Primary progressive aphasias

Peter Bekkhus-Wetterberg, MD, Senior Consultant

Memory Clinic, Dept. of Geriatrics,

Oslo University Hospital at Ullevål

What are primary progressive aphasias?

- Language led dementias
  - Language disturbance is the primary and leading symptom
- Progressive
- Caused by different pathologies
- With differing language profiles

History

- Pick (1892) og Serieux (1893): A progressive disorder of language associated with atrophy of the left frontal and temporal regions
- Mesulam (1982): «Slowly progressive aphasia», renamed «primary progressive aphasia (PPA)» (1992)
- Warrington (1975): Progressive disorder of semantic memory
  - Snowden (1989): Same disorder described as «Semantic dementia»
  - Hodges (1992): Comprehensive characterisation of semantic dementia
- Grossman (1996): «Progressive nonfluent aphasia»
- Consensus meeting (Neary et al 1998): Criteria for PPA, thereafter classified as Semantic dementia or Progressive non-fluent aphasia
- Gorno-Tempini (2004): Logopenic progressive aphasia

Gorno-Tempini et al. *Classification of primary progressive aphasia and its variants.* Neurology 2011;76:1006–1014

Current PPA-terminology

- A consensus process 2006-2009 resulted in a classification published in 2011
- Three types of primary progressive aphasia
  - Nonfluent, agrammatic variant PPA
  - Semantic variant PPA
  - Logopenic variant PPA

- In addition, similar language disturbances may occur as part of a more generalized dementia

Gorno-Tempini et al. *Classification of primary progressive aphasia and its variants.* Neurology 2011;76:1006–1014

Criteria for (any) primary progressive aphasia

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

Mesulam. Primary progressive aphasia. Ann Neurol 2001;49:425– 432.
Gorno-Tempini et al. Classification of primary progressive aphasia and its variants. Neurology 2011;76:1006–1014

Three main types of PPA are recognised

- Semantic PPA
  - Word meaning
  - Temporal poles
- Nonfluent, agrammatic PPA
  - Motor speech and grammar
  - Posterior left frontal lobe

Mainly associated with fronto-temporal degeneration

- Logopenic PPA
  - Repetition
  - Left temporoparietal junction

Mainly associated with Alzheimer's disease

Gorno-Tempini et al. *Classification of primary progressive aphasia and its variants.* Neurology 2011;76:1006–1014
Botha & Josephs. *PPA and Apraxia of Speech*. Continuum (Minneap Minn) 2019;25(1 , Dementia):101–127.
Mendez. *Early-onset Alzheimer Disease and Its Variants*. Continuum (Minneap Minn) 2019;25(1 , Dementia):34–51.

Semantic variant PPA

svPPA

- ***The meaning of words***
- ***Temporal poles***

Typical reply, semantic variant PPA

- DOCTOR: Could you tell me something about your background?
- PATIENT: Background? What do you mean by that? I’ve never heard that word.

Criteria for semantic variant PPA

- Both of the following core features must be present:
  1. Impaired confrontation naming
  2. Impaired single-word comprehension
- At least 3 of the following other diagnostic features must be present:
  1. Impaired object knowledge, particularly for low frequency or low-familiarity items
  2. Surface dyslexia or dysgraphia
  3. Spared repetition
  4. Spared speech production (grammar and motor speech)

Gorno-Tempini et al 2011

Semantic variant PPA

- Anomia (naming difficulties)
  - Naming problems are present in other variants of PPA and in other neurodegenerative diseases with aphasia
  - The naming deficit in semantic variant PPA is severe, particularily when compared to the relative sparing of other language domains

Gorno-Tempini et al 2011

Semantic variant PPA

- Single-word comprehension is severely impaired
  - Especially for low-frequency items
  - Inability to comprehend low-familiarity words can be the only symptom accompanying anomia at the earliest stages
- A manifestation of a widespread semantic memory deficit that causes impairments in object and person recognition

Gorno-Tempini et al 2011

Semantic variant PPA

- Even with severe semantic impairment, repetition and motor speech are spared
- Grammar is usually correct

Gorno-Tempini et al 2011

Semantic variant PPA

- Surface dyslexia and surface dysgraphia
  - Deficits in reading and writing words with an irregular or atypical relationship between spelling and pronunciation
  - Words are pronounced «regularly» when reading
    - In Norwegian, «beige» will be pronounced as [beige] instead of the correct [beːʃ]
  - Words are spelt in a «regular» manner
    - Norwegian «giro» [ʃiːro] will be spelt as «sjiro»

