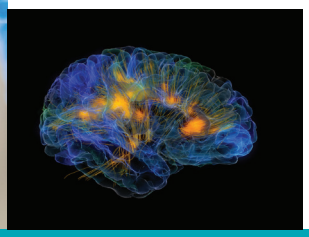
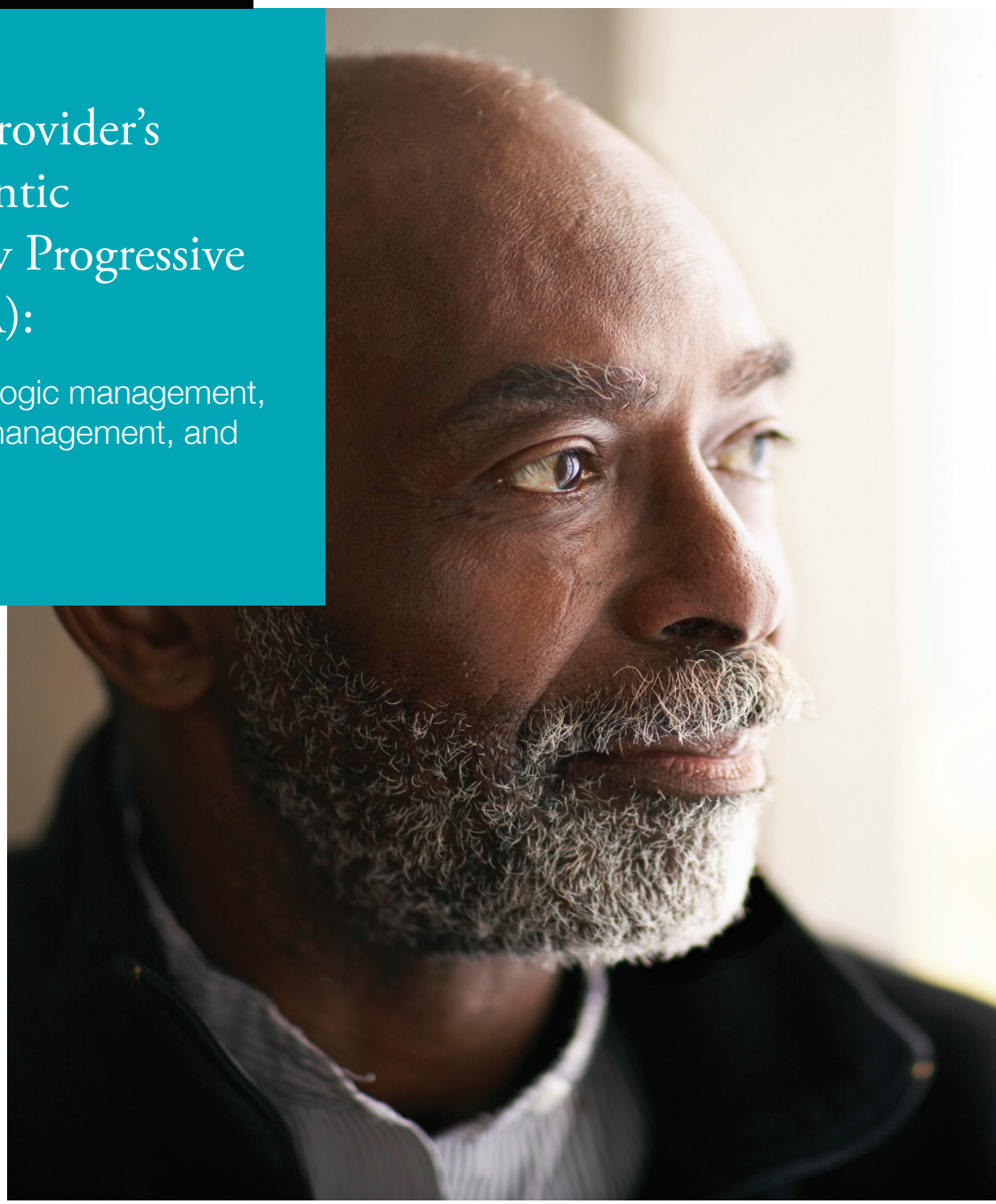


A Healthcare Provider's Guide to Semantic Variant Primary Progressive Aphasia (svPPA):

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



This material is provided by UCSF Weill Institute for Neurosciences as an educational resource for health care providers.

