



## A Healthcare Provider's Guide To The Nonfluent Variant Of Primary Progressive Aphasia (nfvPPA):

Diagnosis, pharmacologic management,  
non-pharmacologic management, and  
other considerations

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## A Healthcare Provider's Guide To The Nonfluent Variant Of Primary Progressive Aphasia (nfvPPA): Diagnosis, pharmacologic management, non-pharmacologic management, and other considerations

### Diagnosis

#### Definition

Primary progressive aphasia (PPA) is an isolated language deficit with an insidious onset and gradual progressive impairment of language production, object naming, syntax, or word comprehension that is apparent during conversation or through speech and language assessments.

Early on, activities of daily living may be unaffected except those related to language (e.g., using the telephone). Aphasia is the most prominent deficit at symptom onset and with disease progression, although other cognitive deficits may be affected later in the disease.

PPA is a clinical syndrome with heterogeneous neuropathologic causes. The 3 variants of PPA are nonfluent PPA (nfvPPA), semantic variant PPA (svPPA), and logopenic variant PPA (LPA).<sup>1</sup>

#### Etiology

Pathological findings in nfvPPA is most commonly associated with Frontotemporal Lobar Degeneration with tau deposition (FTLD-tau), Frontotemporal Lobar Degeneration with TDP deposition (FTLD-TDP), Alzheimer's disease (AD), or other. The left posterior fronto-insular regions in the brain are primarily affected.

#### Course

First symptoms include anomia and word-finding difficulties typically between the ages of 60 to 65. Speech fluency is impaired and speech production becomes effortful. Patients will have trouble with sentence construction and syntax (agrammaticism).<sup>2</sup> Patients may also exhibit speech apraxia or trouble with the planning and sequencing of the movements required for speech production.<sup>3</sup> During the first two years of nfvPPA, patients typically have preserved skills in other nonverbal cognitive domains and

activities of daily living.<sup>1</sup> After these first two years many patients will exhibit extrapyramidal features of corticobasal degeneration (CBD and progressive supranuclear palsy (PSP) and the behavioral abnormalities of FTD.<sup>4</sup> The average survival in nfvPPA is about 8 to 10 years.<sup>5</sup>

#### Differential Diagnosis

Other things to rule out include side effects of medications, delirium, vascular conditions, reversible metabolic disorders, and neurodegenerative conditions with similar symptoms (for example, Alzheimer's disease).

#### Diagnostic Criteria

Criteria were developed by a panel of experts. Patients meet criteria based on 2 steps.<sup>1</sup>

##### A. Patients must first meet Mesulam's criteria for PPA<sup>1,6,7</sup>

###### 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.

###### Exclusion: criteria 1-4 must be answered negatively for a PPA diagnosis

1. Pattern of deficits is better accounted for by other neurodegenerative nervous system or medical disorders

2. Cognitive disturbance is better accounted for by a psychiatric disorder
3. Prominent initial episodic memory, visual memory, and visual perceptual impairments
4. Prominent, initial behavioral disturbance

**B. Patients must also meet criteria for the nonfluent variant of PPA<sup>1</sup>**

**I. Clinical diagnosis of nonfluent/agrammatic variant of PPA**

At least one of the following core features must be present:

1. Agrammatism in language production
2. 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:

1. Impaired comprehension of syntactically complex sentences
2. Spared single-word comprehension
3. Spared object knowledge

**II. Imaging-supported nonfluent/agrammatic variant diagnosis**

Both of the criteria must be present:

1. Clinical diagnosis of nonfluent/agrammatic variant PPA
2. Imaging must show one of more of the following results:
  - a. Predominant left posterior-fronto-insular atrophy on MRI or
  - b. Predominant left posterior fronto-insular hypoperfusion or hypometabolism on SPECT or PET

**III. Nonfluent/agrammatic variant PPA with definite pathology**

Clinical diagnosis (criterion 1 below) and either criterion 2 or 3 must be present:

1. Clinical diagnosis of nonfluent/agrammatic variant PPA
2. Histopathologic evidence of a specific neurodegenerative pathology (e.g., FTLN-tau, FTLN-TDP, AD, other)
3. Presence of a known pathogenic mutation

**Pharmacologic Management**

**Medications to Use**

Treatment of nfvPPA is predominantly symptomatic. Medications commonly used for Alzheimer's disease show no benefit (and may be linked to some cognitive side effects).<sup>8</sup> Behavioral disturbances

are best treated using the selective serotonin reuptake inhibitors, such as citalopram or escitalopram.<sup>9,10</sup>

**Medications to Avoid**

Medications with strong anticholinergic side effects, such as sedating antihistamines, barbiturates, narcotics, benzodiazepines, gastrointestinal and urinary antispasmodics, CNS stimulants, muscle relaxants, and tricyclic antidepressants should be avoided. Antipsychotics should be used with caution. If used, carefully evaluate effectiveness of medication and consider discontinuing if there is no improvement in six weeks.<sup>11,12,13</sup>

**Non Pharmacologic Management**

**Speech Therapy**

There is some preliminary evidence supporting the benefit of speech therapy. For example, speech and language therapy may slow the decline in naming abilities.<sup>14,15</sup> In a small group of patients with left-hemisphere lesions, singing promoted word intelligibility.<sup>16</sup>

Communication devices, like tablets or type-to-talk instruments, or picture books are other strategies that may promote communication abilities for patients.

