PRIMARY PROGRESSIVE APHASIA

and

OTHER FRONTOTEMPORAL DEMENTIAS

Diagnosis and Treatment of Associated Communication Disorders

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Series Introduction

The Medical Speech-Language Pathology book series provides graduate students, clinicians, and clinical researchers with functional, comprehensive material to enhance practice in a medical setting. The books are designed to bolster transdisciplinary knowledge through infusion of information from neurology, pharmacology, radiology, otolaryngology, and other related disciplines. They capture our current understanding of complex clinical populations, often encountered in medical settings, and offer information to guide evaluation and management strategies. For each clinical population, case studies are used to promote application and integration of the material. Moreover, the handbooks are richly supplemented with figures, tables, and patient samples to enhance accessibility of the information. Each book in the series is authored by experienced professionals and content experts who are able to transform the research literature into clinically applicable and digestible information. The authors integrate theory and practice in a succinct manner, allowing immediate application to everyday practice. This book series advances the medical speech-language pathology community by merging fundamental concepts, clinical strategies, and current theories with research evidence, with the goal of fostering outstanding clinical practice and clinical research.

The first book of the series set the stage regarding the environment of the medical speech-language pathologist (SLP) as an interprofessional team member, the clinical populations encountered by the SLP, and the foundational knowledge needed to understand and interpret neuroimaging, medication influences, and infection control precautions.

In this outstanding second book of the Medical Speech-Language Pathology series, leading experts on the frontotemporal dementias (FTD) and primary progressive apraxia of speech (PPAOS) have created an invaluable resource. The authors transformed decades of clinical experience and the latest cutting-edge research into an understandable tutorial that encompasses differential diagnosis, clinical examinations, speech/language/cognitive assessments, neuroimaging findings, and treatment recommendations. Consistent with the book series focus on clinical applicability, case studies are skillfully used to highlight key diagnostic characteristics as well as theoretically sound treatment goals. Written and spoken language samples from individuals diagnosed with FTD are offered to concretely illustrate the various, complex profiles. Additionally, the authors go a step beyond by providing counseling and educational information, including online resources, for the SLP who is navigating these difficult diagnoses with patients and care providers. Our clinical and scientific practice will undoubtedly be enhanced by this book, allowing us to better serve individuals with the complex, evolving diagnoses of logopenic primary progressive aphasia (PPA), semantic dementia, nonfluent-agrammatic PPA, PPAOS, the behavioral variant of FTD, and amyotrophic lateral sclerosis with FTD.

Medical Speech-Language Pathology
Series Editors
Kristie A. Spencer, PhD, CCC-SLP
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Foreword

Not too many decades ago, the party line on higher-level speech and language difficulties associated with neurodegenerative disease was that they were simply one set of problems embedded within a broad constellation of cognitive deficits. It was not uncommon for such difficulties to be referred to as the *language of Alzheimer's disease* or *aphasic dementia.* When case studies of people with unexplained insidious onset and progression of language difficulty began to appear with some regularity in the 1980s, they were initially viewed by some (many?) as curiosities or not-so-interesting variants of early manifestations of what would quickly evolve to more clinically typical Alzheimer's disease. To illustrate the uncertainty about the importance of these problems at the time, when I discussed two cases with slowly progressive aphasia at the Clinical Aphasiology Conference in 1987 I concluded that the syndrome "probably does exist."

Gradually, and then with considerable momentum, things changed.

Primary progressive aphasia (PPA) is now widely accepted as a distinct clinical syndrome. It is perhaps the most frequently occurring exemplar of neurodegenerative conditions that initially and for an extended period of time are relatively isolated to specific higher-level cognitive, motor, or behavioral/affective functions. There now is general agreement that PPA is not a unitary syndrome and that an imperfect-but-meaningful proportion of cases can be captured clinically under three variants, each with its own imperfect-but-meaningful localization and underlying pathologies. Two of the PPA variants are now often housed within the parent category of frontotemporal dementia (FTD), along with their cousin, behavioral variant FTD. In addition, it is now recognized that apraxia of speech (AOS), known to be a frequent feature of the nonfluent/agrammatic variant of PPA, can also occur in the absence of aphasia (*primary progressive AOS* [PPAOS]). And, confounding the complexity of the relationships among these disorders, a link is now recognized between FTD and amyotrophic lateral sclerosis.