UCSF Weill Institute for Neurosciences

Memory and Aging Center

A Healthcare Provider's Guide to Semantic Variant Primary Progressive Aphasia (svPPA)

Diagnosis, Pharmacologic Management, Non-pharmacologic Management, and Other Considerations

Diagnosis

Definition

Semantic variant primary progressive aphasia (svPPA) is one of the language variants of frontotemporal dementia (FTD). In this variant, selective degeneration of the left anterior temporal lobe leads to a loss of semantic memory.[1,2] Typical symptoms include poor confrontation naming, impaired single word comprehension, poor object/person knowledge, surface dyslexia, spared repetition, and spared motor speech with relatively preserved behavior and cognition.[3] When the degeneration starts on the right side, it leads to the loss of empathy, recognition of the emotions of other people, difficulty recognizing familiar faces, psychosis, and behavioral disinhibition.[4] Later stages of right-sided svPPA can look similar to behavioral variant FTD (bvFTD).[5,6]

Etiology

svPPA account for 20% of FTD cases, but the cause in most cases is unknown. About 5% or less of all patients with svPPA had a family history of FTD.[7] There is early research into possible developmental and autoimmune factors that may predispose someone to svPPA[8,9] as well research into inflammatory markers that may play a role in disease development.[10]

Course

People with svPPA usually know they are having trouble finding words. Word finding problems and anomia are typically the first obvious symptoms. High frequency nouns, verbs, and proper grammar tend to remain accessible for the longest time. Eventually, both temporal lobes suffer atrophy, and the patient typically shows language, cognitive, and behavioral symptoms.

Differential Diagnosis

The specific semantic loss in svPPA differs from that of Alzheimer's disease in that cueing does not typically help recall the lost word. Right-sided svPPA might look like bvFTD or a psychiatric disorder. Neoplasms, cerebrovascular disease, hypothyroidism, depression, bipolar disease, schizophrenia and personality disorder should all be ruled out as possible explanations. Atrophy patterns seen on imaging should help the differential tremendously.

Diagnostic Criteria

International consensus criteria were published in 2011. 2 patients are first diagnosed with primary progressive aphasia (PPA) and then into clinical variant based on specific speech and language symptoms. Classification can then be further specified as "imaging-supported" and "with definite pathology" if further data are available.

I. Primary progressive aphasia (PPA)

Inclusion: Criteria I.A.-I.C. must be answered positively

- I.A. Most prominent clinical feature is difficulty with language
- I.B. These deficits are the principal cause of impaired daily living activities
- I.C. Aphasia should be the most prominent deficit at symptom onset and for the initial phases of the disease

Exclusion: Criteria I.D.-I.G. must be answered negatively for a PPA diagnosis.

- I.D. Pattern of deficits is better accounted for by other nondegenerative nervous system or medical disorders
- I.E. Cognitive disturbance is better accounted for by a psychiatric diagnosis
- I.F. Prominent initial episodic memory, visual memory, and visuoperceptual impairments
- I.G. Prominent, initial behavioral disturbance

II. Clinical diagnosis of semantic variant PPA

Both of the following core features must be present:

- II.A. Impaired confrontation naming
- II.B. Impaired single-word comprehension

At least 3 of the following other diagnostic features must be present:

- II.C. Impaired object knowledge, particularly for low-frequency or low-familiarity items
- II.D. Surface dyslexia or dysgraphia
- II.E. Spared repetition
- II.F. Spared speech production (grammar and motor speech)

III. Imaging-supported semantic variant PPA diagnosis

Both of the following criteria must be present:

- III.A. Clinical diagnosis of semantic variant PPA
- III.B. Imaging must show one or more of the following results: Predominant anterior temporal lobe atrophy, Predominant anterior temporal hypoperfusion or hypometabolism on single-photon emission computed tomography (SPECT) or positron emission tomography (PET)

IV. Semantic variant PPA with definite pathology

Clinical diagnosis (criterion IV.A. below) and either criterion IV.B. or IV.C. must be present:

- IV.A. Clinical diagnosis of semantic variant PPA
- IV.B. Histopathologic evidence of a specific neurodegenerative pathology (e.g., frontotemporal lobar degeneration due to tau or TDP-40, Alzheimer's disease, other)
- IV.C. Presence of a known pathogenic mutation

Pharmacologic Management

Medications to Use

Review expected and realistic goals of treatment (e.g., treatment is for symptomatic improvement and not a cure or reversal of disease). Expected benefits may be mild improvement in memory function, mood, and alertness. If the patient has vascular disease or mixed dementia, they should receive management and education regarding modification of cardiovascular risk factors.

To a limited degree, selective serotonin reuptake inhibitors (SSRI) and serotonin norepinephrine reuptake inhibitors (SNRI)-type compounds may help with the repetitive compulsive behaviors.[11]

Speech and language therapy to focus on retaining a selection of high frequency words may be helpful is started early.[12]

Medications to Avoid

Medications with strong anticholinergic side effects, such as sedating antihistamines, barbiturates, narcotics, benzodiazepines, gastrointestinal and urinary antispasmodics, central nervous system (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.[13,14,15]

Non Pharmacologic Management

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 research is needed to determine the actual mechanisms.[16,17] A heart-healthy diet (lower in sugar and fat and higher in vegetables and fruit) is considered to be 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.[18,19] 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

Sleep

Disrupted sleep can negatively impact memory and thinking, though the mechanisms are not well understood.[20]

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.

