Assessment of Individuals with Primary Progressive Aphasia

Maya L. Henry, Ph.D., CCC-SLP[1] and Stephanie M. Grasso, M.A., CCC-SLP[1]

ABSTRACT

Speech–language pathologists play a crucial role in the assessment and treatment of individuals with primary progressive aphasia (PPA). The speech–language evaluation is a critical aspect of the diagnostic and rehabilitative process, informing differential diagnosis as well as intervention planning and monitoring of cognitive-linguistic status over time. The evaluation should include a thorough case history and interview and a detailed assessment of speech–language and cognitive functions, with tasks designed to detect core and associated deficits outlined in current diagnostic criteria. In this paper, we review assessments that can be utilized to examine communication and cognition in PPA, including general aphasia batteries designed for stroke and/or progressive aphasia as well as tests of specific cognitive-linguistic functions, including naming, object/person knowledge, single-word and sentence comprehension, repetition, spontaneous speech/language production, motor speech, written language, and nonlinguistic cognitive domains. The comprehensive evaluation can inform diagnostic decision making and facilitate planning of interventions that are tailored to the patient's current status and likely progression of deficits. As such, the speech–language evaluation allows the medical team to provide individuals with PPA and their families with appropriate recommendations for the present and the future.

KEYWORDS: primary progressive aphasia, assessment, diagnosis, dementia

Learning Outcomes: As a result of this activity, the reader will be able to (1) describe the purposes of speech–language assessment for individuals with PPA; (2) summarize how a comprehensive assessment battery (including speech, language, and cognition) can inform diagnostic decision making in PPA; (3) select appropriate speech–language and cognitive assessments that can be used to inform diagnosis and treatment for individuals with PPA.

[1]Department of Communication Sciences and Disorders, University of Texas, Austin, Texas.

Address for correspondence: Maya L. Henry, Ph.D., CCC-SLP, Department of Communication Sciences and Disorders, The University of Texas at Austin, 2504A Whitis Avenue (A1100), Austin, TX 78712-0114 (e-mail: maya.henry@austin.utexas.edu).

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Primary progressive aphasia (PPA) is a disorder marked by a gradual loss of communicative function caused by neurodegenerative disease affecting speech and language networks in the brain.[1,2] There are three widely recognized clinical variants of PPA, each with a unique signature of communication deficits and underlying neural changes: the semantic, nonfluent/agrammatic, and logopenic variants. The last two decades have brought a great deal of progress in clarifying these clinical phenotypes and their neuropathologic underpinnings and, increasingly, patients are referred to speech-language pathologists (SLPs) for assessment and treatment. This paper will focus on approaches to assessment in PPA, the purposes of which are threefold: (1) to establish the PPA diagnosis and clinical variant, when possible; (2) to determine appropriate interventions for patients and their families; and (3) to track progression of deficits over time.

PRIMARY PROGRESSIVE APHASIA DIAGNOSIS

Current consensus criteria for PPA diagnosis recommend a two-tiered diagnostic process.[1] First, a PPA diagnosis should be established based on the following general criteria:[1,2] the most prominent clinical feature (at onset and for initial stages of disease) should be communication difficulty and this should be the primary contributor to impaired activities of daily living; symptoms should not be attributable to other neurological, psychiatric, or medical disorders; and prominent nonlanguage cognitive or behavioral impairments should not be present initially.

The second stage of diagnosis involves confirming PPA subtype (semantic variant, nonfluent/agrammatic variant, or logopenic variant[1,3]). It is important to note that not all individuals with PPA can be classified into one of the established clinical variants.[4–8] However, when possible, determination of clinical variant is an important step, as it may help inform the diagnostic picture as well as the nature and likely progression of speech–language deficits. Speech–language phenotype, in conjunction with in vivo biomarkers (e.g., neuroimaging, genetic, and biofluid studies[9]) may assist in predicting disease etiology. Although there is only a probabilistic association between PPA phenotype and underlying pathology, the semantic and nonfluent/agrammatic variants are most commonly associated with the frontotemporal degeneration spectrum of pathologies (most often TDP-43 and tauopathy, respectively) and the logopenic variant is associated with Alzheimer's pathology in most cases.[10] With the emergence of clinical trials targeting specific pathological processes, the SLP may play a contributing role in discerning the likelihood of a given underlying disease based on clinical phenotype. Even more importantly from a rehabilitation standpoint, determination of clinical variant can help elucidate the linguistic nature of deficits (semantic, phonological, or grammatical) and strengths, which may guide treatment planning. Lastly, while there is considerable variability in the rate and nature of progression from patient to patient, diagnosis by variant may aid the clinical team in predicting the most likely progression of cognitive, linguistic, and motoric features.[11–13] As such, establishing PPA subtype may inform the medical and rehabilitative plan of care and help patients and families to prepare for the future.

