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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Presenter Disclosure Information

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OUTLINE

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?

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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

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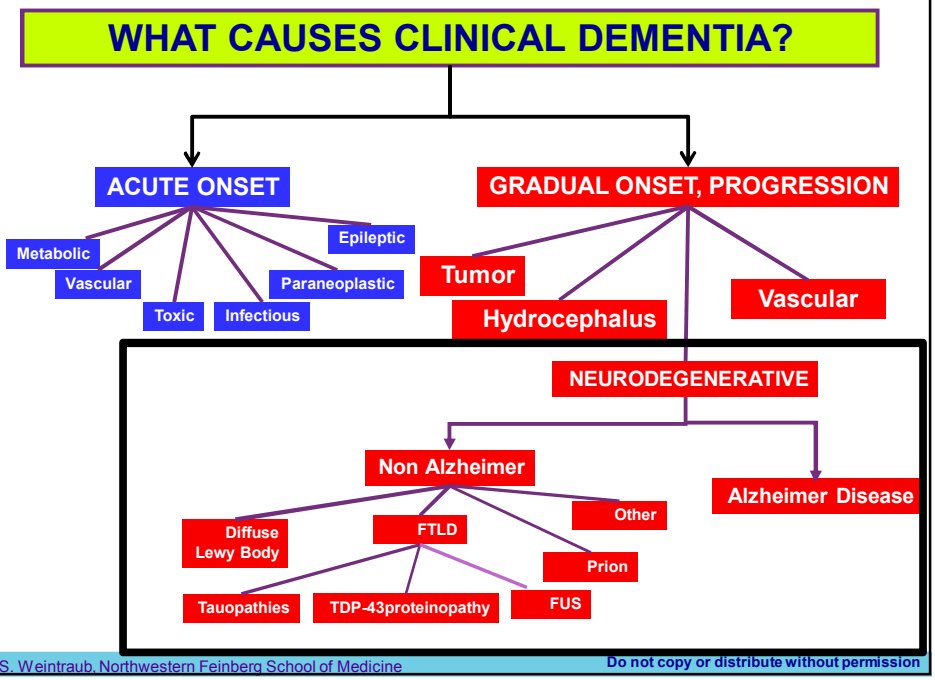

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WHAT IS PPA?

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

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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.

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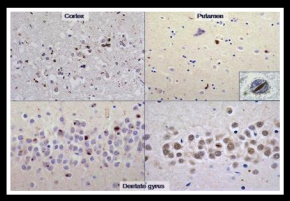
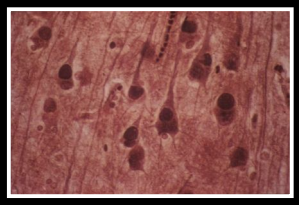
TYPES OF NEUROPATHOLOGY DIAGNOSED AT BRAIN AUTOPSY THAT CAUSE CLINICAL DEMENTIA SYNDROMES

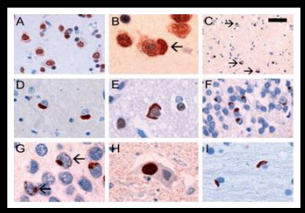
Frontotemporal Lobar Degeneration With TDP-43 Proteinopathy



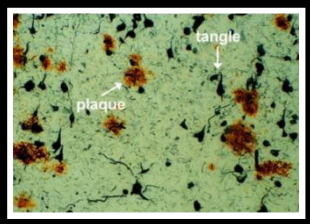
Frontotemporal Lobar Degeneration With Tau Inclusions - e.g. Pick's disease



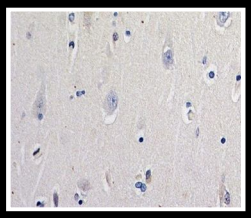
Frontotemporal Lobar Degeneration With FUS Inclusions



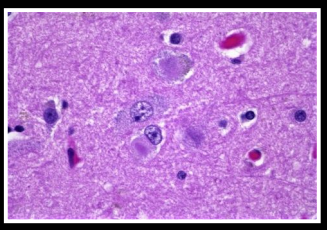
Plaques and Tangles- "Alzheimer's Disease"



NORMAL BRAIN TISSUE



Cortical Lewy Body Disease



Courtesy Eileen Bigio MD NORTHWESTERN CNADC

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Can neurodegenerative disease cause aphasia without any other cognitive deficits?

