Speech-language treatment outcomes in primary progressive aphasia

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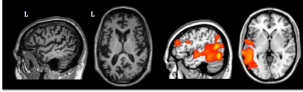University of Texas at Austin, USA

APHASIA RESEARCH AND TREATMENT LAB

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Primary Progressive Aphasia (PPA)

- *Slowly progressive* aphasia caused by neurodegenerative disease
- Most prominent clinical feature is difficulty with speech/language
- Often affects individuals <65 years
- Ultimate progression to mutism
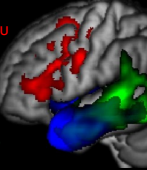
(Mesulam, 2008; Gorno-Tempini et al., 2011)

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3 variants of PPA (Gorno-Tempini et al., 2011)

FTD
- Nonfluent variant
  - Impaired syntax and/or motor speech (AOS, dysarthria)
- Semantic variant
  - Impaired semantics- naming and word comprehension

AD →
- Logopenic variant
  - Impaired phonological processing- naming and repetition

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Three clinical variants linked to underlying patterns of atrophy caused by different diseases

Nonfluent variant =>Tau   Grammar, motor speech

Semantic variant   => TDP-43   Naming, word comprehension

Logopenic variant   => AD   Naming, repetition

Gorno-Tempini et al., 2011; Wilson et al., 2010

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PPA: Is all lost?

5

PPA: Is all lost?

Unraveling Boléro

RADIOLAB
Listen Read Watch

Unravelling Boléro: progressive aphasia, transmodal creativity and the right posterior neocortex

William W. Seeley, Brandy R. Matthews, Richard K. Crawford, Maria Luisa Gorno-Tempini, Dean Foti, Ian R. Mackenzie and Bruce L. Miller

Brain (2008), 131, 39—49

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Slide 7:

Portraits of Artists
Emergence of Visual Creativity in Dementia
Bruce L. Miller, MD; Craig E. Hou, MD
> Author Affiliations | Article Information
Arch Neurol. 2004;61(6):842-844. doi:10.1001/archneur.61.6.842

Art In the Presence of Frontotemporal Dementia

Bruce Miller and William Seeley

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Slide 8:

Can we retrain speech and language in PPA?

- Considerable recent progress understanding the neurobiology of PPA and its cognitive-linguistic underpinnings, but relatively little research effort directed at behavioral rehabilitation

- Despite a robust literature base supporting intervention for speech and language in stroke patients, far less research in progressive aphasia
  - Pessimism on the part of clinical professionals and third party reimbursers

- Is it possible or even worthwhile to try to "train" a degenerating brain?

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Slide 9:

Behavioral treatment for speech and language in PPA and PPAOS: A systematic review

Lisa D. Wauters*, Karen Croot*, Heather R. Dial, Joseph R. Duffy, Stephanie M. Grasso, Esther Kim, Kristin M. Schaffer, Kirrie J. Ballard, Heather M. Clark, Leeah Kohley, Laura L. Murray, Emily J. Rogalski, Mathieu Figeys, Lisa Milman, **Maya L. Henry**
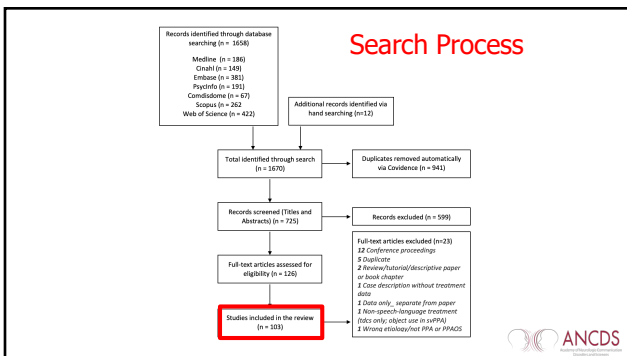
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Slide 10:
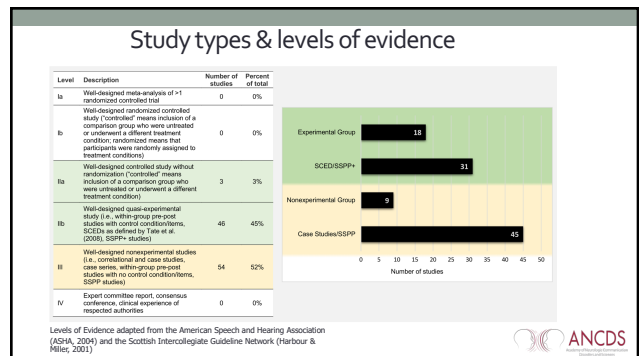
Systematic Review Questions

- What evidence exists for the behavioral treatment of speech and/or language in PPA/PPAOS, and what is the strength of this evidence?

