The ABCs of PPA for SLPs: Clinical Attributes, Biology and Care of Primary Progressive Aphasia

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http://www.brain.northwestern.edu/dementia/ppa/index.html

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PART 1: What is PPA? PPA is a clinical dementia syndrome caused by neurodegenerative disease.

PART 2: How is PPA diagnosed? What are the subtypes of PPA? What tests are used to identify the aphasia profile?

PART 3: What are the educational and treatment needs of patients with PPA and their caregivers? What role does the SLP play? What is the Northwestern PPA Program?
What IS Dementia?

A clinical syndrome:
- Insidious onset
- Progressive changes in cognition and/or behavior from prior customary skills and/or personality
- Interferes with ADL

WHAT CAUSES CLINICAL DEMENTIA?

ACUTE ONSET
- Metabolic
- Vascular
- Epileptic
- Paraneoplastic
- Toxic
- Infectious

GRADUAL ONSET, PROGRESSION
- Tumor
- Hydrocephalus
- Vascular

NEURODEGENERATIVE
- Non Alzheimer
- Alzheimer Disease
- Diffuse Lewy Body
- FTLD
- Tauopathies
- TDP-43proteinopathy
- Prion
- Other
- FUS
WHAT IS PPA?
APHASIC DEMENTIA
A clinical dementia syndrome in which language function slowly declines, due to progressive, neurodegenerative brain disease, eventually affecting additional cognitive, behavioral and functional domains.

What is neurodegenerative disease?
Molecular and cellular abnormalities that attack healthy brain cells and cause them to die.
Disease (type of neuropathology) can only be confirmed by brain autopsy after death.
Can neurodegenerative disease cause aphasia without any other cognitive deficits?
Stroke Model and Focal Cognitive Deficits

ACUTE EVENT
Neuronatomically Focal Determined by VASCULATURE

FOCAL COGNITIVE DEFICIT (e.g., Aphasia)

Can Neurodegenerative Brain Disease: Cause Focal Cognitive Deficits?

PRE 1980 – LACK OF KNOWLEDGE = LATE DETECTION
- Neuropsychologically Widespread Deficits
- Neuroanatomically Diffuse

POST 1980 – INCREASING INFORMATION = EARLY DETECTION
- Neuropsychologically Circumscribed Deficits
- Neuronatomically Focal determined by Large-Scale Network connectivity

Weintraub & Mesulam, 1993, 1996
CLINICAL SYMPTOMS OF DEMENTIA
Changes In Cognition, Behavior, Activities of Daily Living

RELATED TO REGION OF BRAIN DYSFUNCTION
I.E., NEUROANATOMICAL NETWORK
Left, Right, Frontal, Parietal, Temporal, Occipital

RELATED TO NEUROPATH by probabilities
TISSUE DIAGNOSES (%AD, %FTLD, %LBD, %Other)

3 LEVELS OF DEMENTIA CHARACTERIZATION

CLINICAL- THE SYMPTOMS
THE SYMPTOMS THE PATIENT EXPRESSES AND THE CAREGIVER OBSERVES AS CHANGES; WHAT THE CLINICIAN OBSERVES AND TESTS IN THE OFFICE

NEUROANATOMICAL – THE LOCATION OF BRAIN DYSFUNCTION
REGIONS THAT ARE ATROPHIED (MRI) AND/OR PHYSIOLOGICALLY DYSFUNCTIONAL (PET)

NEUROPATHOLOGICAL – THE DISEASE
THE CELLULAR AND MOLECULAR ABNORMALITIES THE NEUROPATHOLOGIST SEES UNDER THE MICROSCOPE
CLINICAL, NEUROANATOMICAL AND NEUROPATHOLOGICAL RELATIONSHIPS

DEMENTIA = What the clinician observes and diagnoses

NEUROANATOMY = BRAIN AREA OF dysfunction/atrophy

DISEASE = What the neuropathologist finds under the microscope

EARLY NEUROPSYCHOLOGICAL PROFILES
Amnesia, Aphasia
Visuospatial, Behavior/Personality/Executive

% AD Neuropathology

% FTLD Neuropathology

% Lewy Body Neuropathology

% OTHER Neuropathology

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EARLY NEUROPSYCHOLOGICAL PROFILE: AMNESIA
Dementia of the AD type