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Stroke MODEL and Focal Cognitive Deficits

ACUTE EVENT

Neuronatomically Focal
Determined by VASCULATURE

FOCAL COGNITIVE DEFICIT
(e.g.,Aphasia)

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Can Neurodegenerative Brain Disease: Cause Focal Cognitive Deficits?

PRE 1980 – LACK OF KNOWLEDGE = LATE DETECTION

Neuropsychologically Widespread Deficits

Neuroanatomically Diffuse

LATE STAGE

POST 1980 –INCREASING INFORMATION = EARLY DETECTION

Neuropsychologically Circumscribed Deficits

Neuronatomically Focal determined by Large-Scale Network connectivity

EARLY STAGE

Weintraub & Mesulam, 1993, 1996

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CLINICAL SYMPTOMS OF DEMENTIA

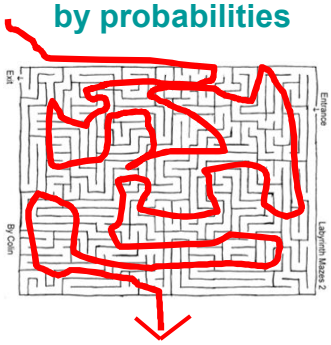
Changes In Cognition, Behavior, Activities of Daily Living

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)

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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

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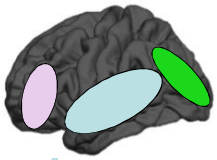
CLINICAL, NEUROANATOMICAL AND NEUROPATHOLOGICAL RELATIONSHIPS

DEMENTIA=
What the clinician observes and diagnoses

NEUROANATOMY=
BRAIN AREA OF dysfunction/ atrophy

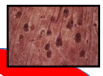
DISEASE= What the neuropathologist finds under the microscope

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

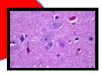


% AD
Neuropathology

% FTLD
Neuropathology



% Lewy Body
Neuropathology



%OTHER
Neuropathology

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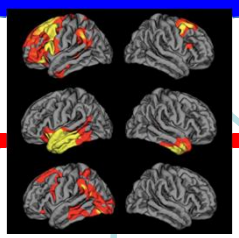
EARLY NEUROPSYCHOLOGICAL PROFILE: APHASIA
Primary Progressive Aphasia



30-40% AD
Neuropathology

60-70% FTLD
Neuropathology

1-2% OTHER
CJD, Cortical Lewy Body

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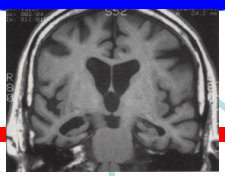
CLINICAL, NEUROANATOMICAL AND NEUROPATHOLOGICAL RELATIONSHIPS

DEMENTIA= What the clinician observes and diagnoses

EARLY NEUROPSYCHOLOGICAL PROFILE: AMNESIA
Dementia of the AD type

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

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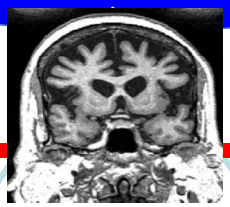
CLINICAL, NEUROANATOMICAL AND NEUROPATHOLOGICAL RELATIONSHIPS

DEMENTIA= What the clinician observes and diagnoses

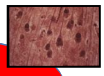
EARLY NEUROPSYCHOLOGICAL PROFILE: Executive/comportmental
Beh variant frontotemporal dementia

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.**

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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)

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HOW IS PPA DIFFERENT FROM DEMENTIA OF THE AD TYPE AND BEHAVIORAL VARIANT FRONTOTEMPORAL DEMENTIA? COMPARISON OF THREE CLINICAL DEMENTIA DIAGNOSES

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

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Classification Of Primary Progressive Aphasia and Its Variants
Gorno-Tempini, Hillis, Weintraub, et al,
Neurology, 2011

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

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CLINICAL DIAGNOSTIC CRITERIA FOR SUBTYPES OF PPA
Gorno-Tempini Hillis, Weintraub, et al, Neurology, 2011