Gorno-Tempini et al 2011

bacon

gips

giro

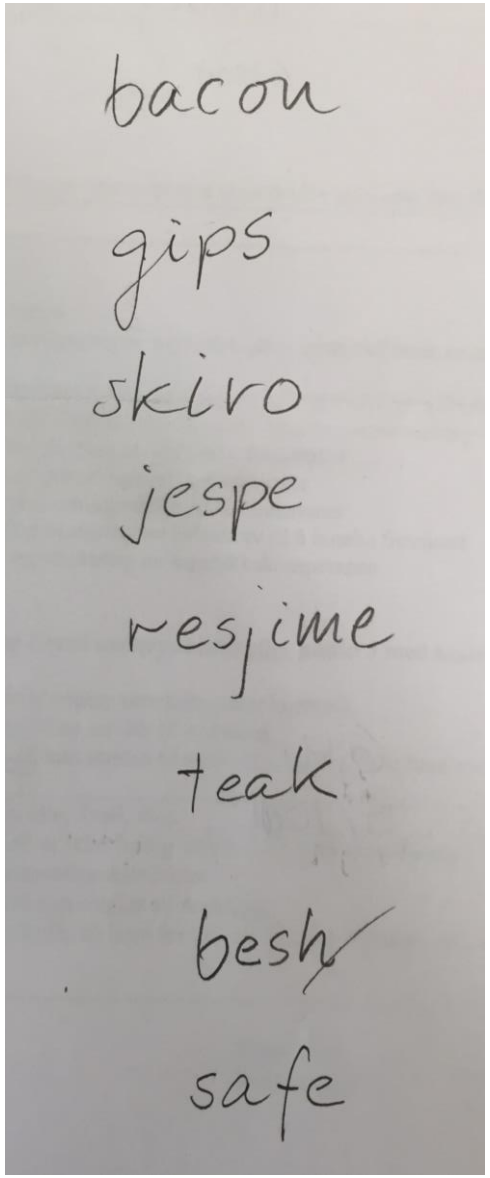
gjespe

regime

teak

beige

safe



Semantic PPA summed up

Areas of difficulty	Areas of relative strength
Difficulties in object naming, single word comprehension, verbal semantic category fluency tasks and non-verbal object knowledge and recognition. Less familiar objects and words are more impaired resulting in a frequency effect. Reading difficulties (acquired surface dyslexia)	Speech is relatively **fluent** and phonologically correct Spared grammar, phonology and number knowledge Accurate repetition Able to stay on topic and expand the topic

