Neuroimaging and SPECT in Primary Progressive Aphasia
# Frontotemporal Lobar Dementia

- Umbrella term with many pathological and clinical subtypes
- Frequently familial and hereditary
- Typically develops in 6th decades and later
- Presentation at young age can mimic neuropsychiatric disorders
- Can be roughly divided into speech deficit and behavioral deficit subtypes
- Rarely, patients can present with parkinsonism or motor neuron disease
- No specific treatments, however accurate diagnosis allays patient and family anxiety about behavior and prognosis
Primary Progressive Aphasia (PPA)

- Rare dementia syndrome characterized by difficulties in speech and language
- Most often considered a presentation of frontotemporal lobar dementia (FTD), though sometimes it overlaps with Alzheimer’s dementia, leading to diagnostic challenges
- As such it can take years and several referrals to make the correct diagnosis of PPA
- During this time period, patients often show minimal or no response to traditional Alzheimer’s therapies, for example
- Importantly, in many common frameworks defining these subtypes, diagnosis can be made using any one of:
  - Clinical only (exhaustive list of features required)
  - Clinical diagnosis supported by imaging (atrophy on MRI, or hypoperfusion/hypometabolism on SPECT or PET)
  - Clinical with combination of pathology or gene mutation

SPECT and FDG-PET can bring important clarity for these patients and their treating physicians
Diagnostic Criteria for Primary Progressive Aphasia (PPA)

Some studies have shown that SPECT is highly accurate in differentiating between FTLD and AD. It can detect active Alzheimer’s disease with approximately 90% accuracy. Generally speaking, a diagnosis of Alzheimer’s disease via SPECT rules out PPA.

### Table 1: Inclusion and exclusion criteria for the diagnosis of PPA: Based on criteria by Mesulam

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<tr>
<th>Inclusion: criteria 1–3 must be answered positively</th>
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<td>1. Most prominent clinical feature is difficulty with language</td>
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<td>2. These deficits are the principal cause of impaired daily living activities</td>
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<td>3. Aphasia should be the most prominent deficit at symptom onset and for the initial phases of the disease</td>
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<th>Exclusion: criteria 1–4 must be answered negatively for a PPA diagnosis</th>
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<td>1. Pattern of deficits is better accounted for by other nondegenerative nervous system or medical disorders</td>
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<td>2. Cognitive disturbance is better accounted for by a psychiatric diagnosis</td>
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<td>3. Prominent initial episodic memory, visual memory, and visuoperceptual impairments</td>
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<td>4. Prominent, initial behavioral disturbance</td>
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Abbreviation: PPA = primary progressive aphasia.

Criteria for PPA Diagnosis

• Subtypes of PPA include non-fluent aphasia, semantic dementia, and logogenic aphasia

1) **Non-fluent aphasia** shows difficulty with grammar and sentence structure, halting speech pattern with difficulties forming correct sounds

2) **Semantic dementia** subtype shows impairments in naming, word comprehension and object knowledge

3) **Logopenic aphasia** has difficulty with word retrieval, halting speech but without grammar difficulties, and difficulties repeating sentences
55-year-old male who presented to the neurology clinic with “difficulty with word finding and a change in speech”, particularly with fluency of speech. He also endorsed mood changes. He had no memory difficulties. His symptoms were progressive over several years with no significant change despite several attempted treatments.

(A) Brain MRI showed predominantly nonspecific T2/FLAIR matter changes without focal abnormalities. It was noted that he had small nonspecific area of white matter change in the right temporal periventricular white matter but the appearance was nonspecific as could be seen in small vessel ischemia, demyelination or gliosis.

(B) There was clinical concern for PPA variant of FTD. FDG-PET was obtained to help corroborate. FDG-PET shows decreased metabolic activity predominantly in the temporoparietal regions, left greater than right. There was also mildly decreased metabolic activity within the left frontal lobe. This is shown below fused with CT. Of note, there were no significant findings on FLAIR (or other MR sequences) corresponding to the above, highlighting the increased specificity of FDG-PET. These findings were supportive of clinical diagnosis of PPA made by the neurologist.
66-year-old male presented to the neurology clinic with worsening speech difficulties over two years. He and his wife endorsed increasingly stuttering and halting, hesitant speech. He also expressed difficulty with writing (agraphia). He denied difficulties with performing his ADLs, loss of sense of direction, or other major cognitive changes. He did not have any clinical response to galantamine.

Fused SPECT obtained with Tc-99m HMPAO and T1 axial MRI show decreased perfusion in the left temporal, frontal and parietal lobes. This was consistent with a clinical diagnosis of PPA made by the neurologist.

Figure 3. Fused Tc-99m HMPAO/MRI shows decreased uptake in the left frontotemporal lobes.
61-year-old male with who presented with 3-4 years of memory impairment, forgetting names of people and objects, difficulty explaining his thoughts. Was on Aricept for presumed Alzheimer’s dementia but did not have improvement. Initial brain MRI showed mild global parenchymal volume loss predominantly in the anterior and medial temporal and parietal lobes. On clinical re-evaluation the disease was felt more consistent with frontotemporal dementia-semantic subtype, though atypical Alzheimer’s could not be excluded. FDG-PET was obtained to differentiate between FTD vs. AD.

(A) FDG-PET showed profound bitemporal hypometabolism compatible with clinically suspected semantic variant primary progressive aphasia (svPPA).
In one 2021 study, the progression of disease in PPA was able to be quantified by volumetrically assessing the rate of atrophy in FDG-PET over time.

This graph shows how atrophy progresses in each specific subtype of PPA over 1-year interval (A) and 2-year intervals (B). Note the characteristic locations affected by each subtype.

This provides a predictive element to neuroimaging that can guide treatment and prognosis.
SPECT and FDG-PET can elucidate the diagnosis of PPA, or rule it out, in clinically ambiguous presentations.

PPA subtypes are characterized by a specific clinical and neuroimaging profiles.

Educating others about earlier usage of SPECT and FDG-PET to detect subtle hypometabolism in patients with otherwise unremarkable imaging.

These techniques can be used to quantify progression.

Neuroimaging in dementia
References