Primary Progressive Aphasia
Three Variants in Assessment and Treatment

Thank you!
- PPA participants and their care partners
- Megan Quimby, Carly Cauley, Julia Halvorson, Courtney Hinz, Sarah Spoor

Primary Progressive Aphasia (PPA)
- A form of cognitive impairment that involves degeneration of speech and language function over time.
- Nerve cell death that occurs in speech and language neural area that is not caused by stroke, head trauma, infection, or cancer

(Cognitive Neurology and Alzheimer's Disease Center, n.d.)

Presentation Overview
1. Understanding PPA
2. PPA Assessment
3. PPA Intervention

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History

- Pick and Serieux (1892) first described language impairments associated with atrophy of left frontal and temporal regions.
- 1980s-early 2000s: Binary classification
  - Fluent vs. nonfluent
  - Semantic dementia vs. nonfluent aphasia
- In 2011, an established criteria was created to classify PPA and variants (Gorno-Tempini et al., 2011)

Statistics

- Prevalence: Approximately 3-15/100,000 individuals (Sapolsky et al., 2011)
- Average age onset: late 50s (Grossman, 2014)
- Survival: 7 years (Sapolsky et al., 2011), or 8-10 years (Harciarek et al., 2011), depending on how early a diagnosis is made and type of variant
- 30-40% caused by Alzheimer’s; 60-70% caused by frontotemporal lobar degeneration (Northwestern U)
- Deterioration of language for at least 2 years before decline in other cognitive functions (Mesulam, 1982)

Etiology

(Mesulam et al., 2014)

- Clinical syndrome with potentially different neuropathologic causes
  - Alzheimer’s Disease
    - Neurofibrillary tangles and plaques
  - Frontotemporal Lobar Degeneration (FTLD)

Potential Factors

(Rogalski, Weintraub, & Mesulam 2013)

- Genetic Factors
  - Mutations in MAPT, GRN, or C9orf72 resulting FTLD
  - ApoE
  - Prion Protein
  - Foxp2
- Focal structural lesions
  - Late manifestation of developmental or genetic weakness of language network
- Learning disability
  - Developmental dyslexia

Inclusion Criteria

(Gorno-Tempini et al., 2011)

- The most prominent clinical feature is difficulty with language
- Language difficulties are the principle cause of impaired daily living activities.
- Aphasia is the most prominent deficit at symptom onset and for the beginning phases of the disease
Exclusion Criteria
(Gorno-Tempini et al., 2011)

- The pattern of deficits cannot be better accounted for by other nondegenerative nervous system or medical disorders
- The cognitive disturbance cannot be better accounted for by a psychiatric diagnosis
- No prominent initial episodic memory, visual memory, and visuoperceptual impairments
- No prominent, initial behavioural disturbance

Two Step Diagnostic Process
(Mesaulum et al., 2011)

1. Presence of PPA
2. Diagnose PPA Variant

Three PPA Variants
- Nonfluent/agrammatic, Logopenic, Semantic
- Categorized by patterns of language impairment and supportive patterns of atrophy on imaging
  - Can be reliably diagnosed in around 75-80% of individuals.
  - Can be subdivided into other variants
    - Primary progressive apraxia of speech (Juby, 2015; Hesse, 2015)
    - Mixed PPA (Mesulam et al., 2014)
  - As atrophy spreads, characteristic patterns of the variants become less distinct over a period of 2 years (Bonakdarpour, 2014)

Three PPA Variants
- Core criteria
- Secondary criteria
- Neuroimaging
- Pathology

Nonfluent/Agrammatic PPA
Core Criteria
(Gorno-Tempini et al., 2011)

- One of these criteria must be present
  - Agrammatism
    - Short, simple phrases
    - Lower mean length of utterance
    - Omits function words and inflections
  - Effortful and halting speech
    - Apraxia of speech
    - Slow labored, speech production
    - Distortions, deletions, substitutions, and insertions
    - Disrupted prosody

Nonfluent/Agrammatic PPA
Secondary Criteria
(Gorno-Tempini et al., 2011)