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

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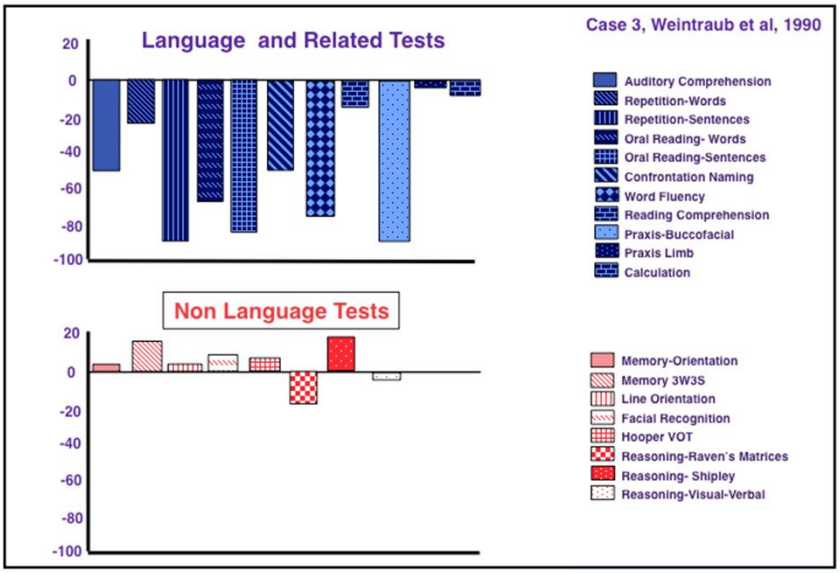
NEUROPSYCHOLOGY OF PPA

Percent Change in Test Scores Over 2 Years



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NEUROPSYCHOLOGY OF PPA
(An "Aphasic Dementia")

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

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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

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THREE WORDS THREE SHAPES EPISODIC MEMORY TEST (3W3S)

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

CONDITION	LEARNING/MEMORY COMPONENT TESTED
COPY	Assures attention to stimuli, verifies writing and drawing ability impact on performance
INCIDENTAL RECALL	How much is remembered without forewarning,i.e., *effortlessly*?
ACQUISITION TRIALS	Re-expose stimuli on two learning trials (30 secs each) followed by immediate reproduction to assure encoding, reach a level of criterion
DELAYED RECALL	Retrieval/retention over time
MULTIPLE CHOICE	Recognition memory

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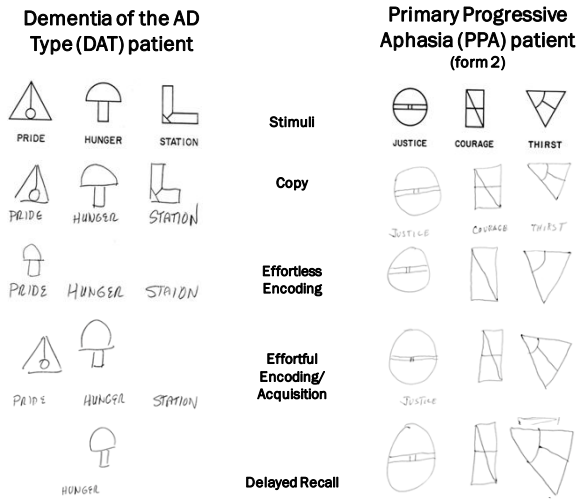
Verbal and Nonverbal Memory In Primary Progressive Aphasia: The Three Words-Three Shapes Test

Weintraub et al, Beh Neurol, 2013



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

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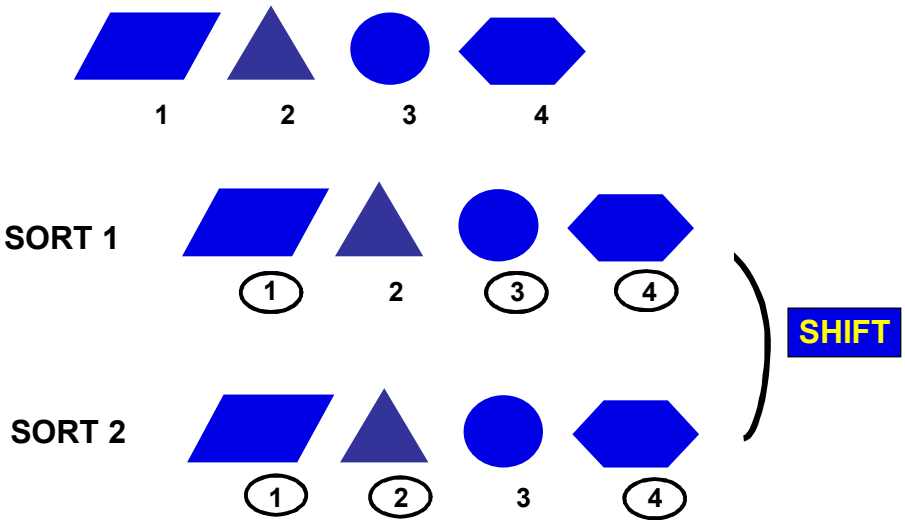
Visual-Verbal Test (Feldman & Drasgow, 1959)