DEMENTIA = What the clinician observes and diagnoses

NEUROANATOMY = BRAIN AREA of dysfunction/atrophy

DISEASE = What the neuropathologist finds under the microscope

85% AD Neuropathology
5-10% FTLD Neuropathology
5-10% OTHER Cortical Lewy Body

EARLY NEUROPSYCHOLOGICAL PROFILE: Executive/comportmental
Beh variant frontotemporal dementia

DEMENTIA = What the clinician observes and diagnoses

NEUROANATOMY = BRAIN AREA of dysfunction/atrophy

DISEASE = What the neuropathologist finds under the microscope

80% FTLD Neuropathology
20% AD, OTHER
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How is PPA Diagnosed Clinically?

- **Neurological examination**: Rate of onset, other localizing symptoms; other illness. Etiology-stroke vs neurodegenerative vs tumor vs other? Are there motor or sensory deficits?

- **Neuroimaging (MRI, CT, PET)**: Rule out other diseases. Evidence of L-sided atrophy or hypometabolic activity?

- **Neuropsychological examination**: Evidence of language domain impairment in absence of other cognitive and behavioral deficits? No episodic memory loss; preserved ADL.

- **Speech/Language Pathology examination**: assess different language modalities: speech, repetition, comprehension, reading, writing; assess different language components: phonology, grammar, semantics; assess functional communication skills for different settings and needs and for planning treatment strategy.
ROOT DIAGNOSIS OF PRIMARY PROGRESSIVE APHASIA
Mesulam 2003; Gorno-Tempini et al, 2011

INCLUSIONARY CRITERIA

1. Language deficits emerge slowly and progress and are most prominent feature of the examination: word-finding pauses, paraphasias, agrammatism, comprehension, reading, etc.

2. Aphasia is the identifiable and principal cause of impairment in ADL, otherwise normal.

3. Aphasia is the sole (or most prominent) deficit at onset and for the initial stages of disease.

EXCLUSIONARY CRITERIA

1. Diseases other than neurodegeneration can account for the symptoms: stroke, tumor

2. Psychiatric diagnosis accounts for the symptoms

3. Predominant initial episodic memory (visual and verbal), visuospatial/perceptual, and/or executive function deficits occur early in the course

4. Prominent initial behavioral disturbances (e.g., marked disinhibition, emotional detachment, hyperorality, an/or repetitive, compulsive behaviors; personality change)

HOW IS PPA DIFFERENT FROM DEMENTIA OF THE AD TYPE AND BEHAVIORAL VARIANT FRONTOTEMPORAL DEMENTIA?

COMPARISON OF THREE CLINICAL DEMENTIA DIAGNOSES

<table>
<thead>
<tr>
<th>CLINICAL DEMENTIA DIAGNOSIS</th>
<th>Dementia of the Alzheimer Type</th>
<th>Behavioral Variant Frontotemporal Dementia</th>
<th>Primary Progressive Aphasia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MAJOR DOMAIN IMPAIRED</strong></td>
<td>Episodic Memory</td>
<td>Comportment</td>
<td>Language</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Forgetfulness, misplacing items, repetitiveness, disorientation</td>
<td>Personality change, lack of judgment and empathy, impulsivity, disinhibition</td>
<td>Word finding, anomia, speech errors, poor auditory comprehension</td>
</tr>
<tr>
<td>Gender</td>
<td>Females&gt;males</td>
<td>Females=Males</td>
<td>Females=Males</td>
</tr>
<tr>
<td>Typical Age at Onset</td>
<td>65+</td>
<td>&lt;65</td>
<td>&lt;65</td>
</tr>
<tr>
<td>Pathology (Disease)</td>
<td>80-90% AD 10% other</td>
<td>80% FTLD 20% other</td>
<td>60-70% FTLD 30-40% AD</td>
</tr>
<tr>
<td>BRAIN REGION</td>
<td>Medial Temporal Regions</td>
<td>Frontal Lobes</td>
<td>L PeriSylvian Region</td>
</tr>
</tbody>
</table>
Classification Of Primary Progressive Aphasia and Its Variants