- Two of three criteria must be present
  - Impaired comprehension of complex sentences
    - Negative passives and object relative clauses
  - Spared single word comprehension
  - Spared object knowledge
Neural Atrophy in Nonfluent/Agrammatic

- Left posterior fronto-insular atrophy
- Inferior frontal gyrus
- Insula
- Premotor
- Supplementary motor areas

Nonfluent/Agrammatic Pathology (Hillis, 2015)

- FTLD-Tau
  - Corticobasal degeneration
  - Progressive supranuclear palsy
  - Pick’s Disease
  - Argyrophilic grain disease
- FTLD-TDP

Additional Factors in Nonfluent/Agrammatic

- Cognitive Factors
  - Mild to moderate difficulty in executive function task
  - Difficulty with tests of set-shifting
  - Visuospatial processing and verbal episodic memory are strengths
- Clinical Observations
  - Intact social skills
  - Aware of performance on tasks and speech production
  - Mild disinhibition and apathy as disease progresses

Nonfluent/Agrammatic PPA @ Advanced Stages

- More prominent speech language impairment
  - Less fluent speech, reading/writing difficulties, mute
- Cognitive difficulties emerges (Mesulam et al., 2014)
  - Impaired executive function and working memory
- Movement impairment merges (Mesulam et al., 2014)
  - Motor speech abnormalities, corticobasal degeneration, progressive supranuclear palsy syndromes
- Features of behavior variant FTD (Mesulam et al., 2014)
  - Apathy, disorganization, inattention, poor judgment, inappropriateness, aggression, hyperorality

Logopenic PPA Core Criteria (Gorno-Tempini et al., 2011)

- BOTH criteria must be present
  - Impaired word retrieval in spontaneous conversation and naming tasks
    - Phonologic paraphasias
    - Slow rate
    - Frequent pauses
  - Impaired repetition of sentences and phrases
    - Phonological loop dysfunction (Mesulam et al., 2014)

Logopenic PPA Secondary Criteria (Gorno-Tempini et al., 2011)

- Three of the four criteria must be present
  - Speech (phonologic) errors in spontaneous and naming
    - Phonologic paraphasias
    - Well articulated, no distortions
  - Spared single word comprehension and object knowledge
  - Spared motor speech
    - Articulation and prosody is good
  - Absence of frank agrammatism
    - Halting, but due to word finding difficulties
Neural Atrophy in Logopenic

(Gorno-Tempini et al., 2011)

- Left posterior perisylvian or parietal atrophy
  - Posterior temporal
  - Supramarginal
  - Angular gyri

(Logopenic Pathology)

- Alzheimer’s Disease
  - Amyloid plaques and neurofibrillary tangles
- FTLD-TDP
- FTLD-Tau

Additional Factors in Logopenic

(Bettcher & Sturm, 2014)

- Cognitive Factors
  - Mild visuospatial deficits like localizing and constructing
  - Difficulties in phonological working memory (problems in Forward Digit Span Test)
  - Impairments in numbers and complex calculations
- Clinical observations
  - Aware of difficulties
  - May display apathy, anxiety, and mild irritability

Logopenic PPA @ Advanced Stages

- Most variable of all the PPA types
  - Persistent lvPPA patterns
  - May become nnvPPA or svPPA
  - Develop cognitive impairments and motor dysfunction

Semantic PPA

Core Criteria

(Gorno-Tempini et al., 2011)

- Both of these characteristics must be present
  - Impaired naming of objects
    - Circumlocution, simplification, semantic paraphasia (Mesulam et al., 2014)
    - Deficits present in most categories (tools, animals, people)
    - Reports of deficits in concrete object concepts than abstract concepts
  - Impaired single word comprehension
    - Earliest and obvious manifestations
    - Impaired in low frequency items
    - Problems in object and person recognition
  - Impaired object knowledge, particularly for low frequency or low-familiarity items
  - Surface dyslexia or dysgraphia
    - Regularization errors “sea” is read as /su/
  - Spared repetition
  - Spared speech production
  - Potential paragrammatic errors

Semantic PPA

Secondary Criteria

(Gorno-Tempini et al., 2011)