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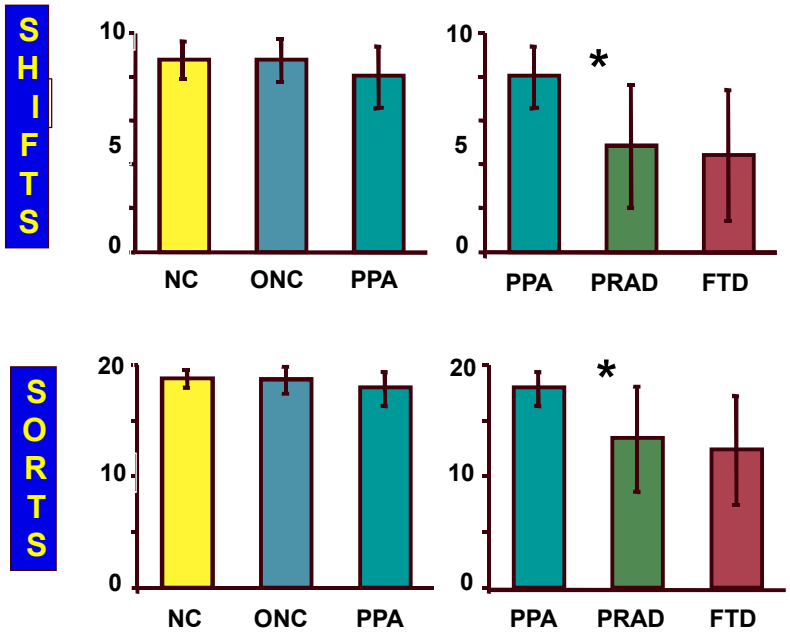
Wicklund, Johnson, Weintraub, 2004



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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

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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)

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APHASIA ASSESSMENT IN PPA

LANGUAGE COMPONENTS

PHONOLOGY
Sound Discrimination, Production

SEMANTICS
Single Word Comprehension, Naming

GRAMMAR (SYNTAX, MORPHOLOGY)
Production, Comprehension

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Classical Aphasiology

Non Fluent = Anterior = Broca's =Agrammatic?

Fluent = Posterior = Wernicke's =Semantic?

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Can Fluency Be Dissociated From Grammar?

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

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Dissociations Between Fluency And Agrammatism In Primary Progressive Aphasia

Thompson CK, Cho S, Hsu CJ, Wieneke C, Rademaker A, Weitner BB, Mesulam M-M, Weintraub S

Aphasiology, 2012

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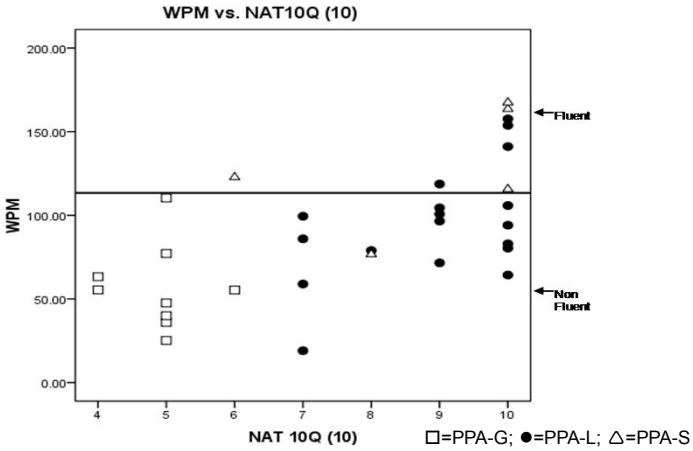
Thompson CK, Cho S, Hsu CJ, Wieneke C, Rademaker A, Weitner BB, Mesulam M-M, Weintraub S

