Clinical Phenotypes of Primary Progressive Apraxia of Speech

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Three General Components of Speaking

1. Cognitive linguistic processing
   - Aphasia

2. Sensorimotor planning/programming
   - Apraxia of speech

3. Neuromuscular execution
   - Dysarthria

Three General Components of Speaking: What if something goes wrong?

1. Cognitive linguistic processing
   - Dementia
   - Progressive aphasia

2. Sensorimotor planning/programming
   - Progressive apraxia of speech

3. Neuromuscular execution
   - Dysarthria
Primary Progressive Aphasia (PPA)

- A rare degenerative, neurological syndrome.
- Insidious onset.
- Language capabilities become slowly and progressively impaired, while other mental functions remain preserved.
- Three variants
  - Semantic dementia
  - Logopenic
  - Non-fluent variant

Gorno-Tempini et al. Diagnosis Criteria (2011)

- Pattern of deficits
  - not accounted for by other nondegenerative nervous system, medical, or disorder.
- Absence of episodic memory, visual memory, and visuo-perceptual impairments at onset.
- Absence of behavioral disturbance at onset.

Semantic variant of PPA

- Anomia with loss of single word meaning.
- Difficulty generating/recognizing familiar words.
  - This happens for rare words first and common nouns for later stages.
  - Verbs and abstract words are often spared.
- Fluent spontaneous speech is retained.
- Some patients have problems recognizing familiar objects and faces.
  - The presence of this sign can help confirm the diagnosis.
Logopenic variant of PPA

- A slow rate of speech, secondary to word retrieval difficulties.
- Phonologic errors may be present.
- Sentence and phrase repetition is impaired.
  - Repetition of single words is spared.
- Reading and writing abilities may be preserved longer than speech.
- Trouble understanding long or complex verbal information.

Agrammatic/ non-fluent variant of PPA

- **Speech is effortful and reduced in quantity.**
- Sentences become shorter and **word-finding hesitations** become more frequent.
- Pronouns, conjunctions and articles are lost.
- Word order may be abnormal, especially in writing or e-mails (agrammatic).
- Reversals (e.g., “he” for “she”; “yes” for “no”).
- Reduced comprehension for long and grammatically complex sentences.

PPA implies a disorder of language impairment.
Aphasia may not even be present!

Primary Progressive Apraxia of Speech
Hallmark Speech Characteristics: Articulation

- INCONSISTENT articulation errors
  - place errors
  - manner errors
  - consonants and vowels may be increased in duration
  - consonant clusters pose more difficulty v. consonants (phonetic complexity)
  - more errors with lengthier words
  - more errors observed with infrequent words
  - more errors observed for nonsense syllables/words
  - more errors for purposeful utterances (v. automatic)
  - Speaker is often aware of errors

Hallmark Speech Characteristics: Prosody

- Prosodic Errors
  - Rate is usually slow for multi-syllabic utterances
  - Inappropriate inter-syllabic pauses
    - Pauses between syllables or words or before initiation of utterances
  - Abnormal
    - Equal stress across syllables and words
    - Stress on the unintended syllable and word
    - Intonation
    - Less variation and loudness contour

Table 2. Inventory of articulation characteristics of apraxia from the apraxia Battery for Adults – 2 (Dabul, 2000) [*only normed and standardized test]

Speech Behavior
1. Exhibits phonemic anticipatory errors (glean glass for green glass)
2. Exhibits phonemic perseverative errors (pep for pet)
3. Exhibits phonemic transposition errors (Artica for Africa)
4. Exhibits phonemic voicing errors (ben for pen)
5. Exhibits phonemic vowel errors (moan for man)
6. Exhibits visible/audible searching
7. Exhibits numerous off-target attempts at the word
8. Errors are highly inconsistent [*not quite true, particularly for severe speakers]
9. Errors increase as phonemic sequence increases [*complexity principle]
10. Exhibits fewer errors with automatic speech than volitional speech
11. Exhibits marked difficulty initiating speech
12. Intrudes schwa sound / between syllables or in consonant clusters
13. Exhibits abnormal prosodic features
14. Exhibits awareness of errors and inability to correct them
15. Exhibits expressive-receptive gap
Patient Perceptions and Complaints

- "Pure" AOS:
  - "my speech won’t come out right"
  - "know what I want to say but doesn’t come out right"
  - not as fluent as before
  - mispronounce words
- with mild or moderate AOS, patients report being surprised by errors that “sneak into” narratives
- complaints usually center around articulation problems
- some patients report having to speak slowly or more carefully to prevent errors
- predict errors on multi-syllabic or difficult to pronounce words
- recognize errors and attempt to correct them
- problems may be more obvious when stressed or fatigued
Diagnostic Criteria

- AOS
  - slow rate
  - distorted sound substitutions
  - articulatory groping
- No evidence of aphasia
- Normal neurological examination
- Normal neuropsychological testing

AOS Types

- Phonetic-PAOS
- Prosodic-PAOS
- M-PAOS = No clear predominance of either

Types suggest the PREDOMINANT feature. It does not suggest the singular feature.