There can be little doubt that the classifications and understanding of PPA, PPAOS, and other FTDs will continue to evolve as a function of refinements in clinical assessment and neuroimaging correlates, and accumulating autopsy findings. This will require ongoing interdisciplinary basic and clinical research collaboration. It is also important to recognize that progress in the diagnosis and classification of these disorders has far outstripped what is known about optimal strategies for managing their often devastating personal, social, and occupational consequences. Nonetheless, general principles for management and the development of specific treatment approaches are providing guidelines and an accumulating evidence base for their implementation by practicing clinicians.

It is very appropriate at this time to take stock of the state of the science and art of research and clinical practice directed at PPA, PPAOS, and related FTDs. This book does just that. As a whole, it provides a very substantive overview of the topic, and its individual chapters provide essential details about the underpinnings, defining clinical features, assessment, differential diagnosis, and management of each of the disorders. The consistent chapter-to-chapter format and case studies provide a reader-friendly cohesiveness that will be appreciated by students, busy clinicians, and clinical researchers. Lastly,

this book will serve as a solid foundation for critically appraising the value of future clinical research that will impact the quality of care for individuals with these increasingly recognized disorders which so insidiously but profoundly siphon away the ability to communicate.

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Preface

This book, *Primary Progressive Aphasia and Other Frontotemporal Dementias: Diagnosis and Treatment of Associated Communication Disorders*, is the second in a series of books addressing medical speech-language pathology. This book is intended to fill an unmet need to assist clinicians, students, and related healthcare professionals in the diagnosis and treatment of the title disorders.

This book is being published as our understanding of the spectrum of frontotemporal dementia (FTD) variants is expanding daily. There is a growing population of individuals diagnosed with various forms of FTD and primary progressive aphasia (PPA), and this number is likely to increase as medical practitioners and speech-language pathologists (SLPs) become more expert at identifying these conditions. More clinicians will be seeing, and treating, patients with a diagnosis of FTD specifically, whereas previously the diagnosis was likely unspecified or assumed to be an Alzheimer's disease dementia. This book explicitly targets a class of disorders that are now becoming more widely recognized, yet most clinicians do not have the breadth of experience to feel confident in assessing and treating these patients. This goal of this book is to expand this clinical knowledge base and support the development of skills beyond diagnosis, but also in the arena of clinical management.

This clinical resource book is targeted toward practicing clinicians, graduate students, or clinical researchers who are interested in the latest conceptualization and research regarding FTD spectrum disorders and the associated communication disorders. The goal of this book is to provide clinical pearls to assist in diagnostic assessments and treatment planning. Each chapter is clinically driven, and empirically supported, with a focus on the communication disorders associated with FTD. This book offers an unprecedented quantity of information on primary progressive aphasia and apraxia of speech. This book is written for clinicians, by clinical researchers and practitioners. It is the hope of the editor and contributing authors that this book will be utilized by SLPs who routinely care for individuals diagnosed with progressive neurogenic communication disorders, and also incorporated into communication sciences and disorders training programs.

Within each chapter, you will find a concise presentation of available evidence-based practice and research findings, with a focus on sharing information that is clinically applicable and digestible for nonresearchers. Of course, there is a proportion of clinical experience and expertise that is not published. The selected authors all engage with diagnosis and treatment and have also wonderfully captured their clinical experience within their text. Each chapter provides a comprehensive outline of testing that will assist in the diagnosis of the cognitive-communication disorders associated with FTD, PPAs, and primary progressive apraxia of speech (PPAOS).

Chapter 1, the introduction, provides an overview of the assessment process and differential diagnosis among FTD subtypes, PPA, and PPAOS. When a patient arrives, one generally does not know which condition will be observed and therefore which chapter is most important to read. The chapter provides a broad overview for identifying the FTD variant and serves as a starting point for selecting a chapter to read more in depth.

Chapters 2, 3, and 4 detail the logopenic, semantic, and nonfluent/agrammatic variants of PPA, respectively. Each chapter discusses the neurophysiological underpinnings and associated disease mechanisms associated with the clinical presentations. Each chapter then details the key features for differential diagnosis, including clinical examinations and neuroimaging findings. Where appropriate, the chapters discuss relevant genetic risk factors and concomitant neuropsychological changes. Importantly, each chapter provides an overview of current treatment research, discussion of the role of the SLP in interdisciplinary and interprofessional teams, and case studies that demonstrate goals that can be utilized in therapy. Finally, each chapter broaches counseling and education for the patients and their care partners. This includes review of current online and community resources.