- Three of the four of the characteristics must be present
  - Impaired object knowledge, particularly for low frequency or low-familiarity items
  - Surface dyslexia or dysgraphia
    - Regularization errors “sea” is read as /su/
  - Spared repetition
  - Spared speech production
  - Potential paragrammatic errors
Semantic Atrophy
(Gorno-Tempini et al., 2011)

- Anterior temporal lobe atrophy
- Ventral and lateral parts of anterior temporal lobes
- Atrophy is bilaterally, but greater on left hemisphere

Semantic Pathology
(Hillis, 2015)

- FTLD-TDP
- AD

Additional Factors in Semantic
(Bettcher & Sturm, 2014)

- Cognitive Factors
  - Difficulties in verbal area in episodic memory (influence results of visual recall or recognition)

- Clinical Observations
  - Changes in social and emotion

Semantic PPA @ Advanced Stages

- Early behavioral and personality changes
  - disinhibition, irritability, inappropriate social interactions and food fads
  - As the disease progresses, utilization behaviors, mental inflexibility, and compulsions

- At advanced stages
  - Semantic jargon, pragmatic disturbance, mutism is common
  - Prominent impairments of additional cognitive domains and motor function can emerge

PPA Assessment

- Clinical Observations
- Speech and Language
- PPA
- Cognitive Factors
Initial Assessment

• Detailed history
• Neurological examination
• Speech and language assessment
• Neuropsychiatric assessment
• Neuropsychological evaluation
• Brain imaging

Speech-Language Assessment

(Nickels, Taylor & Croot, 2011)

• Identify language impairment and its impact on communication activities/participation/quality of life to determine treatment
• Establish baseline for the nature, extent, and rate of change in PPA over time.

Our Challenges

• Choose appropriate difficulty levels of tests, cut-off scores, normative values, and modes of assessment (Mesulam et al., 2014)
• Sensitive measure at early vs. late stage (Harciarek, Sitek, & Kertesz, 2014)

Speech and Language Domains

(Mesulam et al., 2012)

PAA

• Grammatical Ability
• Comprehension
• Repetition
• Object Naming

Speech Production

(Gorno-Tempini et al., 2011; Sapolsky et al., 2011)

• Syntax and grammar
  • Picture description, story retell, constrained-sentence production task, language sample analysis, BDAE seven-point scale for grammatical form, Grammatical Competence and Paraphasias Scale, Northwestern Anagram Test
  • Motor speech
    • Multiple repetitions of multyllablic words and utterances of increasing length and diadochokinesis
  • Articulation
  • Apraxia Battery for Adults
• Fluency
  • BDAE seven-point scale for phrase length, WAB Fluency, spontaneous speech and picture description
• Impaired PPA variant: nfvPPA

Confrontation & Generative Naming

(Sapolsky et al., 2011; Nickels, Taylor & Croot, 2011)

• Boston Naming Test
• Phonemic/category fluency tasks
• Impaired PPA variant
  • svPPA: severe with semantic errors
  • lvPPA: moderate with phonemic errors
Repetition
(Sapolsky et al., 2011)

• Repeat words, phrases and sentences from WAB and BDAE repetition tasks

• Impaired PPA variant
  • LvPPA: phonological errors
  • NfvPPA: motor speech errors

Comprehension
(Sapolsky et al., 2011)

• Single-word comprehension
  • WAB Auditory Word Recognition, BDAE Word Comprehension, PALPA Spoken Word-Picture Matching, Peabody Picture Vocabulary Test

• Sentence comprehension
  • WAB and BDAE following commands tasks, BDAE Complex Ideational Material, CYCLE Sentence-Picture Matching

• Impaired PPA variant
  • NfvPPA: errors on syntactical complexity
  • LvPPA: errors on syntactical length

Semantics
(Henry, Mooney & Morhardt, 2015; Nickels et al., 2011)

• Pyramids and Palm Tree test (Howard & Patterson, 1992)
• PALPA spoken word-picture matching (subtest 47)
• PALPA synonym judgments (subtest 49)
• Peabody Picture Vocabulary Test

• Impaired PPA variant: SvPPA

Reading/Writing
(Sapolsky et al., 2011)