Phonetic PAOS

- Formerly known as “type 1”
- Predominated by distorted sound substitutions or additions
  - Increased in prominence with increased utterance length or syllable or word complexity

PAOS is used here, but these types are seen in progressive AOS with and without aphasia (PPAOS).
Prosodic PAOS

- Formerly known as “type 2”
- Predominated by:
  - syllable segmentation within multisyllabic words or across words in phrases
  - lengthened intersegment durations between syllables, words or phrases
  - “I have to pause to continue.”

How can we distinguish between the types?

- Acoustics
  - Rate
  - Articulatory error score (more on this later)
- AMRs
- SMRs

- Demographic information?
- Imaging?

Acoustics: Rate

- Rate (syll/ sec) for catastrophe for Phonetic and Prosodic PPAOS patients against AES.

AMRs and SMRs
AMR: Summary

- **Mean**: Statistically significant difference between Phonetic and Prosodic PPAOS patients.
  - Phonetic PPAOS patients, on average, are faster than Prosodic PPAOS patients.
- **SD**: no statistically significant difference between Phonetic and Prosodic patients.
Acoustics: SD SMR Production

SMR: Summary
- **Mean**: No statistically significant difference between Phonetic and Prosodic PPAOS patients.
- **SD**: Statistically significant difference between Phonetic and Prosodic PPAOS patients.
  - Phonetic PPAOS patients showing more variability, on average, compared to Prosodic PPAOS patients.

Demographic & clinical differences

<table>
<thead>
<tr>
<th></th>
<th>Phonetic</th>
<th>Prosodic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>% female</td>
<td>50%</td>
<td>80%</td>
<td>0.16</td>
</tr>
<tr>
<td>Age at onset, years</td>
<td>59 ± 9</td>
<td>73 ± 8</td>
<td>0.001</td>
</tr>
<tr>
<td>Western Aphasia Battery Aphas quotient</td>
<td>87 ± 12</td>
<td>95 ± 5</td>
<td>0.07</td>
</tr>
<tr>
<td>Boston Naming Test</td>
<td>12 ± 2</td>
<td>14 ± 1</td>
<td>0.01</td>
</tr>
<tr>
<td>Apraxia of Speech Rating Scale</td>
<td>22 ± 9</td>
<td>17 ± 5</td>
<td>0.17</td>
</tr>
<tr>
<td>% dysarthria</td>
<td>10%</td>
<td>40%</td>
<td>0.12</td>
</tr>
<tr>
<td>Montreal Cognitive Assessment Battery</td>
<td>25 ± 3</td>
<td>27 ± 3</td>
<td>0.19</td>
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<tr>
<td>Unified Parkinson’s disease Rating Scale III</td>
<td>7 ± 4</td>
<td>15 ± 8</td>
<td>0.01</td>
</tr>
<tr>
<td>Neuropsychiatric Inventory-Q</td>
<td>3.3 ± 3.0</td>
<td>0.8 ± 1.3</td>
<td>0.03</td>
</tr>
</tbody>
</table>

PPAOS v. PPA
- **PPAOS** implies that there is pure motor speech disorder and that aphasia is absent.
- **PPA** implies that aphasia is present and that the aphasia dominates the syndrome.
  - Presence of linguistic abnormalities (syntax, semantics, phonology, prosody).
  - May also have apraxia of speech.
What if AOS is dominant?

- What if the presenting syndrome is characterized by AOS and agrammatic aphasia **but the AOS, not the aphasia**, is the most prominent features of the syndrome and cause for functional impairment in day to day life?
- Such patients do not meet criteria for PPA **AND** do not meet criteria for PPAOS

Assessment and differential diagnosis

Step 1: Is aphasia present?
Step 2: Is apraxia of speech present? If so, what dominates?
Step 3: Is dysarthria present?
Largely completed simultaneously!

First step

- Is aphasia present?
Variants of PPA: assessment tips

- Agrammatic variant
  - Loss of function words/ morphological markers
  - Assess spoken language AND writing
- Semantic variant
  - Surface dyslexia
  - Loss of word meaning
- Logopenic variant
  - Anomia without loss of single word meaning
  - Poor sentence repetition
  - Comprehension deficits
  - Phonological errors are present

Second Step

- Is apraxia of speech present?