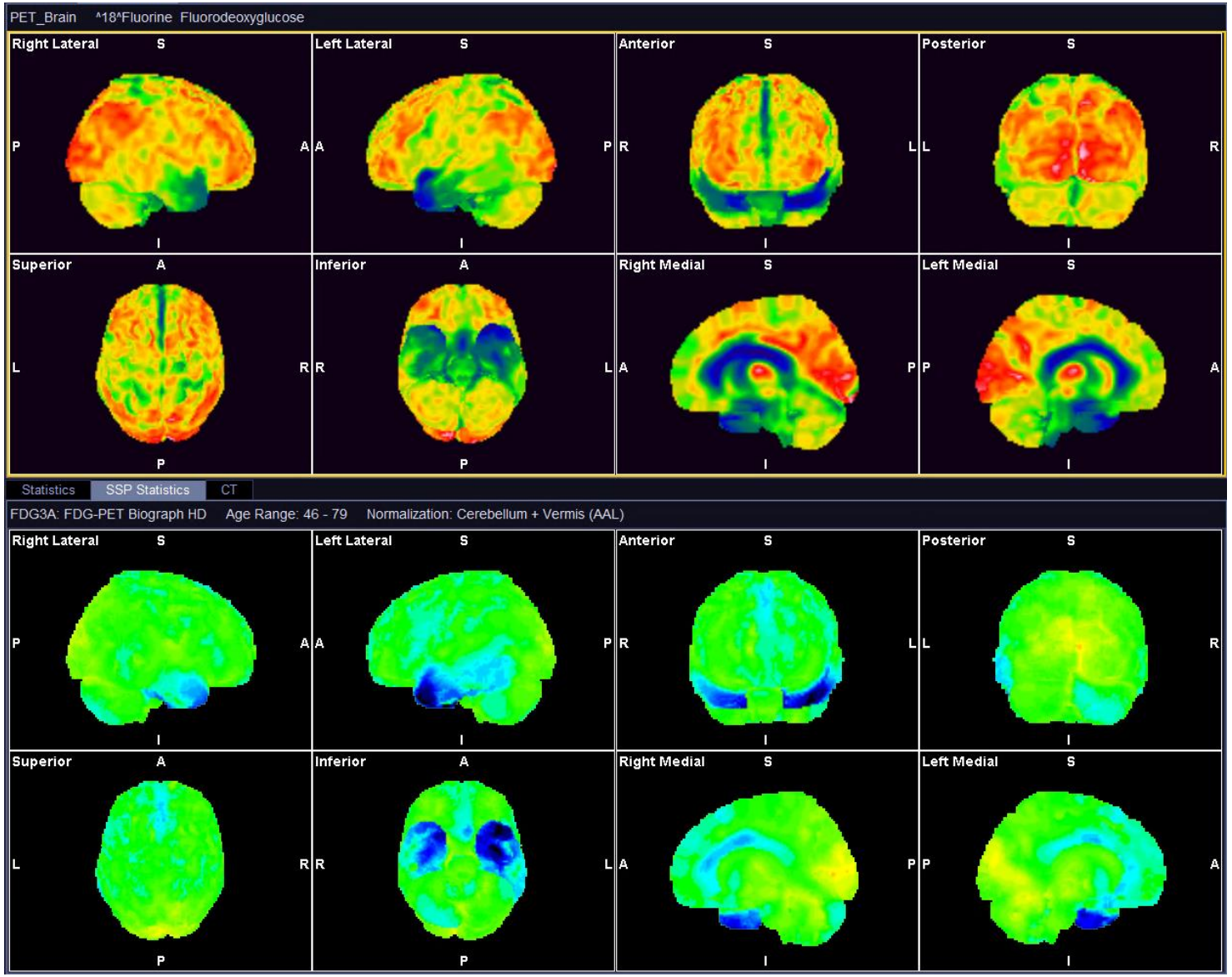
Anna Volkmer, UCL 2020

Imaging findings

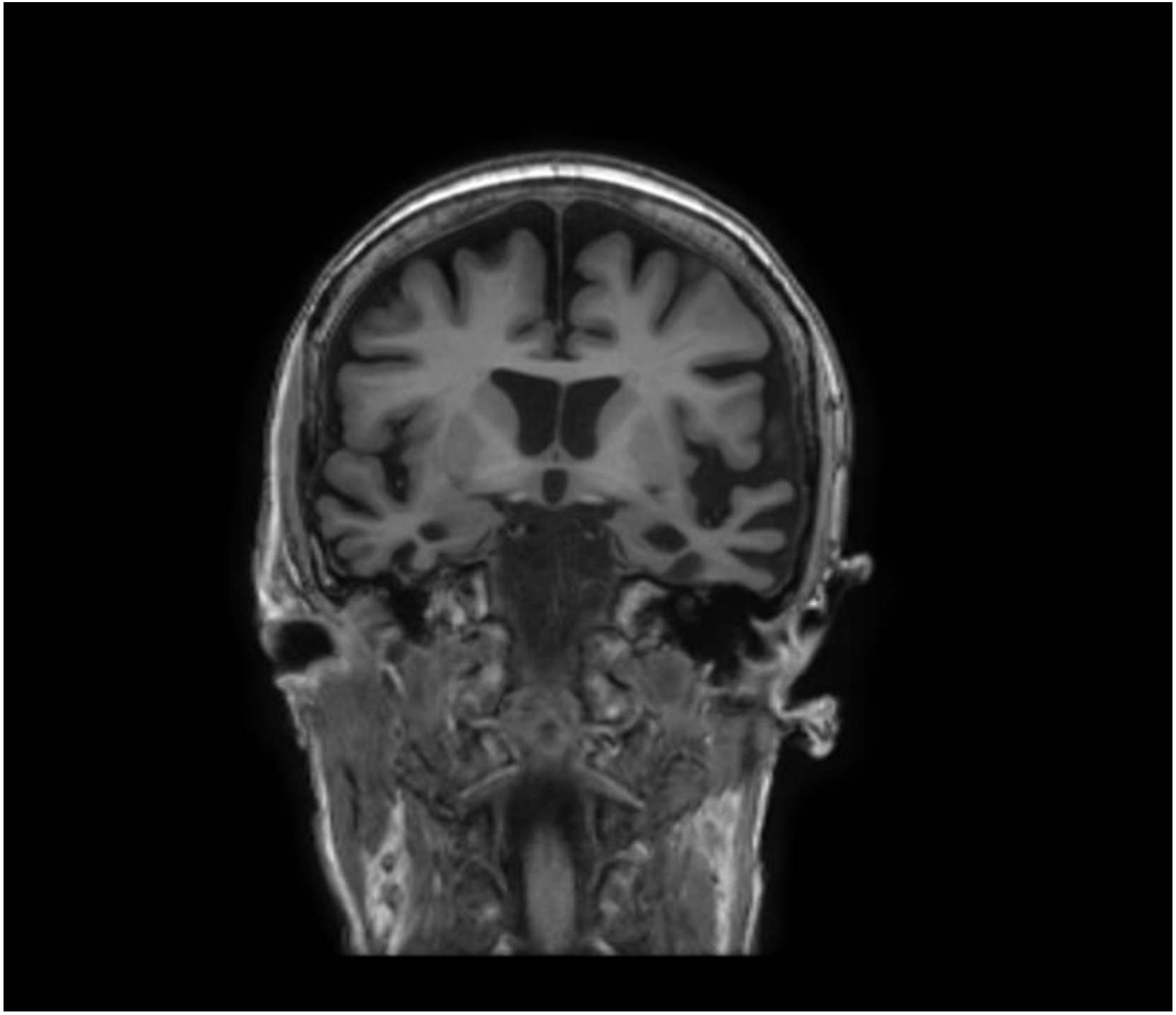
svPPA

↓ FDG uptake

Anterior temporal lobe(s)



Images courtesy of Dr Ebba Gløersen Müller, Division of Radiology and Nuclear Medicine, Oslo University Hospital



Diagnostic considerations in svPPA

- Structural imaging is highly sensitive and specific in svPPA (98 / 93%)
- FDG-PET is extremely sensitive and specific in svPPA (up to 100%)
- The underlying pathology is nearly always (90%) FTLD-TDP43 type C

- Most patients develop a behavioral variant FTD, but progression may be very slow (more than a decade from diagnosis to severe dementia)

Wasim et al. Neuroimaging of PPA variants. Neurographics 2018 Jan/Feb;8(1):1-6
Botha & Josephs. *PPA and Apraxia of Speech*. Continuum (Minneap Minn) 2019;25(1 , Dementia):101–127.
Olney et al. *Frontotemporal dementia.* Neurol Clin. 2017 May ; 35(2): 339–374.

Nonfluent, agrammatic PPA

nfvPPA

- ***Motor speech and grammar***
- ***Posterior left frontal lobe***

Typical reply, nonfluent PPA

- DOCTOR: Could you tell me something about your background?
- PATIENT: W- well, w- went, went enju- enji- enjneer

Criteria for nonfluent, agrammatic PPA (nfvPPA)

- At least one of the following core features must be present:
  - Agrammatism in language production
  - Effortful, halting speech with inconsistent speech sound errors and distortions (apraxia of speech)
- At least 2 of 3 of the following other features must be present:
  - Impaired comprehension of syntactically complex sentences
  - Spared single-word comprehension
  - Spared object knowledge

Gorno-Tempini et al 2011

Agrammatism in nfvPPA

- Short, simple phrases with grammatic details left out, such as function words* and inflections

*Function words

Articles (a, an, the)

Pronouns (I, you, we, they …)

Prepositions (in, on, under, over …)

Conjunctions (and, but, or, so …)

Assistive verbs (be, become …)

Particles (if, then, well, thus …)

Gorno-Tempini et al 2011

Effortful speech in nfvPPA

- Slow, labored speech production
- Articulation planning deficit (apraxia of speech) most common disturbance. Can be the initial sign.
- Inconsistent speech sound errors
  - Distortions, deletions, substitutions, insertions, or transpositions of speech sounds
- Patient often aware of errors
- Prosody is disrupted, and rate of speech is markedly reduced

Gorno-Tempini et al 2011

Early symptoms of nfvPPA

- Subtle apraxia of speech
  - Can be revealed by «pataka» test
- Slight grammatical errors, slight problems with syntax comprehension
  - Can be revealed by
    - Written language production tests
    - Syntax comprehension tasks
      - Negative passives, object relative clauses

Gorno-Tempini et al 2011

Nonfluent PPA summed up

Areas of difficulty	Areas of relative strength
Dysfluent effortful, halting speech with speech sound errors (apraxia of speech) OR **Agrammatic** with simple sentence structures Difficulties understanding sentences	Relatively unimpaired single-word comprehension