Other Considerations

Support Resources

- Alzheimer's Association: alz.org
- Family Caregiver Alliance: caregiver.org
- National Institute of Health/National Institute on Aging: nia.nih.gov/alzheimers
- The Association for Frontotemporal Degeneration: theaftd.org
- National Aphasia Center: aphasia.org

Research and Clinical Trials

The National Institutes of Health maintains an extensive listing of clinical trials at 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.

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.

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 Adult Protective Services (APS) 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/.

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.

- **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 his or her 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.

References

1. Hodges JR, Patterson K, Oxbury S, Funnell E. Semantic Dementia. *Brain.* 1992;115(6):1783-1806. 2. Gorno-Tempini ML, Hillis AE, Weintraub S, et al. Classification of primary progressive aphasia and its variants. *Neurology.* 2011;76(11):1006-1014. 3. Bonner MF, Ash S, Grossman M. The New Classification of Primary Progressive Aphasia into Semantic, Logopenic, or Nonfluent/Agrammatic Variants. *Current Neurology and Neuroscience Reports.* 2010;10(6):484-490. 4. Miller BL, Chang L, Mena I, Boone K, Lesser IM. Progressive Right Frontotemporal Degeneration: Clinical, Neuropsychological and SPECT Characteristics. *Dementia and Geriatric Cognitive Disorders.* 1993;4(3-4):204-213. 5. link to bvFTD information 6. Seeley WW, Bauer AM, Miller BL, et al. The natural history of temporal variant frontotemporal dementia. *Neurology.* 2005;64(8):1384-1390. 7. Goldman JS, Farmer JM, Wood EM, et al. Comparison of family histories in FTLD subtypes and related tauopathies. *Neurology.* 2005;65(11):1817-1819. 8. Miller ZA, Hinkley LB, Herman A, et al. Anomalous functional language lateralization in semantic variant PPA. Neurology. 2014;84(2):204-206. 9. Rosenbloom MH, Smith S, Akdal G, Geschwind MD. Immunologically mediated dementias. *Current Neurology and Neuroscience Reports.* 2009;9(5):359-367. 10. Miller ZA, Rankin KP, Graff-Radford NR, et al. TDP-43 frontotemporal lobar degeneration and autoimmune disease. *Journal of Neurology, Neurosurgery & Psychiatry.* 2013;84(9):956-962. 11. Rosenbloom MH, Smith S, Akdal G, Geschwind MD. Immunologically mediated dementias. *Current Neurology and Neuroscience Reports.* 2009;9(5):359-367. 12. Henry M, Rising K, Demarco A, Miller B, Gorno-Tempini M, Beeson P. Examining the value of lexical retrieval treatment in primary progressive aphasia: Two positive cases. *Brain and Language.* 2013;127(2):145-156. 13. Han L, Mccusker J, Cole M, Abrahamowicz M, Primeau F, Élie M. Use of Medications With Anticholinergic Effect Predicts Clinical Severity of Delirium Symptoms in Older Medical Inpatients. *Archives of Internal Medicine.* 2001;161(8):1099. 14. Roe CM, Anderson MJ, Spivack B. Use of Anticholinergic Medications by Older Adults with Dementia. *Journal of the American Geriatrics Society.* 2002;50(5):836-842. 15. Marcum ZA, Hanlon JT. Commentary on the New American Geriatric Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. *The American Journal of Geriatric Pharmacotherapy.* 2012;10(2):151-159. 16. Barnes DE, Santos-Modesitt W, Poelke G, et al. The Mental Activity and eXercise (MAX) Trial. *JAMA Internal Medicine.* 2013;173(9):797. 17. Jedrziewski MK, Ewbank DC, Wang H, Trojanowski JQ. The Impact of Exercise, Cognitive Activities, and Socialization on Cognitive Function. *American Journal of Alzheimers Disease & Other Dementias®.* 2014;29(4):372-378. 18. Howe TE, Rochester L, Neil F, Skelton DA, Ballinger C. Exercise for improving balance in older people. *Cochrane Database of Systematic Reviews.* September 2011. 19. Podewils LJ. Physical Activity, APOE Genotype, and Dementia Risk: Findings from the Cardiovascular Health Cognition Study. *American Journal of Epidemiology*. 2005;161(7):639-651. 20. Yaffe K, Falvey CM, Hoang T. Connections between sleep and cognition in older adults. *The Lancet Neurology.* 2014;13(10):1017-1028.