• WAB and BDAE written language tasks

• Impaired PPA variant
  • svPPA: regularization errors
  • lvPPA: phonologic errors

Functional Communication
(Harcia et al., 2014)

• Social Networks Package (available online)
• Aphasia Needs Assessment (available online)
• Communicative Effectiveness Index (available online)
• Frontotemporal Dementia Rating Scale (available online)
• Assessment for Living With Aphasia -2

Other Abnormalities

• Cognition
  • Memory, executive function, visuospatial processing

• Motor
  • Weakness, incoordination, limb apraxia

• Neuropsychiatric
  • Social and emotional changes, disinhibition, apathy
Cognitive Tests

- Mini Mental State Exam
- Digit Span Forward
- Digit Span Backward
- Cognitive Linguistic Quick Test
- Trail Making Test
- Addenbrooke’s Cognitive Examination-Revised

Progressive Aphasia Severity Scale (PASS) (Sapolsky et al., 2014)

- A comprehensive assessment of individual domains of speech/language to help diagnose PPA subtypes
- Establish baseline communication strengths and weaknesses and monitor change over time
- Rates the presence and severity of speech and language symptoms across 13 domains
- Uses clinical judgment to make a rating on a 5-point scale based on client’s current ability

PASS (Sapolsky et al., 2014)

1. Informant questionnaire
   - For care partner to complete
   - Multiple choice questions
   - General question detail

2. Interview the patient and care partner
   - Based on answers from the questionnaire

PASS (Sapolsky et al., 2014)

3. A comprehensive language assessment (to establish baseline)
   - A motor speech exam
   - Boston Naming Test
   - WAB-R: The commands, repetition and pic description tasks
   - Cambridge Semantic Battery (CSB) word-picture matching task
   - The Northwestern Anagram Test (Mesulam et al., 2009)

PASS (Sapolsky et al., 2014)

4. Consider all sources of info (questionnaire, interview, test performance) and rate 10 domains of language on PASS worksheet (0 = normal to 3 = severe impairment)
   - Articulation
   - Fluency
   - Syntax & grammar
   - Word retrieval and expression
   - Repetition
   - Auditory comprehension
   - Single word comprehension
   - Reading
   - Writing
   - Functional communication

PASS

- Comprehension and production in any modality is acceptable.
- Obtain PASS at MGH Frontotemporal Dementia Unit website http://www.nmr.mgh.harvard.edu/~bradd/PASS.html
PASS

- How does this help clinically?
- Allows clinician to observe any changes in the client
- Acts as a guide to help clinician assess areas specific to PPA subtypes

(Sapolsky et al., 2014)

Longitudinal Monitoring

- Critical for therapy planning and alternative communication strategies/devices usage
- Retest every 6 months – 1 year, depending on the rate of progression of clinical symptoms
  - Brief symptom-focused check-ups
  - Neurological and psychiatric monitoring is important at PPA-plus stage

(Sapolsky et al., 2011)

Trialing Treatment Strategies

(Khayum et al., 2012)

<table>
<thead>
<tr>
<th>Individuals with PPA</th>
<th>Family</th>
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<tbody>
<tr>
<td>Focus on communicative strategies</td>
<td></td>
</tr>
<tr>
<td>- Aware?</td>
<td></td>
</tr>
<tr>
<td>- Use them?</td>
<td></td>
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<tr>
<td>- Motivated?</td>
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<tr>
<td>- Memory impairment?</td>
<td></td>
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<tr>
<td>- ADL?</td>
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<tr>
<td>Focus on support level</td>
<td></td>
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<tr>
<td>- Understand PPA?</td>
<td></td>
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<tr>
<td>- Use of adaptations?</td>
<td></td>
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<tr>
<td>- Aware of communicative strategies?</td>
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</tbody>
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PPA Intervention

- Pharmacological
  - No current options for medication for PPA
  - Can treat behavioral disturbances
  - Medications could potentially slow down the progression of disease
- Nonpharmacological
Language Treatment Is Worth It!
(Rising, 2014)