Aphasiology, 2012

FLUENCY DEFICITS IN PPA-G AND PPA-L
GRAMMATICAL DEFICITS IN PPA-G, BUT NOT PPA-L



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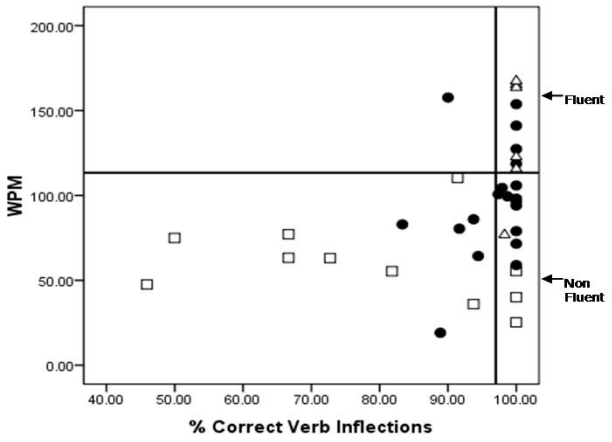
Thompson CK, Cho S, Hsu CJ, Wieneke C, Rademaker A, Weitner BB, Mesulam M-M, Weintraub S
Aphasiology, 2012

MORPHOLOGICAL DEFICITS IN PPA-G BUT NOT PPA-L



□=PPA-G; ●=PPA-L; △=PPA-S

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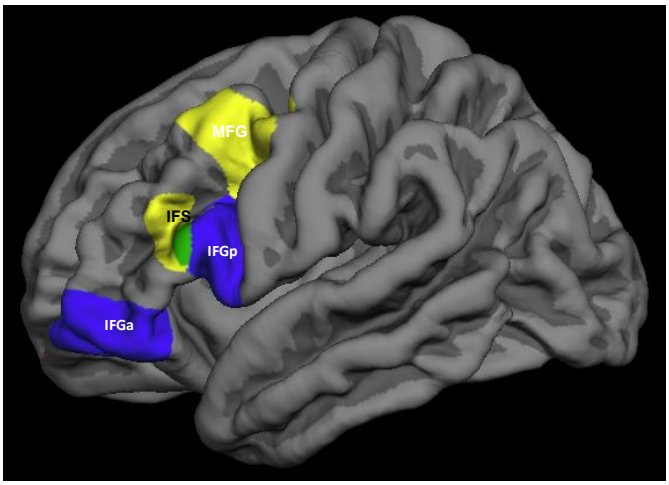
DISSOCIATION OF FLUENCY FROM GRAMMAR IN THE FRONTAL LOBES: NAT VS MLU



Courtesy Emily Rogalski, PhD, CNADC

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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

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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

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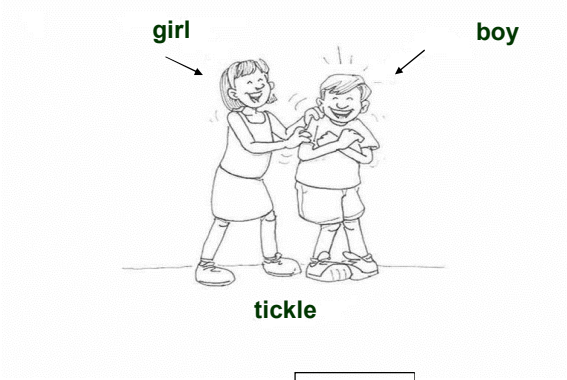
NORTHWESTERN ANAGRAM TEST (NAT)
Weintraub, Mesulam, Thompson



the | girl | tickling | the | boy | is

the | girl | is | tickling | the | boy

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Demographics and Test scores for PPA patients and controls

GROUPS		Age (yrs)	WAB AQ	NAT - 10 (%)
PPA N=31	Mean	62.9	81.5	72.4
	St Dev	8.2	12.0	27.7
NC N=27	Mean	62.3	99.7	98.3
	St Dev	6.6	0.7	4.8

WAB AQ = Western Aphasia Battery Aphasia Quotient
NAT-10 = Northwestern Anagram Test, 10-item version

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Table 1. Samples of Canonical and Noncanonical Sentence Types on the Northwestern Assessment of Verbs and Sentences (NAVS)

