The Thesis Committee for Wylin Marie Daigle
Certifies that this is the approved version of the following thesis:

Treatment for Speech Production and Fluency in Two Individuals with Non-fluent Primary Progressive Aphasia

APPROVED BY
SUPERVISING COMMITTEE:

Supervisor:

Maya L. Henry

Bharath Chandrasekaran

Treatment for Speech Production and Fluency in Two Individuals with Non-fluent Primary Progressive Aphasia

by

Wylin Marie Daigle, B.A., B.S.

Thesis

Presented to the Faculty of the Graduate School of

The University of Texas at Austin

in Partial Fulfillment

of the Requirements

for the Degree of

Master of Arts

The University of Texas at Austin

May, 2015

Dedication

To Thiew Hoon Ng, thank you for giving me my legs, eyes, a breathing body, a beating heart, my life and for this opportunity to study and put these things to use. This is for you. We must be even by now, right?

To Michael Edward Walston, for keeping the heavens from falling alongside me.

Acknowledgements

This project is not possible without the work and time of many talented individuals both here in Texas and across the country. I want to give much gratitude and a Texas-sized thank-you to Maya Henry for this opportunity, your generosity of time, ideas, lab resources, and experience. I could not have asked for a better guide and mentor in taking on this research project. A boulder sized thank you to Stephanie Grasso for your generosity. Thank you for your support and edits of this manuscript. Many thanks to the Aphasia Lab team for making all the moving parts of this project happen. Thank you Bharath Chandrasekaran for your insightful feedback and edits. Thank you to all the faculty for keeping me thinking deeply about issues in this field and for this base of knowledge to work from. Thank you to all my CSD friends and colleagues at the University of Washington and at the University of Texas. You all have kept me in the loop, kept my perspective in check, and kept me laughing for which I am most grateful.

Abstract

Treatment for Speech Production and Fluency in Two Individuals with Non-fluent Primary Progressive Aphasia

Wylin Marie Daigle, M.A.

The University of Texas at Austin, 2015

Supervisor: Maya Henry

Purpose: The current study examined the utility of a script-based treatment protocol for improving speech production and fluency in two individuals with the non-fluent variant of primary progressive aphasia (PPA).

Method: The treatment protocol was a modified version of the "speech entrainment" technique examined in non-fluent stroke aphasia by Fridriksson and colleagues (2012). Personalized scripts were recorded as videos of a healthy speaker's mouth. Scripts were rehearsed via synchronized spoken production in daily homework. Treatment sessions with the clinician targeted memorization and conversational usage. The protocol was modified from the original study in its use of 1.) topics of interest to the participant, 2.) tailored speech rate based on the participant's habitual rate of speech in reading and spontaneous speech tasks, and 3.) tailored level of script difficulty based on the participants' motor and linguistic profile. Speech entrainment is a homework-based treatment and required participants to practice thirty minutes per day over the course of nine weeks of treatment in addition to receiving in-person treatment twice per week. Outcome measures for trained and untrained scripts were percent correct and intelligible scripted words, errors by word class, total number of grammatical errors, and total percent intelligibility.

Results: Both participants showed significant improvement in intelligibility and accuracy of trained scripts and generalized improvement on untrained scripts was observed in one participant. Participants showed a significant reduction in grammatical errors after treatment. One participant showed significant changes in overall intelligibility after treatment, and maintenance of intelligibility and script accuracy at three months post treatment.

Conclusion: Script training using speech entrainment resulted in improved intelligibility, grammaticality, and overall accuracy for scripted material in two participants with PPA. Speech entrainment may be a viable treatment method for individuals with non-fluent PPA, particularly with modifications to support increased intelligibility for those with concomitant motor speech deficits. Because speech entrainment is homework-based, the frequency and dosage of treatment are maximized without necessitating an increase in face-to-face treatment sessions. This has promising implications for individuals facing limited reimbursement for treatment and for individuals who have mobility issues.

Table of Contents

List of Tables

List of Figures

Introduction

Primary progressive aphasia (PPA) is a progressive neurological condition caused by neurodegenerative disease affecting areas of the brain that support communication (Gorno-Tempini, Hillis, Weintraub, Kertesz, Mendez & Cappa, 2011; Mesulam, 2001; Henry, Meese, Truong, Babiak, Miller & Gorno-Tempini, 2013). It is characterized by speech-language difficulties that interfere with activities of daily living, while other cognitive faculties are relatively spared, particularly early in the disease course (Gorno-Tempini et al., 2011). There are three clinical variants: semantic variant (svPPA), which presents with impaired word comprehension and naming; logopenic variant (lvPPA), which presents with anomia and impaired repetition, and non-fluent/agrammatic variant (nfvPPA), which presents primarily with non-fluent spontaneous speech with deficits in motor speech and grammar (i.e. syntax and morphology) (Henry et al., 2013).

PPA is diagnosed clinically and brain imaging plays a complementary role in diagnosis and subtyping by variant. Broadly, brain imaging in PPA reveals atrophy of the language dominant hemisphere (typically left). Imaging in svPPA reveals atrophy predominantly in the anterior temporal lobe (most often left greater than right hemisphere) (Gorno-Tempini et al., 2011; Mesulam, 2001). LvPPA imaging findings are characterized by atrophy in the left posterior perisylvian region. In nfvPPA, imaging shows atrophy in the left posterior fronto-insular region, including Broca's area (Gorno-Tempini et al., 2004; Mesulam, 2001; Henry et al., 2013).