- Treatment gains (in naming) are very promising, especially in view of the progressive nature of the disease (Jokel et al., 2014)

- Individuals with mild PPA may be very good candidates for language rehabilitation (Jokel et al., 2014)

- May not see generalization, but rather maintain language abilities to slow down disease progression

Participation-Directed Intervention
(Harciarek et al., 2014)

- Identify individuals’ strengths and weaknesses in communication (Rogalski & Khayum, 2015)

- Patient-centered therapy goals (Rogalski & Khayum, 2015)
  - Focus on functional outcome
  - Adjust cueing level and use of strategies as the disease progresses

- Personally relevant tx tasks/items
  - Frequent exposure to items in life (i.e., hobbies and interests), motivational level

- Partner involvement/support

Treatment Approaches
(Harciarek et al., 2014)

- 1. Language retraining

- 2. Compensatory strategies

- 3. Partner Training

- 4. Combination of the Approaches

1. Language Retraining
(Rogalski & Khayum, 2015 ASHA)

- Self-cuing strategies to capitalize residual skills
  - Lexical retrieval: Orthrographic, semantic, phonological

- Script training to capitalize automatic retrieval
  - Individuals with PPA and their partners formulate and rehearse scripts to increase ability to speak in a variety of situations

2. Compensatory Strategies
(Khayum, et al., 2012)

- Start early! (Khayum et al., 2012)

- Support multi-modal communication (Khayum & Rogalski, 2015)
  - Unaided: speech, vocalization, gestures, eye gaze, body language, sign language
  - Aided
    - Low-tech: paper/pencil, communication cards/boards/wallets/books, white board, scripts
    - High-tech: speech generating devices, mobile technologies (apps)
  - Communication partner support

Ipad Apps

- Photo Communication
  - Story Creator
  - Scene & Heard
  - Pic Collage
  - Microsoft PowerPoint

- Flashcards (Khayum & Rogalski, 2015)
  - Quizlet

- Communication
  - SmallTalk series
  - Communication Phrases; Daily Activities, Common phrases, Aphasia, etc.

- EESpeech (Lite; Basic)
  - Verbally
3. Partner Training

- Partner training is effective in improving communication activities, participation (Simmons-Mackie et al., 2010) and quality of life (Nickels & Croot, 2014)
- Disease Education (Khayum et al., 2012)
  - Understand PPA and its progressive nature
  - Aware of care options – services, social security disability
  - Planning for the future

- Teaching family or other individuals how to be an effective communicator (Khayum & Rogalski, 2015)
  - Speak slowly, one instruction at a time
  - Simplify sentence structure and use simple vocabulary
  - Provide choices: y/n, written choices
  - Eliminate distractions
  - Increase use of nonverbal cues
  - Face to face. Get attention first
  - Use gestures to supplement speech
  - Use written or picture cues

4. Combine Approaches

- Literature suggests using both language-retraining and compensatory strategies with the aim of improving participation (Harciarek et al., 2014; Rogalski & Khayum, 2015)

Treatment Domains

- Naming
- Speech Production
- Writing
- Traditional Tx with Advanced Technology
**Naming**

- Anomia is a common PPA feature (different underlying cause) (Henry et al., 2013)

- Anomia may result from damage to semantic or phonologic representations, or impaired transmissions of info btw these cognitive representations (Henry et al., 2008)

- Treatment gain appears to induce increased activation of both affected and spared brain regions (Jokel et al., 2011; Beeson et al., 2011)

**Interactive Model of Lexical Processing** (Tippett et al., 2015)

- "spoken word"
- Acoustic Analysis
  - Semantics
  - Orthography
- Visual Analysis
- Phonology
- Speech Motor Control
- "spoken word"
- Written word

**Evidence-Based Suggestions**

- Tx effect appears to be most beneficial at early stages of the disease. (Jokel et al., 2014)

- Variant type may matter: Phonologically based for nfvPPA, semantically based for svPPA (Jokel et al., 2014)

- Semantic features matter (Jokel et al., 2014)

- Generalization may not be a realistic tx goal (Croot et al., 2009)