Current consensus criteria enumerate core and associated speech–language features that must be present for diagnosis by variant.[1] For a diagnosis of semantic variant, both anomia and single-word comprehension impairment must be present, as well as three of the following: impaired object knowledge, surface dyslexia/dysgraphia, spared repetition, and spared grammar/motor speech. For a diagnosis of nonfluent/agrammatic PPA, at least one of the core features of agrammatism or apraxia of speech must be present, and two of the following associated features must also be present: impaired sentence comprehension, spared single-word comprehension, and spared object knowledge. For a diagnosis of logopenic variant, both core features of word-finding difficulty and impaired repetition must be present as well as three of the following: phonological errors in speech, spared single-word comprehension/object knowledge, spared motor speech, and an absence of agrammatism.

THE EVALUATION PROCESS

Case History and Interview

As with any standard diagnostic battery performed by a SLP, it is critical that a thorough case history be obtained from the individual with possible PPA. It is important to gain information regarding the initial presentation, the emergence of any additional symptoms with time, and the degree of linguistic versus cognitive or motoric impairment at the time of assessment. During the interview, clinicians should take note of speech–language features (e.g., word finding difficulties, agrammatism, phonological errors); nonlinguistic cognitive deficits that may emerge with time (e.g., episodic memory impairment); atypical behavioral symptoms that may arise, particularly with semantic variant PPA (e.g., disinhibition, apathy, loss of empathy); or motoric symptomatology (e.g., limb apraxia, parkinsonism, dysphagia) that may develop, most commonly in nonfluent/agrammatic PPA. Any family history of dementia or other relevant medical diagnoses (especially neurodegenerative conditions) should be ascertained, if not already noted in the medical record. Impairments of hearing and/or vision should be documented, as well as the individual's status as a monolingual, bilingual, or multilingual speaker. Impaired hearing or vision may need to be addressed before a valid assessment can be performed, and assessment materials should be linguistically appropriate to the speaker. To inform treatment planning, the clinician should inquire about current functional communication needs and limitations. For example, it is important to ascertain the variety of communication settings (work, home, community settings), partners (family, friends, coworkers), and modes (telephone, face-to-face, written) that are most relevant in the patient's daily life. It is helpful to involve the individual's primary communication partner(s), if possible, to ensure an accurate and complete case history.

Global Assessment of Linguistic Function

In addition to a clinical interview, a thorough speech–language evaluation should be conducted, which allows for characterization of impaired versus preserved speech–language abilities. This evaluation also serves to establish a quantitative index of aphasia severity that can be used as a baseline measure from which to track the progression of symptoms and document potential treatment gains. Standard aphasia batteries developed for use with stroke-induced aphasia are commonly used in PPA research centers as well as typical clinical practice. The Western Aphasia Battery (WAB)—Revised[14] and Boston Diagnostic Aphasia Examination (BDAE)[15] may be used to characterize an individual's overall language profile and to provide a general measure of aphasia severity. Additionally, the WAB has been shown to be a useful tool for distinguishing among PPA subtypes.[16,17] However, it is likely that aphasia batteries developed for stroke may not be adequately sensitive to detect the subtle deficits that are observed in early stages of PPA. Furthermore, using stroke-induced aphasia classification nomenclature (such as Broca's or Wernicke's) is not appropriate when characterizing PPA.