- Does the evidence indicate that treatment results in...
  - **Gains for trained skills/targets**?
  - **Gains for untrained skills/targets** (generalization)?
  - **Maintenance of treatment gains** beyond the immediate post-treatment period?
  - **Socially-validated treatment gains**?

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Slide 11:

Search Process

Records identified through database searching (n = 1658)

Medline (n = 186)
Cinahl (n = 149)
Embase (n = 381)
PsycInfo (n = 191)
Comdisdome (n = 67)
Scopus (n = 262)
Web of Science (n = 422)

Additional records identified via hand searching (n=12)

Total identified through search (n = 1670)

Duplicates removed automatically via Covidence (n = 941)

Records screened (Titles and Abstracts) (n = 725)

Records excluded (n = 599)

Full-text articles assessed for eligibility (n = 126)

Full-text articles excluded (n=23)
12 Conference proceedings
5 Duplicate
2 Review/tutorial/descriptive paper or book chapter
1 Case description without treatment data
1 Data only, separate from paper
1 Non-speech-language treatment (tdcs only; object use in svPPA)
1 Wrong etiology/not PPA or PPAOS

Studies included in the review (n = 103)

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Slide 12:

Study types & levels of evidence

Level	Description	Number of studies	Percent of total
Ia	Well-designed meta-analysis of >1 randomized controlled trial	0	0%
Ib	Well-designed randomized controlled study ("controlled" means inclusion of a comparison group who were untrained or underwent a different treatment condition; randomized means that participants were randomly assigned to treatment conditions)	0	0%
IIa	Well-designed controlled study without randomization ("controlled" means inclusion of a comparison group who were untreated or underwent a different treatment condition)	3	3%
IIb	Well-designed quasi-experimental study (i.e., within-group pre-post studies with control condition/items, SCEDs as defined by Tate et al. (2008); SSPP+ studies)	46	45%
III	Well-designed nonexperimental studies (i.e., correlational and case studies, case series, within-group pre-post studies with no control condition/items, SSPP studies)	54	52%
IV	Expert committee report, consensus conference, clinical experience of respected authorities	0	0%

Experimental Group 18
SCED/SSPP+ 31
Nonexperimental Group 9
Case Studies/SSPP 45

Number of studies (0 5 10 15 20 25 30 35 40 45 50)

Levels of Evidence adapted from the American Speech and Hearing Association (ASHA, 2004) and the Scottish Intercollegiate Guideline Network (Harbour & Miller, 2001)

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Slide 13

Targets of treatment

Target	# of studies
Naming/Lexical retrieval	67
Written naming/Spelling	16
AAC/Multimodal comm	8
Functional comm	7
Semantic knowledge	6
Speech prod/fluency	6
Discourse	5
Syntax/morphology	5
General lang and cog	3
Word comprehension	2
Phonology	1

# of studies (x-axis: 0–80)

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Study quality: Appraisal Point System ratings

APS Scale: 0-14 points

Pie chart: 1 point 1%, 2 points 1%, 3 points 6%, 4 points 8%, 5 points 8%, 6 points 11%, 7 points 12%, 8 points 25%, 9 points 7%, 10 points 17%, 12 points 4%

Appraisal Point System (APS) Categories and Items	n/103	%
Risk of Bias		
2. Comparison/Control	37	35.9
3. Random assignment	0	0
Both risk of bias items	0	0
Reporting Quality		
4. Participants	82	79.6
5. Measures and Materials	85	82.5
6. Procedures	7	6.8
All three reporting quality items	4	3.9
Clinical Relevance		
1. Rationale	95	92.2
8. Clinical significance	80	77.7
9. Discussion/Interpretation	97	94.2
All three clinical relevance items	70	68.0
Data Analysis		
7. Statistical Reporting	68	66.0

Oren et al., 2014, *JSLHR*

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Treatment outcomes: 45 highest quality studies

Number of studies reporting on each outcome type (y-axis 0–50)

Categories: Primary outcomes, Generalization, Maintenance, Social validity

■ Studies in which authors report no effect of treatment
■ Studies in which authors report an effect of treatment in at least one participant