Anna Volkmer, UCL 2020

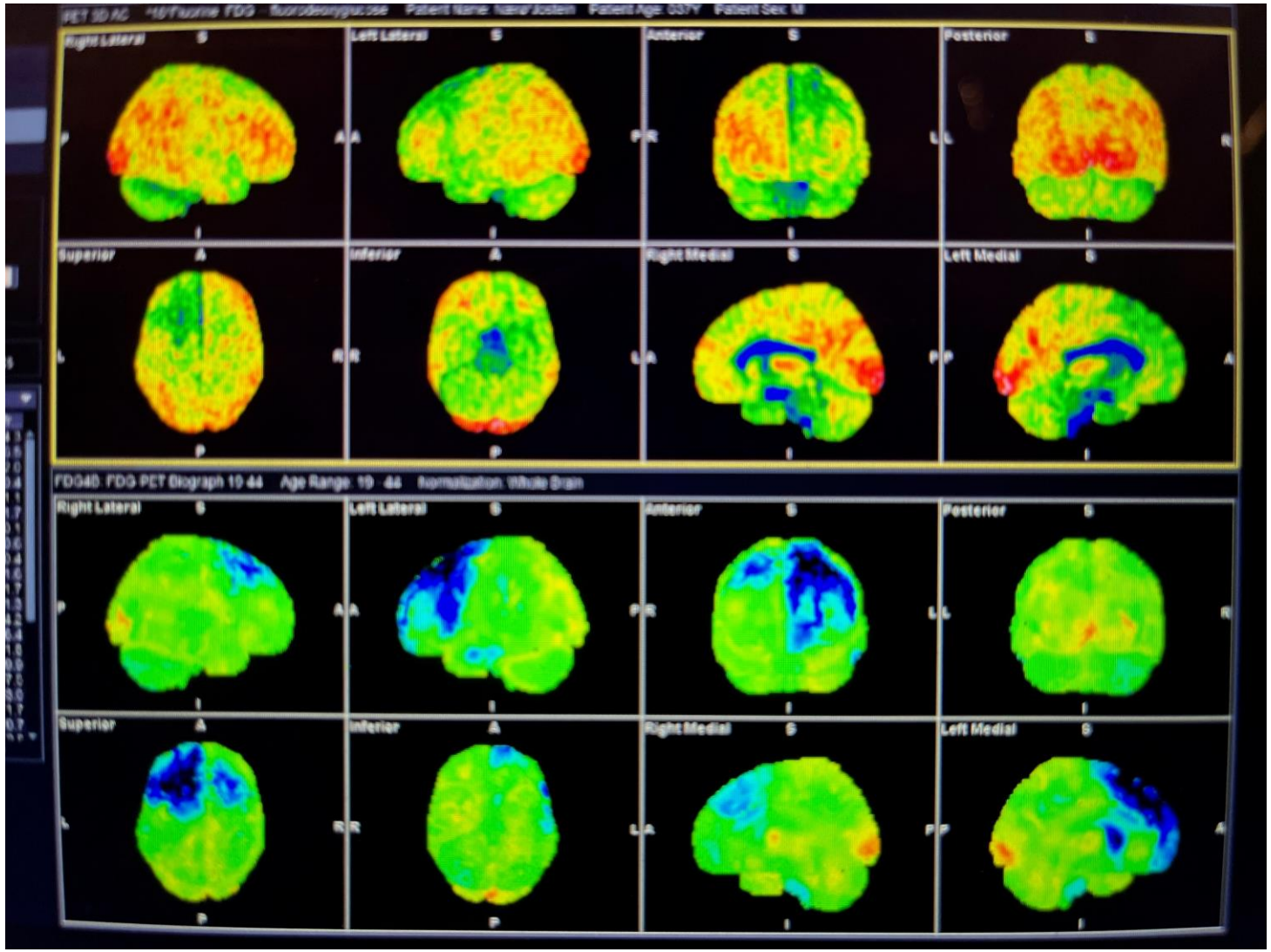
Imaging findings

nfvPPA

↓ FDG uptake

Posterior frontal/insula

Predominantly left side



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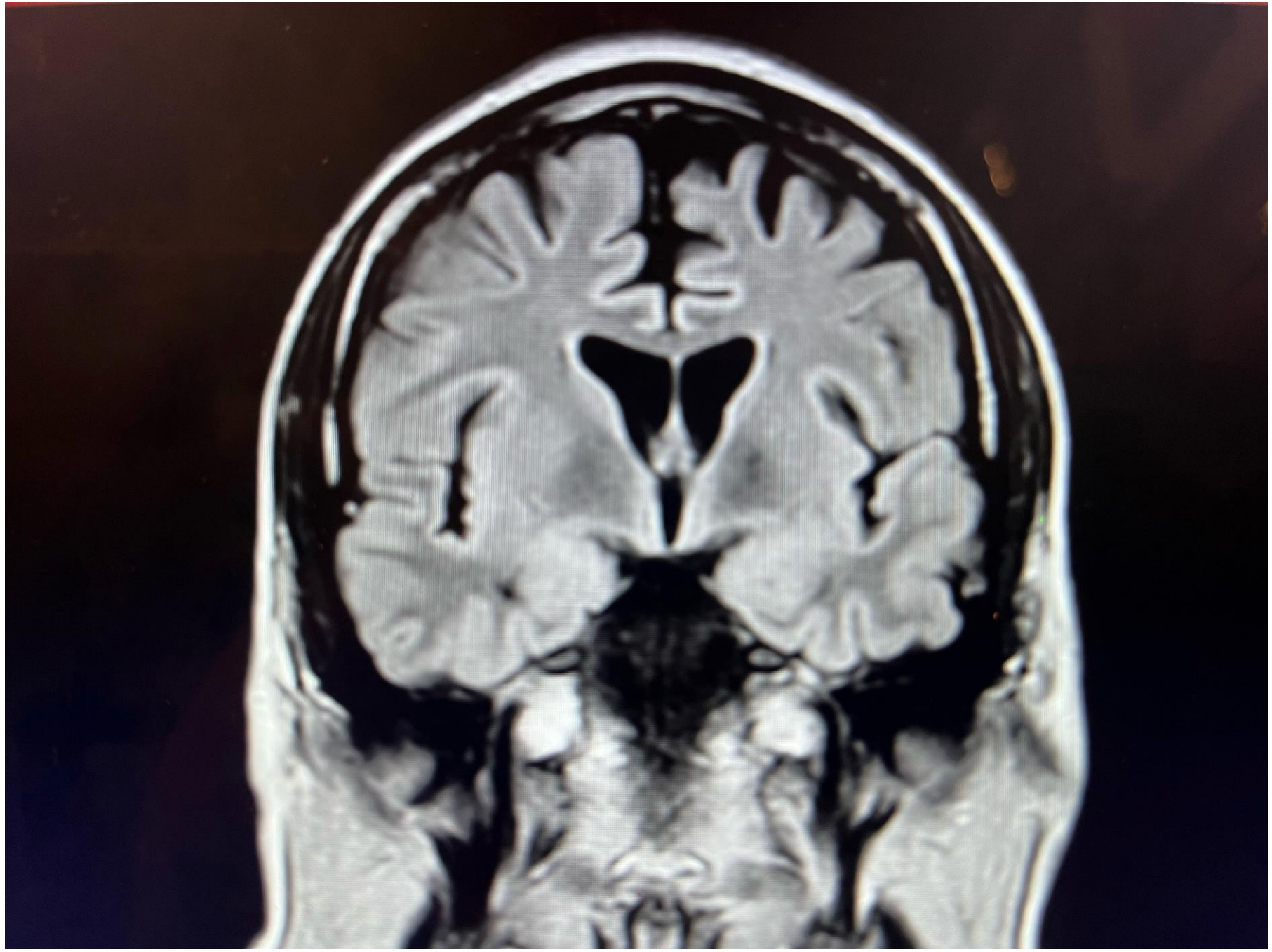

Diagnostic considerations in nfvPPA

- Imaging (MRI and FDG-PET) has low sensitivity (29-67%) but high specificity (91-92%)
- The underlying pathology is most often tau-type FTLD (52%), followed by amyloid pathology (25%) and FTLD-TDP (19%)
- Patients may develop
  - Behavioural variant FTD
  - FTD-associated Parkinson plus-syndromes such as corticobasal syndrome or progressive supranuclear palsy
    - The latter seems to be more common in patients with dominant apraxia of speech

Wasim et al. *Neuroimaging of PPA variants.* Neurographics 2018 Jan/Feb;8(1):1-6
Botha & Josephs. *PPA and Apraxia of Speech*. Continuum (Minneap Minn) 2019;25(1 , Dementia):101–127.

Logopenic PPA

lvPPA

- ***Repetition***
- ***Left temporoparietal junction***

Typical reply, logopenic PPA

- DOCTOR: Could you tell me something about your background?
- PATIENT: Well, I worked for many years at a, eh, um, what is it called? … you know … Anyway, what we did there was that we made these, er, big … things.

Criteria for logopenic PPA, lvPPA

- Both of the following core features must be present
  1. Impaired single-word retrieval in spontaneous speech and naming
  2. Impaired repetition of sentences and phrases
- At least 3 of the following other features must be present
  1. Speech (phonologic) errors in spontaneous speech and naming
  2. Spared single-word comprehension and object knowledge
  3. Spared motor speech
  4. Absence of frank agrammatism

Gorno-Tempini et al 2011

Logopenic PPA

- Language problems in Alzheimer disease are most often of the same character as lvPPA

Gorno-Tempini et al 2011

Logopenic PPA

- Spontaneous speech is slow with frequent pauses for word-finding
- Frank agrammatism is lacking
- Different from nfvPPA
  - In nfvPPA speech is also slow and halting, but characterised by poor prosody, motor speech errors and agrammatism

Gorno-Tempini et al 2011

Logopenic PPA

When testing with confrontation naming

- Usually less pronounced naming problems than in semantic PPA
- Errors tend to be phonological