Chapter 5 discusses the clinical presentation of PPAOS. It reviews the history of this diagnostic category. With the help of case studies, this chapter guides differential diagnosis and treatment planning for these patients. In discusses the evolution of these patients from their initial, predominant motor speech difficulty to the eventual neurologic syndrome: progressive supranuclear palsy or corticobasal syndrome. Coauthored by a speech-language pathologist and behavioral neurologist, this chapter discusses the appropriateness of behavioral treatments and pharmacological interventions for symptom management.

Chapter 6 addresses the role of the SLP in diagnosis and treatment of the behavioral variant of FTD. Finally, Chapter 7 details the assessment and treatment of FTD in the context of motor neuron disease, and more specifically, amyotrophic lateral sclerosis (ALS). Both chapters discuss the clinical presentations, approaches to diagnosis, genetic risk factors associated with this clinical presentation, and provide excellent suggestions for necessary education and counseling for these patients and their care partners.

The impetus for this book is to share the unprecedented amount of information available to us that can inform our clinical practice. To fully grasp what is important in planning the long-term therapy trajectory, we should utilize our fullest understanding of the underlying disease. As clinicians working with degenerative diseases, we can utilize our understanding to adopt an adaptive approach to therapy and engage in dynamic clinical decision-making. The authors and editor believe the information provided will be useful for practitioners to make differential diagnosis efficient and accurate and make treatment planning effective. We hope the community resources, consolidated in the accompanying appendix, will serve our patients and their care partners well.

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CHAPTER 2

The Logopenic Variant of Primary Progressive Aphasia

Kindle Rising and Pélagie M. Beeson

CHAPTER OUTLINE

SUMMARY

The logopenic variant of primary progressive aphasia (lvPPA) is the most recently identified PPA subtype. The established behavioral diagnostic criteria for lvPPA include the presence of **anomia** and sentence-level repetition deficits, potentially with phonologically based speech errors, with preserved single-word comprehension and no **agrammatism**. This behavioral profile is associated with cortical atrophy in left posterior perisylvian cortical regions, and underlying pathology is predominantly thought to be **Alzheimer's disease**. Logopenic PPA continues to present diagnostic challenges due to overlapping behavioral characteristics with other PPA variants and amnestic **Alzheimer's disease dementia (AD)**, but lvPPA does present with a profile distinct from these other syndromes.

There is a paucity of literature regarding the treatment of lvPPA, but a growing body of evidence suggests that behavioral language therapy is warranted in this population. Promising behavioral treatment approaches that leverage spared cognitive-linguistic processes and train communication strategies effect immediate treatment gains, and may contribute to durability and generalization. Supportive communication and compensatory strategies are also important to maximize communication in lvPPA.

HISTORICAL BACKGROUND

Mesulam's (1982) classic systematic description of primary progressive aphasia (PPA) characterized the disorder as a "slowly progressive aphasia without generalized dementia," but the heterogeneity of the behavioral characteristics of those original six patients suggested that PPA may not be a unitary syndrome. In fact, the syndrome was soon classified into two behavioral variants: fluent, which primarily included individuals with semantic dementia (Hodges, Patterson, Oxbury, & Funnell, 1992), and nonfluent (Grossman, Mickanin, & Onishi, 1996), which broadly included individuals with impairments of syntax and motor speech decline. Over time it became clear that some individuals with progressively declining language abilities did not fit this fluency dichotomy, and that other characteristic linguistic and neuroanatomical features were important in determining a specific PPA diagnosis. There emerged in the literature a description of another pattern of language decline which, like semantic dementia, was characterized initially by anomia, but with intact single-word comprehension. Individuals with this pattern of PPA also had difficulty with sentence repetition and demonstrated long pauses for word retrieval in spontaneous speech, giving the impression of reduced fluency. They did not, however, exhibit the frank agrammatism or motor speech difficulties associated with the nonfluent variant of PPA (Gorno-Tempini et al., 2004; Hillis, Selnes, & Gordon, 1999; Kertesz, Davidson, McCabe, Takagi, & Munoz, 2003; Mesulam et al., 2009). In 2008, Gorno-Tempini and colleagues further characterized this third variant of PPA in a cohort of six patients who exhibited phonological working memory impairment consistent with atrophy in left posterior perisylvian cortical regions. Various terms were proposed to describe this apparent third variant of PPA, including progressive conduction aphasia (Hillis et al., 1999), phonological progressive aphasia (Gorno-Tempini et al., 2008), and progressive mixed aphasia (Grossman, 2010), but ultimately the term "logopenic" from the Greek, meaning "lack of words," was codified by Gorno-Tempini and colleagues and adopted by an interna-