Consensus guidelines for unifying classification of PPA and its three variants, Agrammatic (aka PPA-G), Semantic (aka PPA-S) and Logopenic (aka PPA-L)

1. Clearly delimits clinical diagnosis from sources of supporting evidence and etiology (i.e., imaging, neuropathology)
2. Detailed clinical descriptors
3. Supportive Neuroimaging (must fulfill clinical criteria AND have imaging evidence)
4. Supportive Neuropathology (must fulfill clinical criteria AND have post mortem autopsy verification)
5. Systematic data collection

Caveat: clinical instruments not specified; needs validation

### CLINICAL DIAGNOSTIC CRITERIA FOR SUBTYPES OF PPA

<table>
<thead>
<tr>
<th>PPA-G: NONFLUENT/AGRAMMATIC SUBTYPE</th>
<th>PPA-S: SEMANTIC SUBTYPE</th>
<th>PPA-L: LOGOPENIC SUBTYPE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>At least one of the following core features must be present:</strong></td>
<td><strong>Both of the following core features must be present:</strong></td>
<td><strong>Both of the following core features must be present:</strong></td>
</tr>
<tr>
<td>1. Agrammatism in language production</td>
<td>1. Impaired confrontation naming</td>
<td>1. Impaired single-word retrieval in spontaneous speech and naming</td>
</tr>
<tr>
<td>2. Effortful, halting speech with inconsistent speech sound errors and distortions (apraxia of speech)</td>
<td>2. Impaired single-word comprehension</td>
<td>2. Impaired repetition of sentences and phrases</td>
</tr>
<tr>
<td><strong>At least 2 of 3 of the following other features must be present:</strong></td>
<td><strong>At least 3 of the following other diagnostic features must be present:</strong></td>
<td><strong>At least 3 of the following other features must be present:</strong></td>
</tr>
<tr>
<td>1. Impaired comprehension of syntactically complex sentences</td>
<td>1. Impaired object knowledge, particularly for low frequency or low-familiarity items</td>
<td>1. Speech (phonologic) errors in spontaneous speech and naming</td>
</tr>
<tr>
<td>2. Spared single-word comprehension</td>
<td>2. Surface dyslexia or dysgraphia</td>
<td>2. Spared single-word comprehension and object knowledge</td>
</tr>
<tr>
<td></td>
<td>4. Spared speech production (grammar and motor Speech)</td>
<td>4. Absence of frank agrammatism</td>
</tr>
</tbody>
</table>
**NEUROPSYCHOLOGY OF PPA**

**ORDER OF SEVERITY OF IMPAIRMENTS BY DOMAIN**

**Verbal Skills**
- Delayed Recall*
- Cognitive Flexibility and Abstraction*
- Memory Acquisition*
- Attention/Concentration*

**Performance Skill (non verbal, largely)**
- mostly due to the fact that measures of these functions are verbal

Zakzanis, 1999: The Neuropsychological Signature of Primary Progressive Aphasia, Brain and Language
TEST STRATEGIES: How can you tell if someone with aphasia can remember things, or reason, or understand most non language test instructions?

CHALLENGES FOR TESTING NON LANGUAGE DOMAINS

Tests Contain Complex Verbal Instructions: Block Designs, WCST, Picture Completion

Tests Contain Verbal Stimuli: Word lists, stories, MMSE, Trail Making B

Tests Require Spoken Output: WAIS Similarities, Arithmetic, RAVLT, story recall, etc.

Try to select tests that eliminate complex language

THREE WORDS THREE SHAPES EPISODIC MEMORY TEST (3W3S)

Mesulam & Weintraub, 1985, 2000; Weintraub et al, 2000

<table>
<thead>
<tr>
<th>CONDITION</th>
<th>LEARNING/MEMORY COMPONENT TESTED</th>
</tr>
</thead>
<tbody>
<tr>
<td>COPY</td>
<td>Assures attention to stimuli, verifies writing and drawing ability impact on performance</td>
</tr>
<tr>
<td>INCIDENTAL RECALL</td>
<td>How much is remembered without forewarning, i.e., effortlessly?</td>
</tr>
<tr>
<td>ACQUISITION TRIALS</td>
<td>Re-expose stimuli on two learning trials (30 secs each) followed by immediate reproduction to assure encoding, reach a level of criterion</td>
</tr>
<tr>
<td>DELAYED RECALL</td>
<td>Retrieval/retention over time</td>
</tr>
<tr>
<td>MULTIPLE CHOICE</td>
<td>Recognition memory</td>
</tr>
</tbody>
</table>
Verbal and Nonverbal Memory in Primary Progressive Aphasia: The Three Words-Three Shapes Test