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Systematic review findings

- The evidence indicates that behavioral intervention for speech/language changes associated with PPA results in...
  - Gains for trained skills/targets
  - Gains for untrained skills/targets
  - Maintenance of treatment gains beyond the immediate post-treatment period
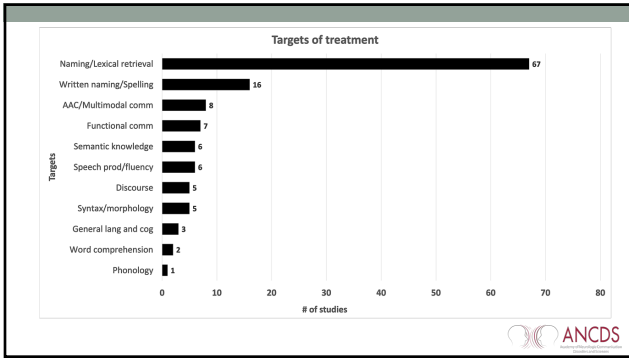 - Socially validated treatment gains (low number of studies reporting)
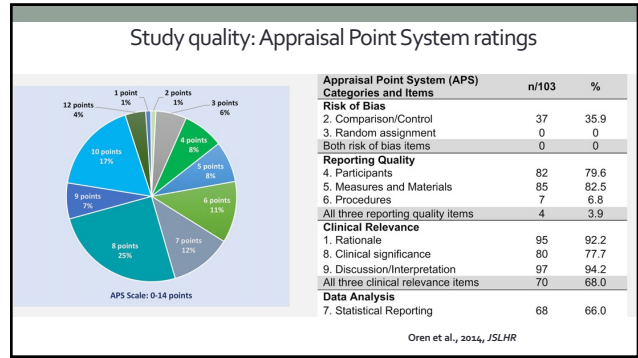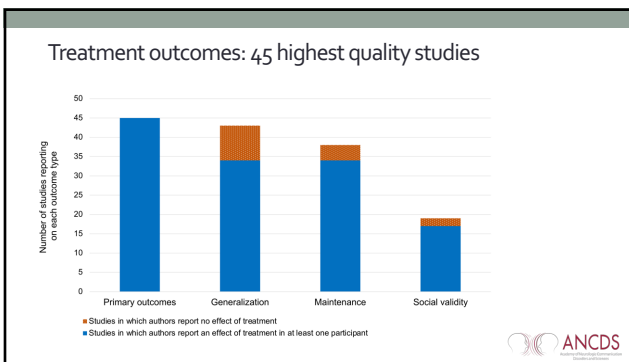- Limitations of the evidence
  - No level 1 studies (no RCTs)
  - Need for more rigorous design (adequate controls, randomization, fidelity reporting)
  - Limited evidence beyond lexical retrieval treatment
  - Need for interventions that take into account progression over time, evolving clinical profile
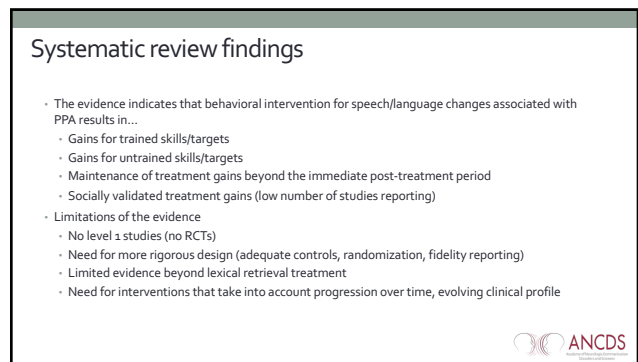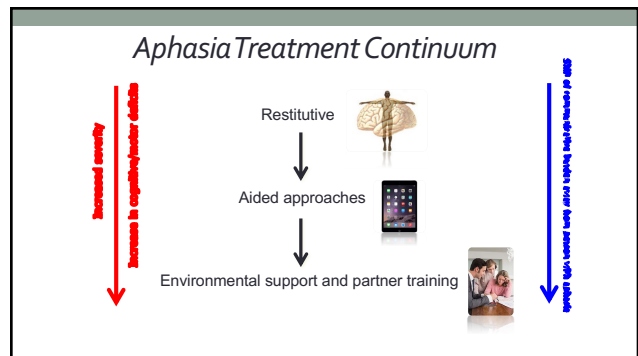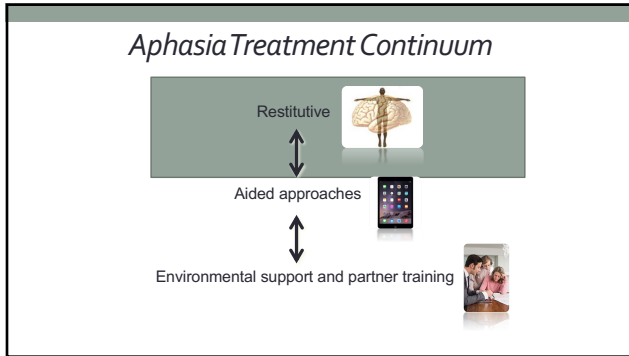
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The goal of speech-language intervention throughout the severity continuum: *Functional communication*

