AD)
- Clinical presentation
  - The hallmark is progressive language disturbance leading to functional impairment in and other cognitive domains (although language dysfunction remains the most impaired)
  - ADLs tend to be maintained except those relating to language (eg, difficulty using the telephone)
- Diagnosis
  - It is a clinical diagnosis, made primarily by detailed history and neurologic examination
  - Neuroimaging (usually MRI):
    - PPA may demonstrate atrophy, hypometabolism, and/or hypoperfusion in the frontal and/or temporal lobes, in a pattern specific to the clinical variant
    - Can exclude focal pathology (cerebrovascular disease and mass/brain tumor)
  - Neuropsychologic testing:
    - Can help distinguish PPA from amnestic dementia (AD) and can help discern which clinical variant
    - Patients with PPA typically perform well on tests of episodic memory, executive function, and visuospatial function in early stages of the disease
  - Diagnostic criteria for PPA: A diagnosis of PPA requires all of the following features
    - Difficulty with language
    - Language deficits are the principal cause of impaired ADLs
    - Aphasia is the first and most prominent symptom
    - Presentation is not better accounted for by other non-neurodegenerative, medical, or psychiatric disorders
    - There are not prominent initial episodic memory, visual, or behavioral disturbances
- Variants of PPA—based on the type of language impairment, and anatomic region of the most atrophy
  1. **Nonfluent variant—motor speech deficit** characterized by effortful production of the linguistic units of sound
    - Slowed speech is caused by articulatory difficulty with effortful, halting speech.
    - Bedside test: repeat word such as “caterpillar” that is challenging to articulate.
    - Peak site of atrophy within the left inferior frontal gyrus and posterior fronto-insular atrophy.
    - Comprehension is typically spared for single words and simple sentences, patients often have difficulty with complex sentences.
  2. **Semantic variant — impaired single-word comprehension and object naming**
    - First symptom is word finding difficulty and fluency, repetition, and grammar are preserved
    - As the disease progresses, comprehension becomes more globally impaired
    - Bedside test: ask the patient to draw animals such as a turtle, those with semantic variant PPA frequently make drawing lacking defining features (eg, no shell for a turtle)
    - At later stages episodic memory declines but visuospatial skills/executive function remain relatively intact
  3. **Logopenic variant — impaired single-word retrieval** with spared single-word comprehension/object knowledge
    - Can sound like nonfluent due to slow rate, however the slow rate is primarily due to word finding pauses rather than difficulty with word production/articulation
    - Most cases of logopenic variant PPA are due to underlying Alzheimer pathology, although hemispheric asymmetry in the distribution of neurofibrillary tangles distinguishes logopenic variant PPA from typical AD