Type of Sentence	Structure	Example
Canonical	Actives	The groom is carrying the bride
	Subject-extracted Wh-questions	Who is carrying the bride?
	Subject clefts	It was the groom who carried the bride
Noncanonical	Passives	The bride was carried by the groom
	Object-extracted Wh-questions	Who is the groom carrying?
	Object clefts	It was the bride who the groom carried

Weintraub et al, 2009

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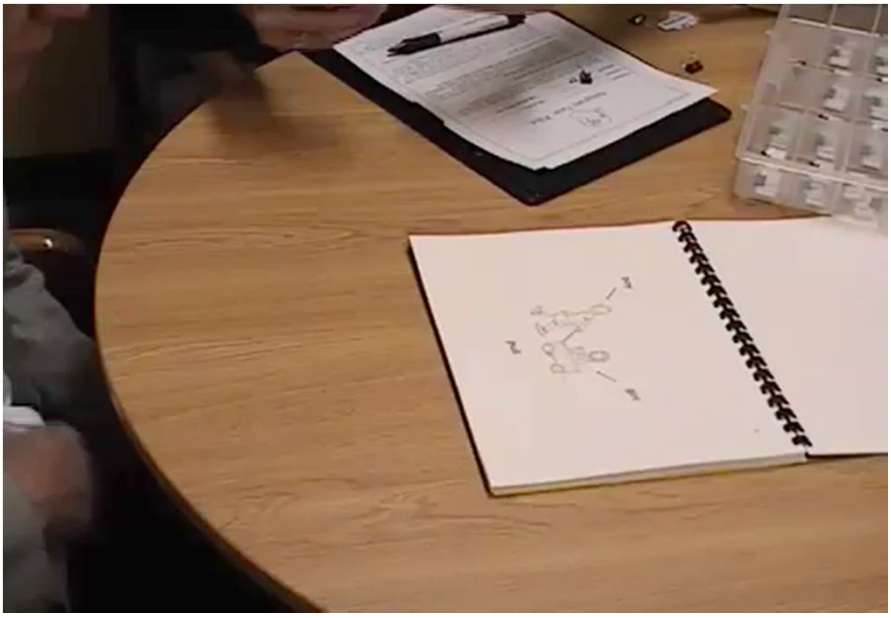

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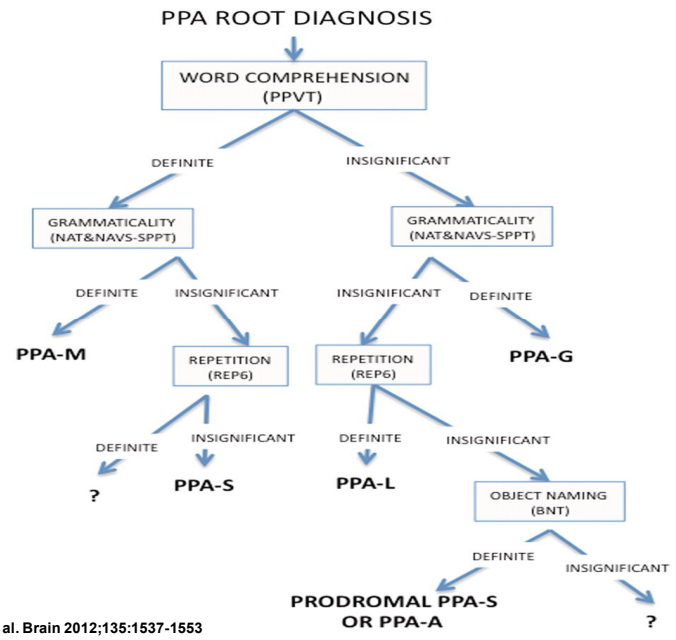

Mesulam M et al. Brain 2012;135:1537-1553

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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

Mesulam, Wienecke, Thompson, Rogalski, Weintraub Brain, 2012

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OUTLINE

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?