tional consensus of experts (Gorno-Tempini et al., 2011). In this consensus paper, the specific patterns of cognitive-linguistic behaviors, neuroanatomical features, and corresponding neuropathological findings were presented for semantic (svPPA), nonfluent/agrammatic (nfvPPA), and logopenic (lvPPA) variants of PPA. Behavioral criteria for a diagnosis of lvPPA require the presence of two core features: impaired word retrieval and impaired phrase and sentence repetition. At least three of the following four features must also be present: (1) phonological speech errors, (2) spared object knowledge and comprehension of single words, (3) spared motor control for speech, and (4) no frank agrammatism. Neuroimaging supporting a logopenic PPA diagnosis should reveal cortical atrophy, hypoperfusion, or hypometabolism in predominantly left temporoparietal regions.

DESCRIPTION OF LOGOPENIC VARIANT PPA

Demographics

Little is known about the incidence and prevalence of PPA in general, and even less about the logopenic variant of PPA specifically. Mesulam (2001) estimated that as many as 20% of all individuals with dementia have PPA. Some experts report that lvPPA patients make up about 30% of their PPA caseload, potentially making this variant the second most prevalent compared to svPPA (39%) and nfvPPA (18%) (Gorno-Tempini et al., 2008; Teichmann et al., 2013). Like the semantic and nonfluent/agrammatic variants, the logopenic variant is also thought to be an early-onset dementia (Migliaccio et al., 2009), and there is some evidence that earlier onset in the logopenic variant specifically may be associated with **developmental learning disability** (Miller et al., 2013); however, little is ultimately understood about the incidence, prevalence, or onset of this variant.

Disease Mechanisms

Alzheimer's disease pathology, characterized by neurofibrillary tangles and extracellular amyloid-beta plaques, is reported in a majority of lvPPA cases (Mesulam et al., 2008; Rabinovici et al., 2008; Rohrer & Warren, 2010; Rohrer, Rossor, & Warren, 2012; Spinelli et al., 2017; Teichmann et al., 2013), although other pathological profiles have been described less frequently, including **TDP-43**, tau, and Lewy body dementia (Montembeault, Brambati, Gorno-Tempini, & Migliaccio, 2018). This variability in the underlying pathology of lvPPA may explain some of the heterogeneity in the atrophy patterns and behavioral profiles that have been reported in this population, particularly as the disease progresses (Rohrer et al., 2010; Tetzloff et al., 2018; Whitwell et al., 2015). Such heterogeneity has prompted discussion about whether lvPPA is a unitary disorder, or whether there may be subvariants, mixed variants, or otherwise "unclassifiable" presentations of PPA that have overlapping behavioral characteristics with lvPPA, but differing neurophysiological underpinnings (Leyton et al., 2015; Rohrer et al., 2010; Spinelli et al., 2017; Teichmann et al., 2013). There is much to be learned about the disease processes underlying the clinical phenotype of lvPPA, and pathology on an individual level cannot be presumed. It is clear, however, that there are characteristic cognitive-linguistic symptoms and corresponding patterns of cortical atrophy that distinguish lvPPA as a clinical entity (Gorno-Tempini et al., 2011).

DIAGNOSIS

Key Features of Logopenic Variant PPA

A diagnosis of PPA must meet the general criteria of language decline in the absence of other cognitive-behavioral symptoms during the initial stages of the disease, and language impairment as the principal symptom affecting activities of daily living (Mesulam, 2001). PPA variant diagnoses take into account specific patterns of language, cognition, and behavior identified through thorough case history interviews and cognitive-linguistic assessment batteries, as well as available neuroimaging data (Gorno-Tempini et al., 2011).