Gorno-Tempini et al 2011

Logopenic PPA

- Repetition of multisyllabic words, sentences and phrases typically impaired in logopenic PPA
  - Most commonly with phonological errors
- Repetition of short single words may be spared

Gorno-Tempini et al 2011

Logopenic PPA

- Another typical feature is phonological paraphasias in spontaneous speech and naming

Gorno-Tempini et al 2011

Logopenic PPA

- Important difference when compared to *semantic PPA:*
  - Single-word comprehension is spared
- Important difference when compared to *nonfluent PPA:*
  - Lack of obvious grammatical errors
  - Unimpaired articulation and prosody

Gorno-Tempini et al 2011

Logopenic PPA summed up

Areas of difficulty	Areas of relative strength
Significant difficulties in word retrieval- tip of the tongue phenomenon common. Phonemic paraphasias are common Poor sentence repetition, digit span, word span and letter span. Sentence comprehension deficits (phonological loop disorder)	Speech is relatively **fluent** Can repeat single words and digits accurately Can understand single words accurately Grammatically basically intact

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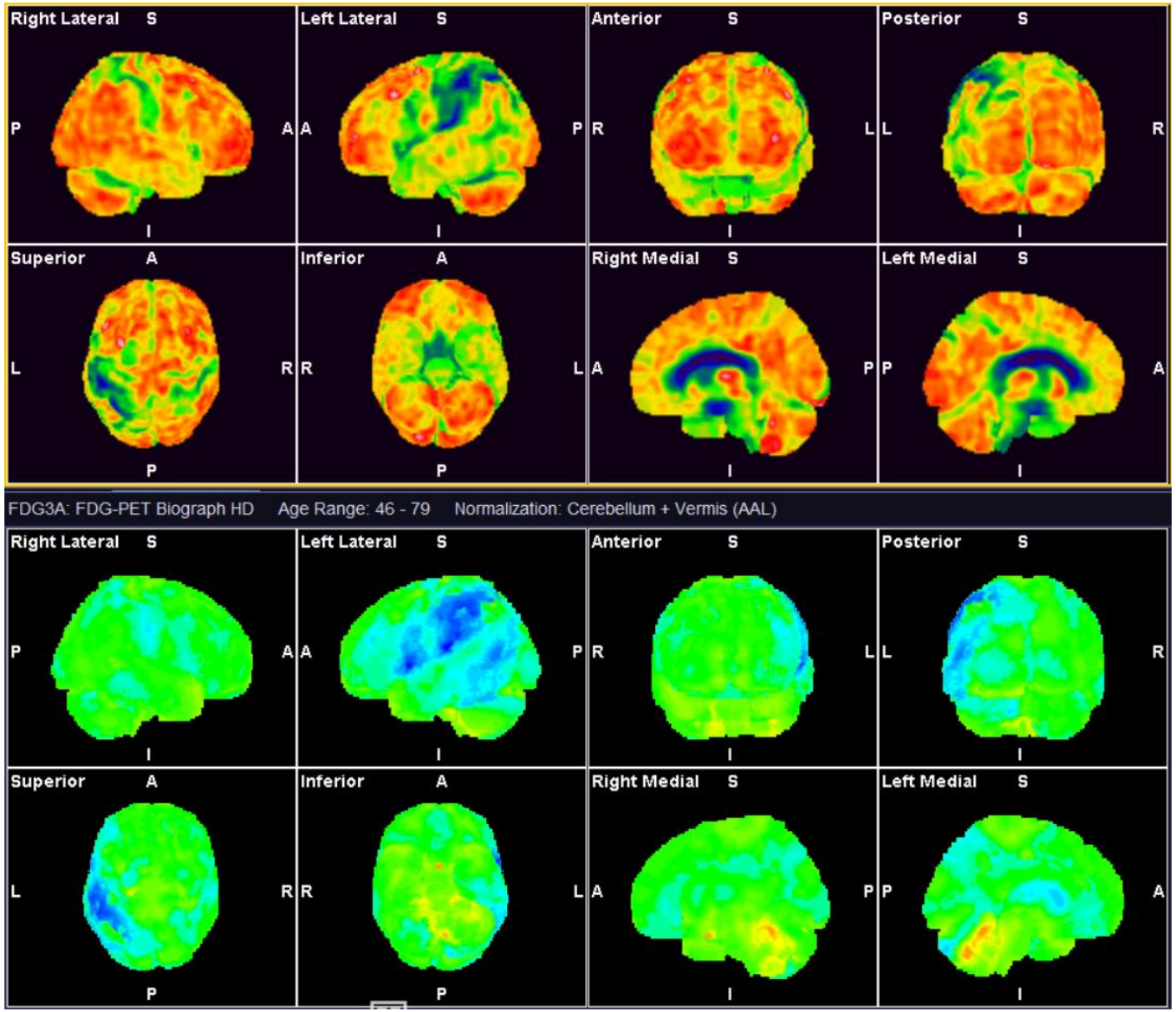
Imaging findings