Tasks for Assessing Motor Speech Programming Capabilities

- General conversational ability
- Imitation (sounds, words and sentences)
- Narrative picture description
- Automatic tasks (counting, days of the week, sentence completion)
- Singing a familiar song
- Reading aloud
- SMRs
- Writing sample
Tests to Assess and Characterize AOS

- Apraxia of Speech Rating Scale (ASRS)
- Articulatory Error Score (AES)

Apraxia of Speech Rating Scale (ASRS)

Articulatory Error Score (AES)

- “Repeat each of the following words three times each.”
  - Cat
  - Catnip
  - Catapult
  - Catastrophe
  - Harmonica
  - Specific
  - Snowman
  - Artillery
  - Statistics
  - Stethoscope
  - Aluminum
  - Rhinoceros
  - Volcano

- “Repeat these sentences one time.”
  - We saw several wild animals.
  - My physician wrote out a prescription.
  - The municipal judge sentenced the criminal.

Third step

- Is dysarthria present?
Differential diagnosis: Dysarthria

- Oral mechanism examination
- AMRs
- SMRs
- Groping?
- Distortions v. substitutions v. distorted substitutions

Other tips for diagnosis

- History is critical!
  - Insidious onset
  - Progression over time

Summary

- Is the disorder progressive?
  - Change over time

- Is aphasia present?
  - Agrammatism
  - Loss of word meaning
  - Phonologic errors
  - Reduced comprehension

- Is apraxia of speech present?
  - Articulatory errors (Phonetic phenotype)
  - Segmentation (Prosodic phenotype)

Thanks!
Questions?
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PRIMARY PROGRESSIVE APRAXIA OF SPEECH

By Rene Utianski, PhD; Joseph Duffy, PhD; and Keith Josephs, MD

Using speech to communicate requires a complex series of actions that begins with selecting appropriate words and organizing them into grammatical sentences. This internally formulated message is then executed as speech through “speech programming,” a crucial subconscious process that creates and conveys instructions for movements of about 100 muscles between the lungs and lips. For adult speakers, this results in the production of at least 14 distinct speech sounds per second.

When the brain and body systems are intact, this extraordinarily complex speech act occurs effortlessly. Unfortunately, spoken communication can break down in several ways. In aphasia, the ability to select and organize words may be compromised. In what is called dysarthria, language function is preserved, but the speech muscles themselves may be compromised by weakness, spasticity, incoordination, or involuntary movements. When the speech programming stage is affected, the problem is called apraxia of speech. These problems may or may not be isolated and, unfortunately, any one of them can have devastating consequences on the ability to communicate.

Speech problems like those described above are often associated with stroke or other traumatic brain injuries. However, they may also be a first and early sign of neurodegenerative disease, a possibility that is often underrecognized by the general public and nonspecialists in medicine. Recently, accumulating research has helped in understanding a neurodegenerative condition that manifests first, or primarily, as apraxia of speech.

On average, it takes between 2½ and three years between initial symptom onset and a diagnosis of primary progressive apraxia of speech (PPAOS). The delay in proper diagnosis can be attributed to a lack of awareness of this condition among both the general public, who, initially at least, may attribute its symptoms to stress or fatigue, and among health care providers, who often misdiagnose this difficulty as aphasia or dysarthria. There is evidence to suggest PPAOS is not as rare as it was once thought, potentially because of misdiagnoses as a functional/psychogenic problem, a variant of aphasia, or another neurodegenerative disease, such as Alzheimer’s disease or amyotrophic lateral sclerosis (ALS).

What Is PPAOS (and What Is It Not)?

When aphasia occurs in isolation or before other neurologic signs, it is called primary progressive aphasia (PPA). Several subtypes of PPA have been described, and their reliable identification has implications for localizing the disease in the brain, identifying the underlying pathology and, most importantly, caring for the patient. Given the current classification system of PPA subtypes, an individual might be classified as having nonfluent aphasia without any language difficulties if the “effortful, halting speech” is secondary to apraxia of speech rather than any language disruption.

Recent research has established that a subset of people who in the past have been classified as having PPA (nonfluent subtype) actually do not have aphasia at all. They can read, write, comprehend speech, and find words and organize grammatical sentences, but instead are unable to program speech movements. This subset of people instead has PPAOS. Importantly, this diagnosis is appropriate only when apraxia of speech is the first, the only, or the most salient feature and there are no additional problems that would meet criteria for a more specific neurologic diagnosis.

Among even expert neurologists and speech-language pathologists, AOS can be difficult to distinguish from other speech and language disorders. This includes its distinction from aphasia. AOS is often overlooked or ignored in patients who receive an aphasia diagnosis, even though one diagnosis does not preclude the other, and they often co-occur. The diagnostic challenge is especially true when aphasia presents as nonfluent or hesitant speech as a result of word-finding deficits or difficulty with grammar. This is in contrast to the delays for speech production seen secondary to restarts and revisions associated with AOS. Furthermore, distorted sound substitutions, secondary to abnormal motor planning, are also often misconstrued as errors associated with aphasia.