Assessments Designed for Differential Diagnosis and Tracking Severity in PPA

A recent systematic review identified nine neuropsychological assessments that were developed or adapted specifically for diagnosis or characterization of PPA.[18] Several of these can be used successfully to differentiate between clinical variants,[19–22] and two were designed specifically to gauge severity and progression in PPA.[19,23] The Sydney Language Battery (SydBat) is a brief battery of tasks (picture naming, word comprehension, semantic association, and repetition) designed to differentiate among PPA subtypes.[22] The Repeat and Point Test is a brief measure developed to differentiate between semantic and nonfluent variants by requiring patients to repeat 10 multisyllabic words and point to the target among semantic and phonological distractors.[21] Discriminant function analysis revealed that SydBat was able to distinguish among PPA variants with 80% accuracy, whereas the Repeat and Point Test distinguished semantic from nonfluent variant cases with 100% accuracy.

The Progressive Aphasia Severity Scale (PASS)[23] is an instrument designed specifically to characterize symptoms and track progression in PPA. With this instrument, clinicians rate the severity of deficits in speech and language domains (articulation, fluency, syntax/grammar, word retrieval/expression, repetition, auditory comprehension for phrases/sentences, single-word comprehension, reading, writing, and functional communication) as well as pragmatic aspects of communication on a 3-point scale. The SLP completes the scale after a questionnaire is filled out by an informant and a structured interview is conducted with both patient and informant. The Progressive Aphasia Language Scale (PALS)[19] also involves clinician ratings of speech–language features (motor speech and grammatical features in spontaneous speech, naming, single-word repetition and comprehension, and sentence repetition and comprehension) but is based on signs observed during a prescribed set of speech–language tasks, rather than symptoms reported via an interview or questionnaire. An algorithm using four key features from this assessment (motor speech impairment, grammar, single-word comprehension, and sentence repetition) proved highly accurate (96% correct) at subtyping PPA participants by variant (relative to expert clinical diagnosis). Lastly, although not designed specifically for PPA, the Clinical Dementia Rating (CDR),[24] a dementia severity rating scale based on a semistructured interview as well as clinical judgment, now includes a language domain.[25] This confers additional sensitivity (relative to the original CDR) for detecting and tracking symptoms and functional impairments in language-prominent dementias such as PPA.

Assessment of Specific Cognitive-Linguistic Domains Using Tailored Tasks

In addition to general aphasia batteries and rating scales, specific tasks and assessments may be utilized to further inform differential diagnosis of PPA variant (see Table 1 for a summary of a subset of assessments/tasks). These assessments also provide crucial information regarding spared and impaired speech–language and cognitive processes that may be relevant when designing an intervention plan. A comprehensive battery of such assessments might include the following components: confrontation naming, tests of object/person knowledge, single-word and sentence comprehension measures, repetition tasks, spontaneous speech/language production tasks, motor speech assessment, written language measures, and assessments of nonlinguistic cognitive status. Several assessments have been developed or adapted to measure a specific linguistic or motoric domain in PPA, including assessments of lexical retrieval,[26] syntax,[20,27] nonverbal semantic processing,[28] and apraxia of speech.[29] Other assessments were developed for stroke aphasia; however, given the overlapping symptomatology across etiologies and these measures' inclusion of normative data for age-matched controls, they are valid instruments for detecting impairment in PPA as well. We outline relevant assessments from each of these categories below.

ASSESSMENT OF LEXICAL RETRIEVAL

Naming impairment is a ubiquitous feature in PPA and is a core feature of both semantic and logopenic variants. Confrontation naming may be assessed using a graded picture naming test such as the Boston Naming Test.[30] From this measure, the severity of the naming impairment can be determined and types of naming errors can be noted, which may assist in distinguishing among the variants of PPA. Individuals with the semantic variant are likely to be anomic on all but the highest frequency items, and are likely to produce superordinate or coordinate semantic errors or to omit words.[31,32] These individuals are unlikely to be aided by phonemic cues and may also do poorly when given multiple-choice options.[33] When matched for overall severity of aphasia, individuals with the logopenic variant are likely to have naming impairment that is less severe than that of individuals with semantic variant PPA, but more severe than those with the nonfluent/agrammatic variant.[3] Additionally, logopenic individuals are more likely to produce phonemic paraphasias than those with semantic variant. In the nonfluent/agrammatic variant, naming errors may be phonetic (indicating motor speech impairment) or phonemic in nature.[34] Individuals with the logopenic and

Table 1 Impaired domains and predicted performance on speech–language assessments by PPA variant