Weintraub et al, Beh Neurol, 2013

<table>
<thead>
<tr>
<th>Dementia of the AD Type (DAT) patient</th>
<th>Primary Progressive Aphasia (PPA) patient (form 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stimuli</strong></td>
<td>Amnesia in DAT interferes with effortless encoding of shapes and delayed recall of words and shapes and all recognition is abnormal</td>
</tr>
<tr>
<td><strong>Copy</strong></td>
<td>Aphasia in PPA interferes with effortless encoding and delayed retrieval of words but not shapes and all recognition is normal</td>
</tr>
<tr>
<td><strong>Effortless Encoding</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Effortful Encoding/Acquisition</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Delayed Recall</strong></td>
<td></td>
</tr>
</tbody>
</table>

Amnesia in DAT interferes with effortless encoding of shapes and delayed recall of words and shapes and all recognition is abnormal

Aphasia in PPA interferes with effortless encoding and delayed retrieval of words but not shapes and all recognition is normal

Visual-Verbal Test (Feldman & Drasgow, 1959)

1 2 3 4

SORT 1

1 2 3 4

SORT 2

1 2 3 4

SHIFT
APHASIA ASSESSMENT IN PPA
Western Aphasia Battery (WAB-R)

APHASIA QUOTIENT
Composite Score = Mild, Moderate, Severe
Object/Color/Letter/Number/ Shape Comprehension
Object/Color/Letter/Number/ Shape Naming
Complex Commands
Spontaneous Speech (Fluency, Content)
Reading, Writing
APHASIA ASSESSMENT IN PPA

Boston Diagnostic Aphasia Examination (BDAE)

Boston Naming Test (BNT)

Northwestern Naming Battery (NNB)

Northwestern Anagram Test (NAT)
  https://flintbox.com/public/project/19927/

Northwestern Assessment of Verbs and Sentences (NAVS)
  http://flintbox.com/public/project/9299/

Psycholinguistic Assessment of Aphasia (PALPA)

Multilingual Naming Test (MINT; Gollan et al, 2012, 2013)

LANGUAGE COMPONENTS

PHONOLOGY
  Sound Discrimination, Production

SEMANTICS
  Single Word Comprehension, Naming

GRAMMAR (SYNTAX, MORPHOLOGY)
  Production, Comprehension
1. Fluent Non Fluent Distinction Oversimplifies
   - PPA patients can be at least intermittently nonfluent even though they do not have impairments in producing syntactically correct sentences

2. Such a dissociation is key for distinguishing the agrammatic from the logopenic subtype of PPA

3. PPA with agrammatism predicts tauopathy
Dissociations Between Fluency and Agrammatism
In Primary Progressive Aphasia
Aphasiology, 2012

FLUENCY DEFICITS IN PPA-G AND PPA-L
GRAMMATICAL DEFICITS IN PPA-G, BUT NOT PPA-L
Dissociations Between Fluency And Agrammatism
In Primary Progressive Aphasia
Aphasiology, 2012

MORPHOLOGICAL DEFICITS IN PPA-G BUT NOT PPA-L

DISSOCIATION OF FLUENCY FROM GRAMMAR
IN THE FRONTAL LOBES: NAT ▲ VS MLU ▼
CONCLUSIONS

1. Different regions of brain atrophy are associated with reduced fluency and reduced grammatical processing in PPA

2. Impairments of fluency and grammar do not always go together in PPA

Challenges For Testing Grammar Production

1. If speech production is decreased, it is difficult to know if output is grammatically correct or not

2. Need for a test of grammatical processing that:
   - eliminates speech production
   - reduces working memory load
   - reduces impact of word finding deficits
Demographics and Test scores for PPA patients and controls