- Maximize communication at each stage of illness
- Consider the individual in the context of their environment(s) and functional needs
- Tailor treatment approach to current status; take into account likely progression

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Slide 19

Aphasia Treatment Continuum

Restitutive

↓

Aided approaches

↓

Environmental support and partner training

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Slide 20

Aphasia Treatment Continuum

Restitutive

Aided approaches

Environmental support and partner training

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Slide 21

Restitutive interventions

- Two treatment approaches for mild-moderate PPA: immediate and long-term outcomes
  - Naming treatment for semantic (sv) and logopenic (lv) PPA
  - Script training for speech production and fluency in nonfluent/agrammatic (nfv) PPA

svPPA = anomia → Naming treatment

lvPPA = anomia → Naming treatment

nfvPPA = impaired speech production/fluency → Script training

National Institute on Deafness and Other Communication Disorders — R01DC016291

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Enrollment (current multi-site trial with UCSF)

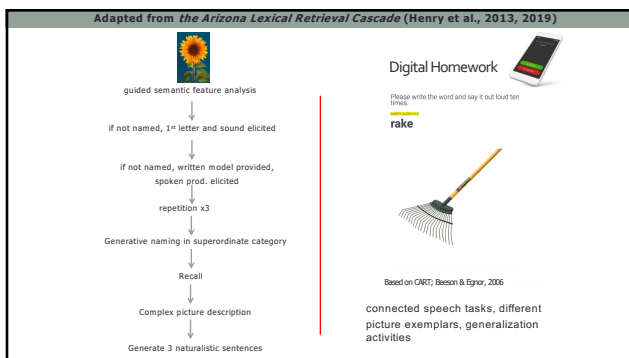|	# enrolled	# MRI scanned	Pre-Testing	Treatment	Post-Testing	3 month f/u	6 month f/u	1 yr f/u
Nonfluent variant	41	21	37	34	34	32	30	25
Semantic variant	27	13	25	22	21	19	18	15
Logopenic variant	42	24	42	41	41	40	38	32
Total	110	58	104	97	96	91	86	72

ClinicalTrials.gov: NCT04881617

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Slide 23

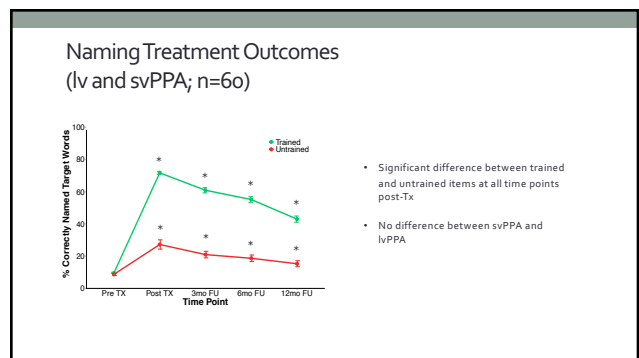### Treatment for word-finding in PPA
(Henry et al., 2013, *Brain and Language*; Henry et al., 2019, *JSLHR*; Grasso et al., 2021, *Brain Sci*)

- Anomia is a pervasive feature in PPA
- Training hierarchy designed to capitalize on spared cognitive-linguistic processes and encourage self-cueing (Arizona Lexical Retrieval Cascade; Henry et al., 2013)
  - Two one-hour sessions per week (4-8 weeks total)
  - Daily home practice
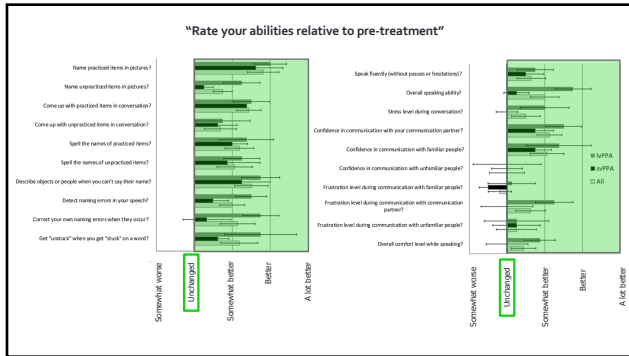 - Individually-tailored, functional treatment sets (personal photos)