Impaired domains by PPA variant	Speech–language assessments/tasks and predicted performance
Semantic variant: Impaired confrontation naming; impaired knowledge of people and objects; surface dyslexia/dysgraphia	BNT[29] = Impaired performance with the presence of semantic errors PPT[39] = Impaired performance PPVT[41] or other single-word comprehension task = Impaired performance NAT[26] = Spared performance Repetition task (e.g., WAB subtest[13]) = Spared performance Motor speech tasks[50,51] = Spared performance Connected speech task = Anomic during connected speech, with empty language (e.g., use of the words *thing* and *stuff*); may show semantic errors (e.g., *cat* for *dog*) Reading/Writing tasks[55] = Surface dyslexia/dysgraphia (impairment on irregular word reading and spelling, especially for low-frequency words); may show phonologically plausible errors (e.g., spell *tomb* as *toom*)
Nonfluent/agrammatic variant: Impaired grammar and/or motor speech (i.e., apraxia of speech); agrammatism in writing	BNT[29] = May show mild impairment with the presence of articulatory or phonological errors PPT[39] = Spared performance PPVT[41] or other single-word comprehension task = Spared performance NAT[26] = Impaired performance if agrammatic Repetition task (e.g., WAB subtest[13]) = Impaired; may show grammatical errors (e.g., omitting obligatory functors) or motor speech errors (e.g., sound distortions) Motor speech tasks[50,51] = Impaired performance with features of apraxia of speech and possible concomitant dysarthria Connected speech task = Simplified grammatical structures, agrammatism, and may present with slow, effortful speech production (consistent with AOS) Reading/Writing tasks[55] = May show worse performance on pseudowords. May show agrammatism when reading and writing at the text level (e.g., written picture description, passage reading)
Logopenic variant: Impaired confrontation naming; impaired repetition (particularly for sentences of increasing length); phonological dyslexia/dysgraphia	BNT[29] = Impaired, often with phonological paraphasias PPT[39] = Spared performance PPVT[41] or other single-word comprehension task = Spared performance NAT[26] = Spared performance Repetition task (e.g., WAB subtest[13]) = Impaired, especially with phrases and sentences of increasing length Motor speech tasks[50,51] = Spared performance Connected speech task = May present with phonological paraphasias; pauses during instances of word retrieval difficulty Reading/Writing tasks[55] = Phonological dyslexia/dysgraphia (impairment most prominent on pseudowords); may show lexicalization errors (word substituted for pseudoword)

Abbreviations: BNT, Boston Naming Test; NAT, Northwestern Anagram Test; PPT, Pyramids and Palm Trees; PPVT, Peabody Picture Vocabulary Test; WAB, Western Aphasia Battery.

nonfluent/agrammatic variants of PPA typically demonstrate spared semantic knowledge for items they cannot name (i.e., the ability to circumlocute) and may be aided by phonological cues and multiple-choice options. The Northwestern Naming Battery assesses both noun and verb production as well as comprehension and has proven sensitive to different patterns of deficits in agrammatic PPA (impaired verb naming and spared comprehension) versus semantic variant PPA (impaired noun naming and comprehension).[26]

ASSESSMENT OF OBJECT/PERSON KNOWLEDGE AND SINGLE-WORD COMPREHENSION

Impaired object/person knowledge is often a feature of semantic variant of PPA.[35–38] To assess object knowledge, nonverbal semantic processing assessments such as picture association tests and picture–sound or object–function matching tests can be used. A short version of the Pyramids and Palm Trees Test,[39] a picture association test, has proven sensitive to object knowledge deficits in semantic variant PPA as compared with the other clinical variants. To test knowledge of people, individuals may be asked to identify photographs of famous individuals and celebrities.[35,40] Single-word comprehension is usually tested via spoken or written word-picture matching tasks (e.g., Peabody Picture Vocabulary Test[41]). These measures are especially sensitive for identifying individuals with semantic variant PPA, for whom single-word comprehension deficits are a core feature. By contrast, single-word comprehension is largely spared in nonfluent/agrammatic and logopenic variants of PPA.