The classic characterization of speech and language characteristics in logopenic PPA include impaired naming and sentence repetition with phonological errors, spared object knowledge, single-word comprehension, and speech production, and an absence of frank agrammatism (Gorno-Tempini et al., 2011). Patients with logopenic PPA often report lexical retrieval difficulties as an early and prominent symptom that prompts them to obtain a clinical diagnosis. Examination of abilities on confrontation naming tasks (e.g., Boston Naming Test [BNT]; Kaplan, Goodglass, & Weintraub, 2001) and in connected speech tasks such as picture descriptions may reveal naming errors that are phonological in nature (i.e., speech sound errors such as "helitopper" for "helicopter").

Analysis of the spontaneous speech of individuals with lvPPA will also provide information about fluency, which may be marred by frequent pauses and attempts at self-correction. Historically, this PPA fluency profile was classified as "nonfluent" in contrast to the seemingly hyperfluent speech of individuals with svPPA (Harciarek, Sitek, & Kertesz, 2014). In the context of aphasia classification, however, the "fluent" versus "nonfluent" dichotomy refers to more than the rate and ease of spoken output. Fluency is a multidimensional construct that comprises syntactic structure, phrase length, speech rate, and motor speech characteristics such as articulatory agility (Wilson et al., 2010). Given this framework, fluency in lvPPA may be "intermediate" compared to semantic and nonfluent variants of PPA. Wilson and colleagues (2010) analyzed the spontaneous speech of 50 patients with PPA and identified a maximum speech rate in lvPPA that is greater than that of individuals with nfvPPA but slower than svPPA patients. Furthermore, lvPPA speech samples did not reveal speech sound distortions (i.e., **apraxia of speech**) or frank syntactic errors as noted in those with nfvPPA. The errors in syntax exhibited by those with lvPPA also differ from nfvPPA. In contrast to agrammatism characterized by omission of function words and morphological markers, patients with lvPPA demonstrate **paragrammatic** errors described as "unacceptable juxtapositions of phrases and misuse of words" (Goodglass et al., 1994). The following examples illustrate the difference in the grammatical errors for individuals with lvPPA and nfvPPA:

> **Stimulus:** Picture of a truck parked outside of a garage
>
> **lvPPA (paragrammatic):** "The truck is sitting and . . . haven't putting it into the, the place you're supposed to . . . drive for"
>
> **nfvPPA (agrammatic):** "The truck . . . outside house"

Oral repetition difficulties in lvPPA may be detected using word and sentence repetition tasks on standardized language tests, such as the repetition subtest of the Western Aphasia Battery (WAB) (Kertesz, 1982, 2006). Repetition errors increase with sentence length, while sentence grammaticality and compre-

hension may be relatively spared, as evidenced by responses that retain the syntactic structure and semantic gist of the sentence (e.g., "The pastry cook was elated." repeated as "The baker was very happy."). Sentence comprehension may be impaired as sentence length increases, but comprehension does not appear to be affected by increased syntactic complexity. Single word comprehension (as measured by spoken word to picture matching tasks, for example) remains intact well into the course of the disease (Gorno-Tempini et al., 2008; Henry & Gorno-Tempini, 2010).

Several studies examining the nature of the language deficits in lvPPA suggest that impaired phonological skills underlie the core language behaviors (Gorno-Tempini et al., 2008; Henry et al., 2015; Leyton, Ballard, Piguet, & Hodges, 2014). In one of the earliest papers characterizing the logopenic variant of PPA, Gorno-Tempini and colleagues (2008) examined the status of the "phonological loop" of six lvPPA patients using various span tasks (i.e., digit, letter, and word span). The participants all demonstrated impaired span (no more than three items) regardless of stimuli, and did not demonstrate improvement with phonological dissimilarity in letter strings, as do controls. These results were interpreted to indicate an impairment of phonological working memory, but it was unclear if other aspects of phonological processing might be impaired. Henry and colleagues (2015) investigated phonological processing skills in a group of 36 individuals with PPA and 13 control participants. Both patients with lvPPA and those with nfvPPA performed significantly worse than svPPA and controls on spoken phonological tasks such as phoneme blending, phoneme deletion, and phoneme replacement, with lvPPA patients showing a greater lexicality effect (i.e., poorer performance on **nonwords** than real words) on two of the three tasks and significantly poorer performance on nonword spelling than all groups, suggesting impairment of phonological processing and phonology-orthography transcoding.