<table>
<thead>
<tr>
<th>GROUPS</th>
<th>Age (yrs)</th>
<th>WAB AQ</th>
<th>NAT - 10 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPA N=31</td>
<td>Mean</td>
<td>62.9</td>
<td>81.5</td>
</tr>
<tr>
<td>St Dev</td>
<td>8.2</td>
<td>12.0</td>
<td>27.7</td>
</tr>
<tr>
<td>NC N=27</td>
<td>Mean</td>
<td>62.3</td>
<td>99.7</td>
</tr>
<tr>
<td>St Dev</td>
<td>6.6</td>
<td>0.7</td>
<td>4.8</td>
</tr>
</tbody>
</table>

WAB AQ = Western Aphasia Battery Aphasia Quotient
NAT-10 = Northwestern Anagram Test, 10-item version
<table>
<thead>
<tr>
<th>Type of Sentence</th>
<th>Structure</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canonical</td>
<td>Actives</td>
<td>The groom is carrying the bride</td>
</tr>
<tr>
<td></td>
<td>Subject-extracted</td>
<td>Who is carrying the bride?</td>
</tr>
<tr>
<td></td>
<td>Wh-questions</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Subject clefts</td>
<td>It was the groom who carried the bride</td>
</tr>
<tr>
<td>Noncanonical</td>
<td>Passives</td>
<td>The bride was carried by the groom</td>
</tr>
<tr>
<td></td>
<td>Object-extracted</td>
<td>Who is the groom carrying?</td>
</tr>
<tr>
<td></td>
<td>Wh-questions</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Object clefts</td>
<td>It was the bride who the groom carried</td>
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</table>
PPA Subtyping Algorithm For Mild and Moderate Stage PPA

1. Single Word Comprehension- PPVT IV

2. Grammar- Northwestern Anagram Test (NAT), Northwestern Assessment of Verbs and Sentences (NAVS) Sentence Production Priming Test (SPPT)

3. WAB Repetition- 6 Complex Phrases

4. Naming- Boston Naming Test
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LEVEL OF IMPAIRMENT MEASURED BY THE ADLQ

- SEV
- MOD
- MILD

PERCENT IMPAIRMENT

- AD
- FTD
- PPA
ROLE OF THE SPEECH-LANGUAGE PATHOLOGIST IN WORKING WITH PATIENTS WITH PPA

VERY DIFFERENT FROM THE STROKE OR TBI MODEL

Patients recover from stroke: treatment aims to restore function

Patients get worse with PPA: treatment must change with the course of illness

• Strategies must aim for compensation rather than restoration; since patients retain many cognitive abilities while language is declining, these can be capitalized on for compensatory strategies

• Strategies need to focus on improving communication rather than language

• Involvement of caregivers from the beginning to focus on the communication dyad and anticipate changes over time

• Use of later stage strategies from the beginning that will not be discarded when disease progresses – e.g., augmentative communication device may be too hard to use after initial stages
PPA RESOURCES AT THE NORTHWESTERN CNADC

For Patients/Families
- Information about PPA (in multiple languages)
- Support Groups
- Research Programs
- Links to resources (e.g., NAA, AFTD, Other)

For Researchers/Clinicians
- Detailed diagnostic criteria (including video)
- Add resources/studies
- Add subjects for collaboration

DISTRIBUTION OF PARTICIPANTS ACROSS THE UNITED STATES IN THE NORTHWESTERN PPA RESEARCH PROGRAM
Clinicians may view video case samples of PPA subtypes on this website but must first register.

Next Webinar

June 27, 2013
1:00 PM EDT

Melanie Fried-Oken, Ph.D., CCC-SLP
Maya Henry, Ph.D., CCC-SLP

• Treatment For Persons With PPA: An Adaptable Communication Support Approach
COGNITIVE NEUROLOGY AND ALZHEIMER'S DISEASE CENTER
of the Northwestern University Feinberg School of Medicine
announces the
FRONTOTEMPORAL DEGENERATION (FTD) and PRIMARY PROGRESSIVE APHASIA (PPA)
CAREGIVER AND PROFESSIONAL EDUCATION & SUPPORT CONFERENCE

SAVE THE DATE
MONDAY, NOVEMBER 4, 2013

For questions or information about sponsorship opportunities, please contact Kristen at 312-998-5725 or kweisler@northwestern.edu
www.nunca.northwestern.edu

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