**Healthy Lifestyle**

There are lifestyle habits that promote health and well-being. Research suggests that the combination of good nutrition, physical activity, and mental and social engagement may provide benefit in promoting health although more study is needed to determine the actual mechanisms.<sup>17,18</sup> A heart-healthy diet (lower in sugar and fat and higher in vegetables and fruit) is considered good for both the body and the brain. An example is the Mediterranean diet that promotes nutrition based on fruit, vegetables, nuts, and grains with limits on consumption of red meat and saturated fats. Physical exercise has been associated with improvement of mood and mobility, and a decrease in the risk for falls.<sup>19,20</sup> Physical activities that are socially engaging (walking or swimming with a friend and participating in exercise groups) can be especially enjoyable. Engagement in activities that are mentally stimulating (crossword puzzles, sudoku, computer games) is encouraged as long as the activity is enjoyable.

The Alzheimer's Association has more information on tips for maintaining your health: [alz.org/we\\_can\\_help\\_brain\\_health\\_maintain\\_your\\_brain.asp](http://alz.org/we_can_help_brain_health_maintain_your_brain.asp)

**Sleep**

Disrupted sleep can negatively impact memory and thinking, though the mechanisms are not well understood.<sup>21</sup>

Components of sleep hygiene include:

- Avoid napping during the day
- Avoid stimulants such as caffeine, nicotine, and alcohol too close to bedtime
- Get regular exercise
- Avoid eating right before sleep



- Ensure adequate exposure to natural light
- Establish a regular relaxing bedtime routine
- Associate your bed with sleep. It's not a good idea to use your bed to watch TV, listen to the radio, or read.

For more details on sleep hygiene, you can refer to the National Sleep Foundation at [sleepfoundation.org/ask-the-expert/sleep-hygiene](https://sleepfoundation.org/ask-the-expert/sleep-hygiene).

## Other Considerations

### Support Resources

- Alzheimer's Association: [alz.org](https://www.alz.org)
- Family Caregiver Alliance: [caregiver.org](https://www.caregiver.org)
- National Institute of Health/National Institute on Aging: [nia.nih.gov/alzheimers](https://nia.nih.gov/alzheimers)
- The Association for Frontotemporal Degeneration: [theaftd.org](https://www.theaftd.org)
- National Aphasia Association: [aphasia.org](https://www.aphasia.org)
- The Primary Progressive Aphasia Program at Northwestern University: [brain.northwestern.edu/dementia/ppa/index.html](https://brain.northwestern.edu/dementia/ppa/index.html)
- Primary Progressive Aphasia support, an online support forum: [groups.yahoo.com/neo/groups/PPA-support/info](https://groups.yahoo.com/neo/groups/PPA-support/info)

### Research and Clinical Trials

The National Institutes of Health maintains an extensive listing of clinical trials at [clinicaltrials.gov](https://clinicaltrials.gov). Academic medical centers may be engaged in research and clinical trials.

### Safety

If wandering or getting lost is a concern, refer the patient and family to the MedicAlert +Alzheimer's Association Safe Return program (operated by the Alzheimer's Association) [alz.org/care/dementia-medic-alert-safe-return.asp](https://www.alz.org/care/dementia-medic-alert-safe-return.asp).

Other strategies for ensuring safety concerns may include door alarms and increased supervision.

### Driving

Depending on cognitive and motor findings, the patient may be requested to stop driving, complete test of driving abilities through the Department of Motor Vehicles (DMV), or be referred to a driver's safety course that will assess driving ability. Reporting to the department of motor vehicles should be consistent with state laws. Some states have mandatory reporting requirements: the diagnosis is reported to local health departments who then report to the DMV. Individual state requirements can be found at: [dmvusa.com](https://www.dmvusa.com).

### Living Situation and Environment

It is important to determine if the patient's residential setting best meets his or her functional and cognitive abilities. Areas of concern may include personal safety (ability to manage medications safely, ability to manage nutritional requirements, ability to manage personal hygiene) and quality of life (activities and engagement that match the person's needs and abilities).

Types of living situations range from living at home alone or living at home with supervision, to board and care, assisted living, or memory care units.

### Elder Abuse

Patients with dementia and their caregivers are vulnerable to abuse. Refer to (AFS) if there is concern for the well-being of the patient or the caregiver.

To locate an APS office in your state, see: [napsa-now.org/get-help/help-in-your-area/](https://www.napsa-now.org/get-help/help-in-your-area/).

### Legal Planning

Provide information about advance directives and durable power of attorney while the patient is in the early stages of disease and able to articulate his or her wishes. Make referrals for legal and financial advice, especially if there are concerns about the patient's judgment, decision-making, or vulnerability. A formal evaluation for capacity may be warranted. The Alzheimer's Association provides

a brochure that covers legal planning: [alz.org/national/documents/brochure\\_legalplans.pdf](http://alz.org/national/documents/brochure_legalplans.pdf).

- **Advanced Directives**

These documents allow individuals to state their preferences for medical treatments and to select an agent or person to make health care decisions in the event they are unable to do so or if they want someone else to make decisions for them.

- **Power Of Attorney**

A Power of Attorney (POA) is a legal document that gives someone of an individual's choosing the power to act in their place. POAs can be for medical or financial matters.

- **Living Will**

A living will is a written, legal document that spells out medical treatments that an individual would and would not want to be used to keep them alive, as well as other decisions such as pain management or organ donation.

## Teaching Video for Providers

An example of a physician telling a patient she has dementia: [alz.org/health-care-professionals/dementia-diagnosis-diagnostic-tests.asp#alzheimers\\_diagnosis](http://alz.org/health-care-professionals/dementia-diagnosis-diagnostic-tests.asp#alzheimers_diagnosis).



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