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Slide 25

Adapted from *the Arizona Lexical Retrieval Cascade* (Henry et al., 2013, 2019)

guided semantic feature analysis
↓
if not named, 1st letter and sound elicited
↓
if not named, written model provided, spoken prod. elicited
↓
repetition x3
↓
Generative naming in superordinate category
↓
Recall
↓
Complex picture description
↓
Generate 3 naturalistic sentences

Digital Homework

Please write the word and say it out loud ten times.

rake

Based on CART; Beeson & Egnor, 2006

connected speech tasks, different picture exemplars, generalization activities

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Slide 26

Naming Treatment Outcomes
(lv and svPPA; n=60)

- Significant difference between trained and untrained items at all time points post-Tx
- No difference between svPPA and lvPPA

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Slide 29:

"Rate your abilities relative to pre-treatment"

Name practiced items in pictures?
Name unpracticed items in pictures?
Come up with practiced items in conversation?
Come up with unpracticed items in conversation?
Spell the names of practiced items?
Spell the names of unpracticed items?
Describe objects or people when you can't say their name?
Detect naming errors in your speech?
Correct your own naming errors when they occur?
Get "unstuck" when you get "stuck" on a word?

Somewhat worse | Unchanged | Somewhat better | Better | A lot better

Speak fluently (without pauses or hesitations)?
Overall speaking ability?
Stress level during conversation?
Confidence in communication with your communication partner?
Confidence in communication with familiar people?
Confidence in communication with unfamiliar people?
Frustration level during communication with familiar people?
Frustration level during communication with communication partner?
Frustration level during communication with unfamiliar people?
Overall comfort level while speaking?

■ lvPPA
■ svPPA
☐ All

Somewhat worse | Unchanged | Somewhat better | Better | A lot better

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Slide 30:

Gray matter correlates of treatment response in semantic variant PPA (Dial et al., under review)

Heather Dial, PhD
NIH/NIDCD F32DC016812

- Response to naming treatment associated with anatomical sparing of the
  - **left hippocampus**
    - trained and untrained items
  - **supramarginal gyrus/angular gyrus**
    - trained items
- Importance of regions supporting **episodic memory** and **phonological processing** in improved naming

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Slide 31:

Gray matter predictors of treatment response in logopenic variant PPA

Heather Dial, PhD
NIH/NIDCD F32DC016812

- Response to naming treatment associated with
  - **Left and right middle and inferior frontal gyri (IFG)**

  - **Left IFG**
    - trained and untrained items
    - implicated in **semantic and phonological aspects of word retrieval**
      - role in **generalized improvement** of word retrieval

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Slide 32:

Treatment for speech production in nonfluent/agrammatic PPA
(Henry et al., 2018, *Brain*; Schaffer et al., 2020, *Neuropsych Rehab*; Schaffer et al., 2021, *AJSLP*)

- Video-Implemented Script Training for Aphasia (VISTA)
  - At-home script training practice (30 minutes per day) with an audio-visual model
    - Adapted from **speech entrainment** technique (Fridriksson et al., 2012)
  - Sessions with clinician to promote memorization and conversational usage
    - Trained and untrained functional topics developed collaboratively with the clinician

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Slide 33:

Home practice video:

Easy script:

Football is a great sport. My favorite NFL team is the Green Bay Packers. My college team is the UW Badgers. I love to watch football all the time.

Hard script:

Fly-fishing is a passion of mine for numerous reasons, but mostly for the wonderful places it takes me to. The waters and the ecosystems are inevitably beautiful and interesting. I also enjoy the fact that fly-fishing is so demanding, challenging and totally absorbing. It serves a therapeutic role that releases me from the stresses of everyday life. When I am not fishing, I often find myself planning a trip to one of the places I love to fish most, including Connecticut, Montana, Alaska, Canada, or Texas.
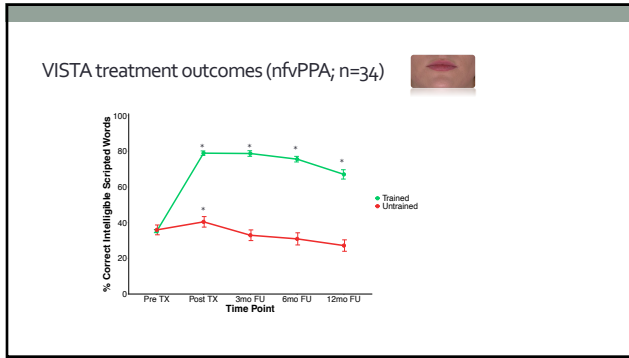
30 minutes of unison speech production per day