Logopenic PPA

↓ FDG uptake

Posterior perisylvian or parietal area

Predominantly left-sided



Images courtesy of Dr Ebba Gløersen Müller, Division of Radiology and Nuclear Medicine, Oslo University Hospital

Diagnostic considerations in lvPPA

- Structural imaging (MRI) is not very sensitive but highly specific in lvPPA (57 / 95%)
- FDG-PET is more sensitive than MRI, and specific (92 / 94%)
- The underlying pathology is nearly always Alzheimer-type amyloid pathology, though some studies report FTLD-type pathology

- Most patients develop a generalized, Alzheimer-type dementia over time

Wasim et al. Neuroimaging of PPA variants. Neurographics 2018 Jan/Feb;8(1):1-6
Botha & Josephs. *PPA and Apraxia of Speech*. Continuum (Minneap Minn) 2019;25(1 , Dementia):101–127.
Mendez. *Early-onset Alzheimer Disease and Its Variants*. Continuum (Minneap Minn) 2019;25(1 , Dementia):34–51.

Unclassifiable PPA

- Several studies have shown that a large proportion of cases of PPA are not readily classifiable with the current criteria (up to 40%)

Sajjadi et al. Neurology 2012;78:1670-77
Mesulam et al. Brain 2012;135(pt5):1537-53
Wicklund et al. Neurology 2014;82(13):1119-26
Botha et al. Cortex 2015;69:220-236

Primary progressive apraxia of speech, PPAOS

- Speech and Language are different concepts
- The construct «nonfluent / agrammatic PPA» consists of a mixture of speech and language problems
  - Many researchers prefer to subdivide differently
  - The group from the Mayo Clinic (Keith A Josephs) have published widely on the subject of progressive apraxia of speech, PAOS

Primary progressive apraxia of speech

- Diagnostic criteria
  - Insidious onset and progressive worsening of speech disturbance
  - Apraxia of speech is the only or dominant speech disturbance at the time of testing
  - Dysarthria may be present but must be less severe than apraxia of speech
  - Any evidence of aphasia makes the diagnosis less certain

Botha & Josephs. PPA and Apraxia of Speech. Continuum (Minneap Minn) 2019;25(1 , Dementia):101–127.

Primary progressive apraxia of speech

- All patients with PPAOS develop parkinsonian signs with axial rigidity
- 40% of patients develop a PSP/CBS-like disorder five years into the disease
  - Gaze palsy, ideomotor apraxia, falls, frontal lobe syndrome, dysphagia, incontinence, dysarthria and aphasia with agrammatism
- In the remaining 60% worsening apraxia of speech is the main issue

- The overwhelming majority of autopsied cases have a 4-repeat tauopathy with corticobasal degeneration

Botha & Josephs. PPA and Apraxia of Speech. Continuum (Minneap Minn) 2019;25(1 , Dementia):101–127.

Refer the patient with PPA or PPAOS to a speech and language therapist (SLT) for assessment and treatment!

- “Speech and language therapists have developed several impairment-based interventions and compensatory strategies for use in the clinic.”

Volkmer et al. *Speech and language therapy approaches to managing primary progressive aphasia.* Pract Neurol. 2020 Apr;20(2):154-161. doi: 10.1136/practneurol-2018-001921. Epub 2019 Jul 29.

Take-home messages

- There are several distinct types of progressive aphasia
  - There is also a rare syndrome of isolated progressive apraxia of speech
- Semantic variant PPA is the best defined entity both clinically and neuropathologically
- SLT treatment is possible and can be meaningful

Suggested reading

- Gorno-Tempini et al. **Classification of primary progressive aphasia and its variants.** Neurology 2011;76:1006–1014
- Marshall, Hardy, Volkmer et al. **Primary progressive aphasia: a clinical approach.** J Neurol. 2018 Jun;265(6):1474-1490. doi: 10.1007/s00415-018-8762-6. Epub 2018 Feb 1.
- Bekkhus-Wetterberg, Brækhus, Müller et al. **Primary progressive aphasia.** [Article both in English and Norwegian] Tidsskr Nor Laegeforen. 2022 Nov 21;142(17). doi: 10.4045/tidsskr.22.0100. Print 2022 Nov 22.
- Volkmer et al. **Speech and language therapy approaches to managing primary progressive aphasia.** Pract Neurol. 2020 Apr;20(2):154-161. doi: 10.1136/practneurol-2018-001921. Epub 2019 Jul 29.