ASSESSMENT OF SYNTAX

Standardized aphasia tests such as the WAB, BDAE, and Northwestern Assessment of Verbs and Sentences (NAVS)[42] contain sentence comprehension tasks and can be useful in identifying impairments of receptive syntax. Impaired comprehension of syntactically complex sentences (e.g., subject-relative or object-relative clauses) is typical in individuals with nonfluent/agrammatic PPA.[43] However, individuals with logopenic PPA may show impairment on items that contain sentences of greater length, or that have lower probability,[44] due to deficits in phonological working memory. The Make A Sentence Test (MAST) and the SEntence Comprehension Test (SECT) were designed to test syntax production and comprehension, respectively, and have proven to correlate with grammatical difficulties in spontaneous speech of individuals with PPA.[20] For patients with very limited output or concomitant motor speech impairment, the Northwestern Anagram Test (NAT), which does not require spoken production, may be used to assess expressive grammar.[27] This assessment requires individuals to arrange anagrams in the correct order to generate sentences of varying syntactic difficulty that correspond to pictures presented by the clinician. Notably, this assessment, in conjunction with a test of lexical semantics (Peabody Picture Vocabulary Test), has proven effective in distinguishing among PPA variants.[6,45]

ASSESSMENT OF REPETITION

To assess repetition, subtests or tasks from comprehensive aphasia batteries may prove useful (e.g., WAB, BDAE). Difficulty with repetition due to dysarthria, apraxia of speech, and/or agrammatism is characteristic of the nonfluent/agrammatic variant of PPA.[46] By contrast, logopenic individuals have difficulty repeating words and sentences due to deficits in phonological short-term memory.[44,47,48] As such, they are likely to perform more poorly on longer, lower probability items and those without semantic content, such as nonwords or anomalous sentences (e.g., "Hairpins leap fluttering riddle games"[49]).

EVALUATION OF MOTOR SPEECH AND FLUENCY

In addition to repetition tasks, a motor speech evaluation, such as the hierarchy of tasks outlined by Wertz and colleagues[50] or Duffy,[51] provides information to assist in distinguishing between the nonfluent/agrammatic and logopenic variants of PPA, each of which presents with reduced fluency of output, but for different underlying reasons (motoric/grammatical vs. phonological). These batteries include tasks

such as diadochokinetic measures (rapid repetition of alternating speech sounds such as "puh-tuh-kuh") and repetition of utterances of increasing articulatory complexity (from single sounds to long sentences), as well as multiple repetitions of words containing difficult articulatory sequences, such as *impossibility* or *artillery*. This type of assessment can reveal characteristics of mild dysarthria or AOS, which may not be salient in conversational speech. The presence and severity of features of AOS may be quantified using the Apraxia of Speech Rating Scale (ASRS), which has been implemented in patients with neurodegenerative disease.[29] Characteristic features of nonfluent/agrammatic PPA include a slow rate of articulation, effortful or errorful speech production, and, in some cases, alterations in voice quality or prosodic features.[46]

"Fluency" is a multidimensional construct that encapsulates several speech and language features which may be variably disrupted in the clinical subtypes of PPA. To assess speech–language fluency, a picture description task (such as the "Cookie Theft" picture from the BDAE or the "Picnic Scene" from the WAB) can be used to obtain a connected speech sample. From this measure, speech rate, utterance length, grammatical competence, lexical retrieval ability, and motor speech features can be assessed. Speech and language measures derived from a picture description task have been shown to aid in distinguishing among the PPA variants.[52] Participants with semantic variant PPA will show preservation of prosodic and motoric features of speech as well as grammar, but will demonstrate marked word retrieval difficulty, particularly for nouns, resulting in "empty" but fluent language. Nonfluent patients will show simplified grammar or agrammatic constructions with a relative paucity of verbs relative to nouns. Speech fluency may also be disrupted by slowed rate and effortful, distorted production resulting from motor speech impairment (AOS and, in some cases, dysarthria). By contrast, individuals with the logopenic variant will show frequent pauses for word finding, phonological paraphasias, and may demonstrate use of paragrammatic constructions related to abandoned or rephrased utterances in the context of word retrieval failure.