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Slide 34:

Video Script Training Tx Session

Structured Tasks

1. Recognize script sentences from foils
2. Put script sentences in order
3. Read script aloud
4. Produce script sentences in response to questions
5. Produce entire script from memory
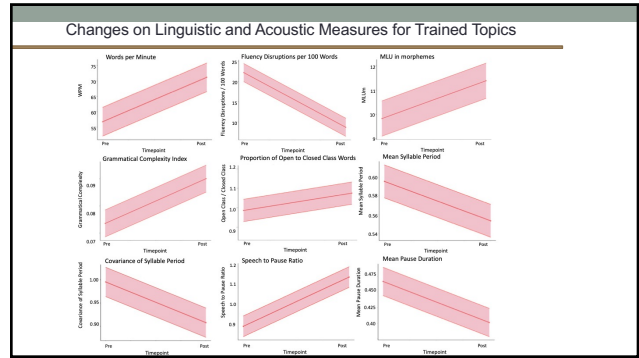6. Respond to questions with scripted sentences (not in scripted order)

Functional Application

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Slide 35
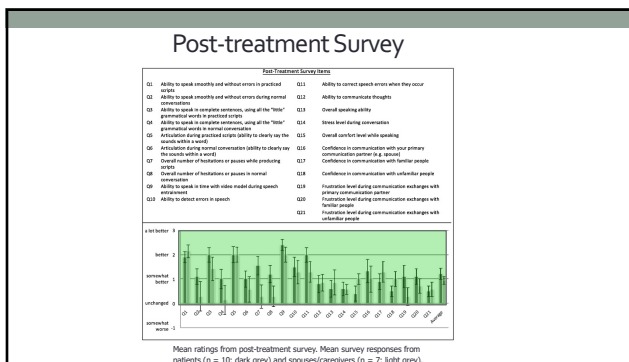
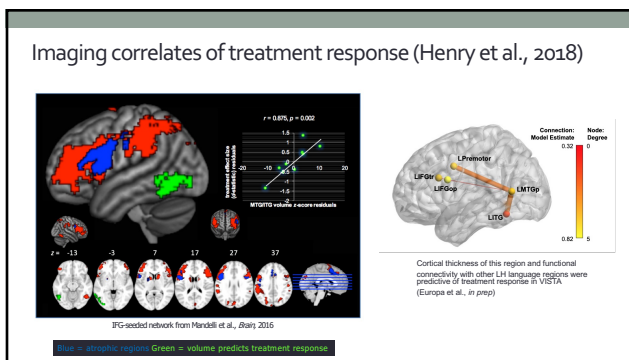### VISTA treatment outcomes (nfvPPA; n=34)

Chart: % Correct Intelligible Scripted Words (y-axis, 0–100) vs Time Point (x-axis: Pre TX, Post TX, 3mo FU, 6mo FU, 12mo FU). Legend: Trained (green), Untrained (red).

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Slide 36

Changes on Linguistic and Acoustic Measures for Trained Topics

Panels: Words per Minute (WPM), Fluency Disruptions per 100 Words, MLU in morphemes (MLUm); Grammatical Complexity Index, Proportion of Open to Closed Class Words (Open Class / Closed Class), Mean Syllable Period; Covariance of Syllable Period, Speech to Pause Ratio, Mean Pause Duration. X-axis: Pre / Post Timepoint.

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Slide 37

Post-treatment Survey

Post-Treatment Survey Items

Q1	Ability to speak smoothly and without errors in practiced scripts	Q11	Ability to correct speech errors when they occur
Q2	Ability to speak smoothly and without errors during normal conversations	Q12	Ability to communicate thoughts
Q3	Ability to speak in complete sentences, using all the "little" grammatical words in practiced scripts	Q13	Overall speaking ability
Q4	Ability to speak in complete sentences, using all the "little" grammatical words in normal conversation	Q14	Stress level during conversation
Q5	Articulation during practiced scripts (ability to clearly say the sounds within a word)	Q15	Overall comfort level while speaking
Q6	Articulation during normal conversation (ability to clearly say the sounds within a word)	Q16	Confidence in communication with your primary communication partner (e.g. spouse)
Q7	Overall number of hesitations or pauses while producing scripts	Q17	Confidence in communication with familiar people
Q8	Overall number of hesitations or pauses in normal conversation	Q18	Confidence in communication with unfamiliar people
Q9	Ability to speak in time with video model during speech entrainment	Q19	Frustration level during communication exchanges with primary communication partner
Q10	Ability to detect errors in speech	Q20	Frustration level during communication exchanges with familiar people
		Q21	Frustration level during communication exchanges with unfamiliar people

Mean ratings from post-treatment survey. Mean survey responses from patients (n = 10; dark grey) and spouses/caregivers (n = 7; light grey).