Reports of the written language profiles of individuals with lvPPA are variable, with phonological **alexia/agraphia** (i.e., greater impairment of nonword reading/spelling compared to performance on real words) reported most commonly (Brambati, Ogar, Neuhaus, Miller & Gorno-Tempini, 2009; Faria et al., 2013; Henry, Beeson, Alexander, & Rapcsak, 2012; Henry et al., 2015), consistent with an underlying phonological impairment. Surface agraphia (i.e., a regularity effect in spelling characterized by difficulty spelling irregular words versus regular words) has also been reported in some patients with lvPPA (Faria et al., 2013; Sepelyak et al., 2011). This surface profile is a bit surprising in logopenic PPA because it suggests an overreliance on a phonological strategy for spelling, but it may reflect impaired access to lexical orthography at a time when phonological skills are still relatively preserved. Occasional reports of word length effects have also been reported, suggesting impairment of the graphemic buffer in some individuals (for review of spelling profiles in PPA, see Graham, 2014).

There is little information published regarding text-level reading and writing abilities of individuals with logopenic PPA, and this topic warrants more attention as written language may be an area of early decline (Rapp & Glucroft, 2009). A sample of sentence-level writing can be obtained using the same picture stimuli used to elicit spoken picture descriptions. In our experience, the language impairment is clearly apparent in written narratives. Writing provides self-moderated timing, so the final product does not show the pauses and delays that are evident in spoken language, but errors in word selection are common and sentence construction may contain some of the same paragrammatic constructions observed in spoken language. By way of example, the following was written about the picnic scene

from the WAB (with the target word, "pouring," added in brackets):

> Two of the people are sitting in beside a tree. A guy is reading and the woman is potting [pouring?] to bringing into a grass place. It looks that the two will be eating in the big place near the tree.

As in spoken production, the sentences are of typical length, but the meaning is hard to extract and there is an excess of misplaced functors. The errors and misuse of grammatical words and morphological markers may be a reflection of weakened phonological support. There is evidence that self-generated writing at the sentence level is sensitive to residual phonological impairment in those with focal brain damage to left perisylvian regions (Beeson, Rising, DeMarco, Howard, & Rapcsak, 2016), suggesting that a closer examination of narrative writing in lvPPA is warranted in clinical and research contexts.

As the disease progresses, the language impairment of lvPPA is associated with nonlinguistic cognitive decline, including deficits in visuospatial skills, memory, attention, and executive function (Butts et al., 2015; Eikelboom et al., 2018; Leyton, Hsieh, Mioshi, & Hodges, 2013). These problems are associated with the underlying AD pathology, which may correspond to more aggressive progression of the disease and ultimately more widespread cognitive-linguistic impairment compared to other variants of PPA (Leyton et al., 2013; Teichmann et al., 2013). Difficulty with calculation has been reported by individuals with lvPPA, and observed on calculation tests (Gorno-Tempini et al., 2004; Rohrer et al., 2010). **Limb apraxia** may also be associated with lvPPA (Gorno-Tempini et al., 2004). The deficits related to calculation and limb apraxia are consistent with a long history of neuropsychological research regarding the consequences of left parietal pathology as well as more recent neuroimaging studies of left parietal lobe function (Buxbaum & Randerath, 2018; Cohen, Dehaene, Chochon, Lehericy, & Naccache, 2000; Dehaene, Piazza, Pinel, & Cohen, 2003; Gerstmann, 1940).

Differential Diagnosis of Logopenic Variant PPA

The logopenic variant of PPA shares some behavioral characteristics with both the nonfluent and semantic variants of PPA and also with amnestic AD, thus posing a clinical challenge in differential diagnosis. The diagnostic decision can be particularly challenging in the early stages of the disease when language impairments are relatively mild, but also in later stages of disease progression as concomitant cognitive impairments become more pronounced (Harciarek et al., 2014). Given that PPA diagnosis requires a cluster of behaviors, differential diagnosis requires information from several behavioral measures to suggest the likelihood of lvPPA over other progressive syndromes.

Logopenic Versus Nonfluent/ Agrammatic Variant PPA

Early PPA classification schemes often included lvPPA patients in the "nonfluent" category due to frequent pausing and hesitations in speech that may give the impression of nonfluency. It continues to be difficult to differentiate these variants, particularly in relatively early clinical presentations when those with nfvPPA may not present with the overt agrammatism that contrasts with the paragrammatic speech of lvPPA patients. An early differentiating feature between the two variants may be anomia, which presents earlier and tends to be more severe in patients with lvPPA. Naming errors in both variants may be phonologically based (**phonemic**