ASSESSMENT OF WRITTEN LANGUAGE

Writing and reading of single words and text should be incorporated into the PPA evaluation, as characteristic deficits may help differentially diagnose its variants[1,53,54] and may indicate whether written language can be utilized as an alternate communication modality. Stimuli for assessment of single-word reading and spelling should vary by frequency (high vs. low), regularity (regular words, such as *stop* and irregular words, such as *tomb*), and lexical status (words vs. pseudowords). The Arizona Battery of Reading and Spelling[55] is a publicly available resource (http://aphasia.arizona.edu/Aphasia_Research_Project/Assessment_Materials.html) that systematically manipulates these features. Other word lists that control for these parameters are available in the Psycholinguistic Assessment of Language Processing in Aphasia (PALPA).[56] Individuals with the semantic variant of PPA present with surface dyslexia/dysgraphia, or difficulty reading/spelling irregular words, particularly those that are low in frequency.[35,57–59] Attempts to read or spell irregular words may result in phonologically plausible errors (e.g., *choir* spelled as *qwire*). Acquiring a written language sample in response to a picture scene can reveal agrammatism that is not evident in spoken discourse for individuals with nonfluent/agrammatic PPA. Individuals with the logopenic variant of PPA show pronounced deficits in reading and spelling nonwords, which require sound-letter conversion and are particularly taxing for the phonological system.[53] Individuals with logopenic PPA may default to real words when attempting to read or spell nonwords, resulting in lexicalization errors, a characteristic feature of phonological dyslexia/dysgraphia (e.g., *dringe* read as *drink*).

ASSESSMENT OF NONLINGUISTIC COGNITIVE ABILITY

Assessment of cognitive status is important to establish baseline cognitive performance, to rule out other possible diagnoses (e.g., Alzheimer's dementia), or to detect the emergence of concomitant cognitive deficits with disease progression. Impairment of nonlinguistic cognitive domains should be less prominent than that of language function. However, subtle executive

function deficits and other cognitive impairments may be present.[60] Standard cognitive screening tools such as the Mini-Mental State Exam[61] or the Montreal-Cognitive Assessment[62] should be used with caution. These measures are largely language based and, as such, may overestimate cognitive impairment in PPA.[63] Several neuropsychological assessment tools have been developed specifically for individuals with frontotemporal dementia spectrum disorders and are freely available to the public, including the frontotemporal lobar degeneration module[64] from the National Alzheimer's Coordinating Center (NACC; https://www.alz.washington.edu/WEB/forms_ftld.html) and a tablet-based assessment (TabCat; https://memory.ucsf.edu/tabcat), developed at the University of California San Francisco, that includes tests of executive function, memory, visuospatial skills, and socioemotional functions. Even a relatively brief neuropsychological battery can be informative for differential diagnosis, which may obviate the need for lengthy batteries that may be difficult or impossible for patients with dementia to complete.[65]

CONCLUSION

In this study, we have discussed assessments that may be used when evaluating the speech–language and cognitive characteristics of individuals with PPA. Initially, it is important that the medical team (including the SLP) establishes that the individual meets criteria for a diagnosis of PPA. Subsequently, subtyping by clinical variant will allow for interventions to be developed and administered with greater precision. As clinical drug trials become more widely available for specific underlying pathologies, accurate subtyping of PPA variant may aid in determining appropriate candidates for these studies. Furthermore, the behavioral profile associated with each variant can guide clinicians to tailor interventions to the individual's current profile, while anticipating and addressing the inevitable changes that are expected to emerge.

The three variants of PPA present with unique linguistic and cognitive features that may be discerned via a detailed case history and formal evaluation. The current consensus criteria should be consulted when selecting assessments to ensure that the test battery targets the established core and associated impairments characteristic of each clinical subtype. Many of the assessments reviewed in this study were initially developed to characterize speech–language changes secondary to stroke (e.g., WAB), or to capture changes in cognitive status in dementia more broadly (e.g., MMSE). Nevertheless, some assessments have been developed in the past decade to aid specifically with subtyping PPA variant (e.g., SydBat), to evaluate deficits characteristic of each clinical variant (e.g., NAT), and to track symptom progression in PPA (e.g., PASS). Collectively, this compendium of assessments enables the SLP to characterize the cognitive-linguistic features of PPA, supporting diagnostic decision making, informing treatment planning, and helping to monitor and predict changes in communication status over time.

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