**Evidence-Based Suggestions**

- Patient-centered tasks/items: Choose highly functional items and link these items to existing knowledge (Croot et al., 2009)

- Lots of practice needed (Jokel et al., 2014)

- Technologically based tx needs further research (i.e., transcranial magnetic stimulation) (Jokel et al., 2014)

**Evidence-Based Suggestions**

- Errorless learning may be more effective than traditional errorful learning
  - Implicit memory facilitates learning (errorless)
  - Declines in explicit memory (errorful) (Jokel et al., 2010)
  - Impaired semantic processing (Jokel et al., 2010)
  - Space-retrieval vs. simple repetition (Garthery-Goulart et al., 2013)

**Anomia Treatment Approaches**

- Remediate Impaired Linguistic Domain
- Capitalize on Preserved Skills
Remediate Impaired Linguistic Domain: SvPPA  
(Rising, 2014)

• Retrain specific semantic concepts
• Engage residual semantic representations
⇒ Effective for item-specific gains

Capitalize on Preserved Skills: SvPPA

• Phonological (first sound, rhyme) and orthographic cues  
  (Rising, 2014)
• Episodic memory (personally relevant context/cue)  
  (Rising, 2014)
• Nonverbal problem solving and visual perceptual skills  
  (Jokel, Rochon & Anderson, 2010)
• Self-cueing strategies (Lexical retrieval cascade in Henry et al., 2013)
⇒ Engage multiple processes may help generalization and maintenance of learning

Lexical Retrieval Cascade for SvPPA  
(Henry et al., 2013)

1. Semantic self-cue: “tell me about it”
2. Orthographic self-cue: “can you write it?”
3. Phonemic self-cue: “what sound does this letter make?”
4. Oral reading: “What does this say?”
   • Provide spoken model if needed
5. Repetition x 3

LvPPA

Remediate impaired linguistic domain: Engage residual phonological abilities  
(Rising, 2014)

• Capitalize on preserved ability
  • Spared semantic knowledge
  • Spared cognitive linguistic processes
  • Self-cueing strategies (Lexical retrieval cascade in Henry et al., 2013)

Lexical Retrieval Cascade for LvPPA  
(Henry et al., 2013)

1. Semantic self-cue: “tell me about it”
2. Orthographic self-cue: “can you write it?”
3. Phonemic self-cue: “what sound does this letter make?”
4. Oral Reading
   • Provide written model and elicit spoken production
5. Repetition x 3
6. Semantic plausibility judgment
  • Ask y/n questions about semantic features of target
7. Recall 2 semantic features + spoken/written names

nfvPPA

• Anomia is not a prominent deficit at early stage
• May capitalize on preserved ability
  • Relatively preserved semantic knowledge  
    (Beeson et al., 2011)
• Maintenance or generalization need further research
Speech Production in nfvPPA

- Combine pictures with gestures (Schneider, Thompson, & Luring, 1996)
- Use script training (Khayum et al., 2012; Henry et al., 2015)
  - Create a script
  - Recognize script sentences and sequence them
  - Read the sentences out loud and produce them in response to questions (in scripted order)
  - Recall the script from memory
  - Respond to questions with the sentences (not in scripted order)
- Personalizing recording

Spelling/Writing

- svPPA: Make phonologically plausible errors (Tsapkini et al., 2014)
  - toast → "tost"  splash → "splash"
- nfvPPA & lvPPA: Make semantic-based errors (Tsapkini et al., 2014)
  - chair → "table"  yacht → "boat"
- lvPPA (Tsapkini & Hillis, 2013)
  - Learned phoneme-to-grapheme correspondences with key word
  - Showed tx gain but no maintenance or generalization
Language Therapy + Transcranial Direct Current Stimulation

- Transcranial Direct Current Stimulation
- Electrical stimulation to train via small electrodes
- tDCS (left inferior frontal gyrus) + spelling (phoneme-to-grapheme conversion) (Tsapkini et al.)
- 2 nVPPA, 4 lVPPA
- “tDCS + spelling” 1x more effective than spelling ix alone (still preliminary)
- Sustained tx effect 2 months post tx
- Improve spelling for untrained items

References


Questions?