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Slide 38

Neural correlates of treatment response

- Lesion studies
  - Compensates for left frontal damage (Fridriksson et al., 2015; Bonilha et al., 2019)

Fig. 2 – Results from lesion-symptom mapping analysis for standardized spontaneous speech scores (red) and improvement in speech fluency (green). These results are thresholded at p < .005 using permutation thresholding to control for multiple comparisons.

- fMRI studies
  - "Entrained" speech capitalizes on spared ventral pathway to activate speech motor programs (Venezia et al., 2016)

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Imaging correlates of treatment response (Henry et al., 2018)

r = 0.875, p = 0.002

Connection: Model Estimate / Node: Degree

LIFGtr, LIFGor, LIFGop, LPremotor, LMTGp, LITG

Cortical thickness of this region and functional connectivity with other LH language regions were predictive of treatment response in VISTA (Europa et al., in prep)

IFG-seeded network from Mandelli et al., Brain, 2016

Blue = atrophic regions Green = volume predicts treatment response
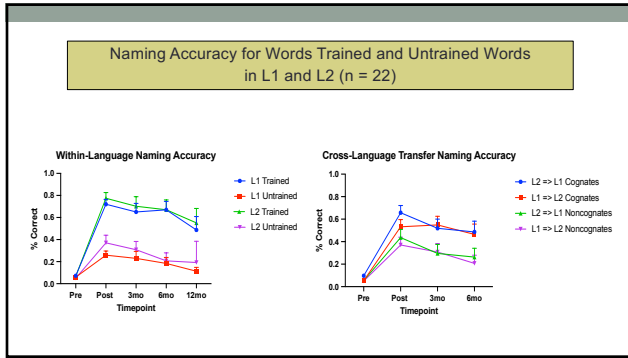
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Slide 40
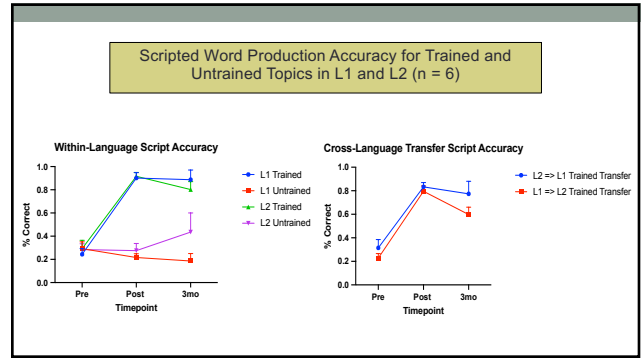
Treatment for Bilingual Speakers with PPA

Stephanie M. Grasso, PhD, CCC-SLP
NIH/NIDCD F31DC016229

- LRT and VISTA
  - Two phases of intervention
    - One language of intervention per phase
    - Distinct targets in each language
    - Counter-balancing individuals who receive treatment in dominant language in first phase
- Within-language gains
  - Does one language demonstrate greater improvement?
    - Dominance and L1/L2 status
- Cross-linguistic transfer effects
  - Is transfer viable in each variant?
  - Is transfer greater from nondominant language to dominant language?
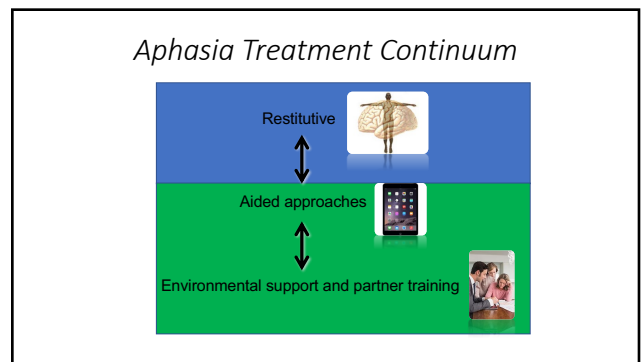 - Does the inclusion of cross-linguistic cognates support greater transfer effects?