AOS can be confused with dysarthria, which arises from a disruption of the neuromuscular control of speech rather than the inability to generate motor programs for speech movement. For instance, speech may present as segmentated and slowed in association with ataxic or spastic dysarthria due to cerebellar or upper motor neuron damage, respectively. However, there are many features suggestive of apraxia of speech that are not present when dysarthria is the accurate and sole diagnosis.

Some examples of other diagnostic labels that are roughly synonymous with PPAOS include slowly progressive anarthria
for dysarthria, progressive aphasia, phonetic disintegration, buccofacial apraxia, and anterior opercular syndrome.

Who Is Affected by PPAOS?

Both men and women are affected by PPAOS, with women being more frequently diagnosed. The average age of onset is in the late 60s to early 70s; however, the age range is broad, and onset can be as early as the late 40s or as late as the early 80s.

How Is PPAOS Identified?

Information gained from careful speech and language examination is the gold standard for the clinical diagnosis of PPAOS. Overall, hallmark characteristics include slow overall speech rate, an increase in distorted sound substitutions with increased utterance length or complexity, segmentation (i.e., brief gaps between syllables) within words and between words, and audible or visible articulatory grooving of the lips or tongue, suggesting several attempts to produce sounds or syllables, with variable success.

Research by the authors suggests that there may be subtypes of PPAOS. In what the authors call type 1, speech is dominated by difficulty with articulation (i.e., productions of speech sounds), with distorted sound substitutions, and stop and start attempts to correct errors, including audible or visible grooping. That pattern of difficulty tends to be more evident when aphasia is also present. In what the authors call type 2, there are predominant prosodic abnormalities, with slowed speaking rate and segmentation between syllable and words; however, there is relatively less difficulty with articulation, as in type 1. The type 2 pattern tends to be more evident in PPAOS. In the type 3 pattern, there is no clear predominance of the articulatory vs prosodic abnormalities; they are both nearly equally evident.

Assessment and characterization of speech patterns is critical in guiding diagnosis, but neuroimaging is also helpful for confirming the diagnosis. An example of key neuroimaging findings associated with PPAOS and PPA is presented in Figure 1 online.

Pathophysiology of PPAOS

Interestingly, autopsy data thus far suggest that PPAOS is consistently associated with the abnormal deposition in the brain of a protein called tau. Tau is also associated with Alzheimer’s disease, but the tau found in association with PPAOS, known as 4-repeat tau, is somewhat different from the form of tau found in Alzheimer’s disease (known as 3- and 4-repeat tau).

What Is the Prognosis and Treatment for PPAOS?

For most people with PPAOS, speech intelligibility for the ability to be understood declines over time. The rate of this decline varies from person to person. In somewhat less than one-half of affected individuals, progression to mutism may occur within four years, but the progression of speech decline can be considerably slower in others. In addition to changes in speech, our research and experience with affected patients reveal that other deficits typically emerge during disease progression.

In some patients, severe parkinsonism, vertical eye gaze problems, urinary incontinence, balance difficulty with falls, swallowing problems, or limb apraxia develop; these findings are similar to a neurodegenerative condition known as progressive supranuclear palsy. In another subset of patients, asymmetric rigidity of the extremities, alien limb, limb apraxia, and other parkinsonian features may emerge, similar to another neurodegenerative condition known as corticobasal syndrome. Although there is typically no evidence of memory loss, impulsivity, or other neuropsychological or neurobehavioral deficits early in the disease course, they may become evident over time.

Available Treatments for PPAOS

One of the most frustrating features of PPAOS is the patient’s normal insight into his or her deficits and difficulties. While there are currently no curative or stabilizing options for this neurodegenerative process, there are several options available to compensate for the loss of speech. When language and thought processes are preserved (i.e., there is no aphasia), handwriting and other electronic applications, some with synthesized speech, permit continued effective communication. In some cases, speech therapy may improve or help to maintain speech intelligibility for a period of time. Once the diagnosis is made, and sometimes before, it is recommended that patients seek treatment with a speech-language pathologist who can make recommendations regarding speech therapy and appropriate augmentative and alternative communication devices.

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— Keith Josephs, MD, is a consultant of neurology at Mayo Clinic in Rochester, Minnesota, and professor of neurology at the Mayo Clinic College of Medicine. He is the principal investigator of many National Institutes of Health-funded grants, including a grant to study primary progressive aphasia and primary progressive apraxia of speech.

For references and a figure, view this article on our website at www.TodaysGeriatricMedicine.com.