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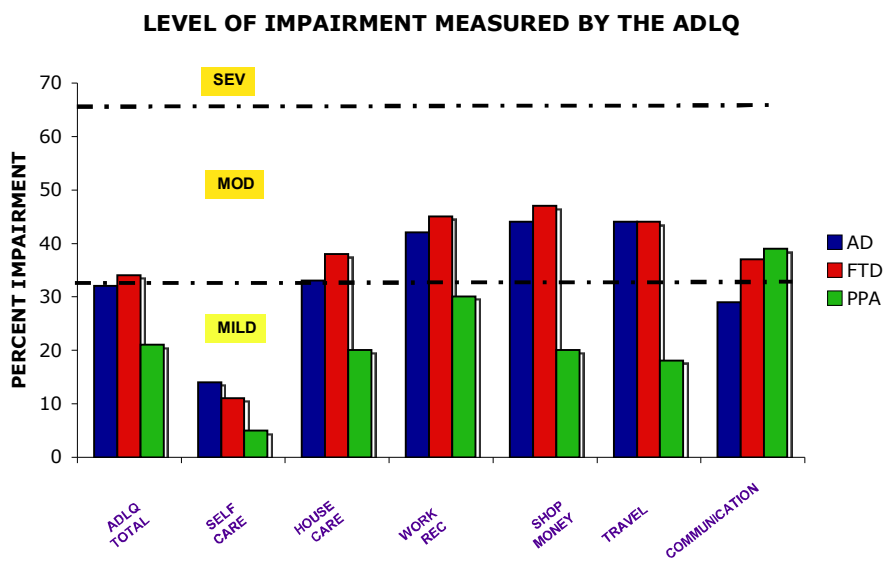

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ROLE OF THE SPEECH-LANGUAGE PATHOLOGIST IN WORKING WITH PATIENTS WITH PPA

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**

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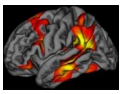
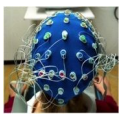
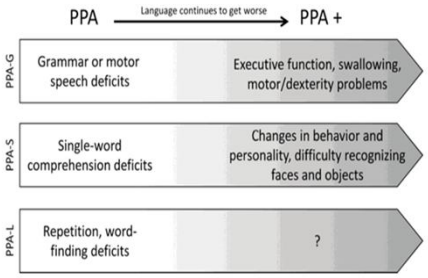
Primary Progressive Aphasia Clinical Evaluation Program @ Northwestern:

- **Neurology**
- **Neuropsychology**
- **Speech-Language Pathology**
- **Social Work**

Language in Primary Progressive Aphasia Research Program @ Northwestern:

- **Neuropsychological Evaluation**
- **MRI Scans**
- **Electrophysiological Studies**
- **Neuropathology/Genetics Studies**



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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

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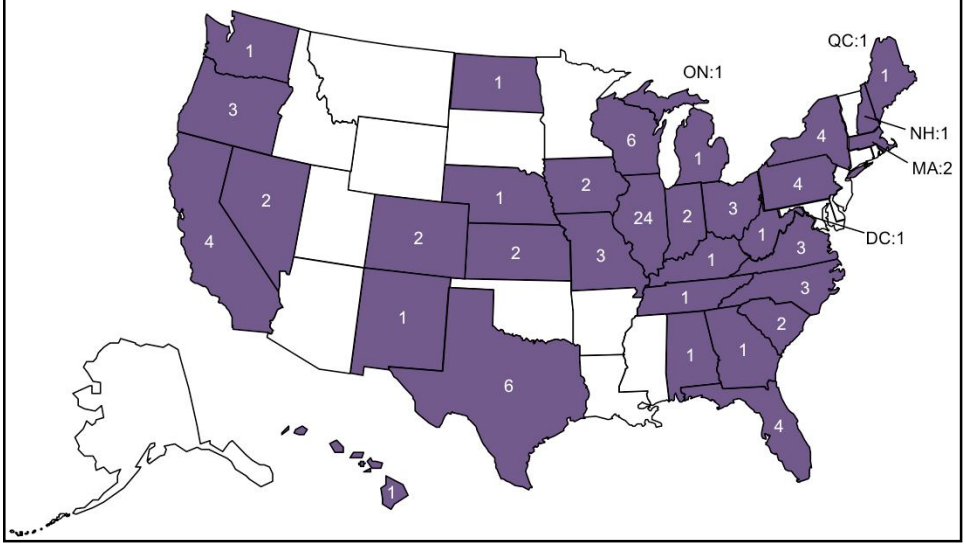
DISTRIBUTION OF PARTICIPANTS ACROSS THE UNITED STATES IN THE NORTHWESTERN PPA RESEARCH PROGRAM



IMPPACT

International PPA Connection

www.ppaconnection.org

- Clinicians may view video case samples of PPA subtypes on this website but must first register

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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**

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and
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