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Naming Accuracy for Words Trained and Untrained Words in L1 and L2 (n = 22)

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Scripted Word Production Accuracy for Trained and Untrained Topics in L1 and L2 (n = 6)

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Potent ingredients for restitutive intervention in PPA

- Strategic nature of naming treatment
- Individually-tailored treatment stimuli
  - Pictures of participants' own items that they are consistently unable to name
  - Functional scripts developed collaboratively and tailored to individual speech-language profile
- Daily home practice to augment sessions with the clinician
  - Electronically-delivered and tracked
- Ongoing practice

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Aphasia Treatment Continuum

Restitutive

Aided approaches

Environmental support and partner training

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The Treatment Challenge:

*"To put the patient's residual lexicon **visually in front of him/her** so that the patient can access needed vocabulary to participate in daily activities as language skills decline."*

--M. Fried-Oken

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Low tech options

- Communication books
- Photo albums
- Pictures
- Newspapers
- Communication boards
- Cards
- Remnants
- Paper and pencil

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High tech options

- Dedicated speech generating devices
- Mobile technology options

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Environmental support, communication partner training

The 'Better Conversations with Primary Progressive Aphasia (BCPPA)' program for people with PPA (Primary Progressive Aphasia): protocol for a randomised controlled pilot study

Anna Volkmer, Aimee Spector, Jason D Warren and Suzanne Beeke

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New Directions: Interweaving restitutive, compensatory, and partner-focused training
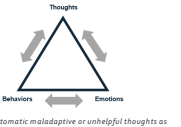
- Stage 1 study (n=21) evaluating the utility of a novel, person-centered treatment targeting functional communication by incorporating elements of restitutive, compensatory, and care-partner-focused interventions

Tell me about it
- This is a **type of...**
- This is **similar to...**
- I **use it** to...
- Describe **how it looks**
- Describe **memories** of it
- What is the first letter or sound?

Write it | Find it in the book

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New Directions: Combined restitutive and psychosocial intervention (Schaffer et al., 2021, *AJSLP*)

- Counseling = Aphasia-modified CBT
- Speech-language treatment =
  - Script training (VISTA; Henry et al., 2018)
  - Lexical Retrieval Treatment (LRT; Henry et al., 2019)
- n = 9 (3 per PPA variant)

Nonfluent/agrammatic variant (n = 3)

identify automatic maladaptive or unhelpful thoughts as they occur and respond to them in a more adaptive way

Logopenic variant (n=3); Semantic variant (n=3)

Kristin M. Schaffer, PhD, CCC-SLP
NIH/NIDCD 1F31DC019044

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Preliminary Results

- **Acceptability**
  - Average participant satisfaction rating of 30 (out of 32; CSQ-8; Larsen et al., 1979)
- **Feasibility**
  - All participants complied with both intervention components (0% attrition)
- **Speech/Language Outcomes**
  - Comparable relative to comparison cohort who did not receive counseling
- Group-level **phenomenological analysis** indicates post-treatment themes of
  - *Acceptance, Resilience, Self-efficacy, Gratitude, Desire for social connection, Present-focused thinking*

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Summary

- Speech-language intervention for progressive aphasia is efficacious and warranted
  - Targeted behavioral treatment results in **significant, generalized, and lasting improvement** of speech and language ability in PPA
- Behavioral restitution is possible in the context of neurodegeneration
  - Anatomically-spared brain regions support recovery of function
- PPA is a complex disorder requiring a person-centred, dynamic, and evolving approach
  - Clinicians must consider evidence-based interventions and broader principles of practice
- Speech-language intervention in PPA should be the standard of care, not the exception
  - Broad ramifications for service provision in patients with neurodegenerative disease who have been historically underserved by rehabilitation specialists

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  - Carly Miller, M.S., CCC-SLP
  - Stephanie M. Grasso, M.A., CCC-SLP
  - Heather Dial, Ph.D (now at Univ. of Houston)
  - Lisa Wauters, M.A., CCC-SLP
  - Kristin Schaffer, M.S., CCC-SLP
  - Rachel Tessmer, M.A., CF-SLP
  - Gary Robinaugh, M.A., CCC-SLP
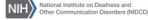 - Karinne Berstis, M.S., CCC-SLP

- ALBA Lab, UCSF Memory and Aging Center
  - Maria Luisa Gorno-Tempini, M.D., Ph.D
  - Eduardo Europa, Ph.D, CCC-SLP (now at Cal State Chico)
  - Zoe Ezzes, M.S., CCC-SLP
  - Maria Luisa Mandelli, Ph.D
  - H. Isabel Hubbard, Ph.D, CCC-SLP (now at Univ. of New Mexico)

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NIH National Institute on Deafness and Other Communication Disorders (NIDCD)

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