1.1 Speech-language treatment in PPA

The treatment literature in PPA has focused mostly on individuals with the semantic variant, with less attention given to individuals with the logopenic or non-fluent variants (Henry et al., 2013). Treatment for individuals with non-fluent PPA has targeted sentence production, (Schneider & Thompson, 2003) phonological processing, (Louis, Espesser, Rey, Daffaure, Cristo & Habib, 2001), multisyllabic word production (Henry et al., 2013), and lexical retrieval (Jokel, Cupit, Rochon & Leonard, 2009). No treatment research has directly addressed fluent speech production in connected speech in individuals with non-fluent PPA, despite this being the most prominent deficit in these patients. Various approaches to training speech production and fluency have been implemented in individuals with non-fluent speech caused by stroke.

1.2 Treatment Overview for the non-fluent variant of PPA and AOS

Only one study, Henry et al., (2013), has explored treatment approaches to improve speech production in individuals with apraxia of speech (AOS) associated with the non-fluent variant of PPA. Treatment consisted of structured oral reading of text with systematic rehearsal of multisyllabic word production in sentence context. The participant was trained to self-detect major speech errors, which included sound deletion, insertion, transposition, substitution, or distorted substitutions/insertions. If the word in error was a multisyllabic word, the word was divided into syllables and the participant produced and repeated the word (syllable by syllable) until each syllable was produced correctly in isolation. Once the word was mastered in isolation the participant repeated the sentence with the target word in an attempt to produce it correctly. If the word was produced in error, the participant returned to rehearsing the word's constituent syllables in isolation. Results revealed that multisyllabic word production in trained text became more accurate and stable over the course of treatment, and was completely error-free over the last four treatment sessions. The participant showed a decrease in major speech errors on multisyllabic words when reading difficult untrained texts as well as an increase in successfully self-corrected speech errors post-treatment. With continued home practice, improvement was maintained up to one year following treatment.

1.3 TREATMENT OVERVIEW FOR SPEECH PRODUCTION AND FLUENCY IN NON-FLUENT APHASIA CAUSED BY STROKE

Fluent speech production has been targeted as a speech and language therapy goal in individuals with Broca's aphasia. Broca's aphasia is an acquired language disorder resulting from lesions located in the posterior inferior frontal gyrus, or the anterior speech area of the left hemisphere (Broca, 1861; Geschwind, 1965; Dronkers 1996). Individuals with Broca's aphasia typically present with halting, non-fluent language production, often with comorbid disordered speech symptoms consistent with AOS and/or dysarthria (Brookshire, 2007).

Several treatment options have been proposed to facilitate fluent speech in individuals with Broca's aphasia (Yamaguchi, Akanuma, Hatayama, Otera & Meguro, 2011; Wilson, Parsons & Reutens, 2006; Tomaino, 2012; Schlaug, Marchina & Norton, 2008; Racette, Bard & Peretz, 2006; Concklyn, Novak, Boissy, Bethoux & Chemali, 2012; Belin, Van Eeckhout, Zilbovicius, Rem, Francois & Guillaume, 1996; Sparks, 2008; Albert, Sparks & Helm, 1973; Sparks & Holland, 1976; Stahl, Kotz, Henseler, Turner & Geyer, 2011). One study found that when individuals with aphasia sang or spoke along with an auditory model while learning novel songs, they repeated and recalled more words when singing than when speaking (Racette et al, 2006). Results suggested that singing in unison with an auditory model, or choral singing, is more effective than choral speech in increasing word intelligibility.

Another study examined 15 patients with chronic non-fluent aphasia who received singing therapy, rhythmic therapy, or standard speech therapy (Stahl et al., 2013). Results revealed that both singing and rhythmic therapies yielded improvement in the production of common, formulaic phrases. Conversely, participants who received standard speech therapy did not improve their production of formulaic phrases, but did improve in production of non-formulaic phrases, which included an unlikely but syntactically correct phrase, such as might occur in modern poetry (e.g., "Bright forest, there at the boat, thin like oak"), in contrast to individuals treated with singing and rhythmic therapy. Improvement of speech production may be due, in part, to the drawing out of syllables, and to the 50% rate decrease (approximately) that occurs during singing relative to speaking (Racette, Bard & Peretz, 2006). This slower rate is advantageous for individuals with non-fluent aphasia with apraxia of speech and dysarthria because there is more time for these individuals to plan speech and motor movements (Stahl, Kotz, Henseler, Turner & Geyer, 2011).

Melodic Intonation Therapy (MIT) is another treatment approach designed to improve expressive language of individuals with non-fluent aphasia. It is a hierarchically structured intonation-based treatment that uses intoned or sung patterns to exaggerate prosody patterns in normal speech (Morrow-Odom & Swann, 2013; Schlaug, Marchina & Norton, 2008; Belin, Van Eeckhout, Zilbovicius, Remy, Francois & Guillaume, 1996; Breier, Randle, Maher & Papanicolaou, 2010). The melodic intonation comprises prosodic speech patterns using two pitches, and patients gradually work to increase phrase length (Schlaug, Norton, Marchina, Zipse & Wan, 2010). MIT also contains continuous voicing, inherent in singing, and the rhythmic tapping of each syllable using the participant's left hand. Left-hand tapping is intended to "engage a right-hemispheric, sensorimotor network that may, in turn, provide an impulse for verbal production" in the same way that a metronome has been shown to act as a 'pacemaker' in motor activities such as rhythmic entrainment (Schlaug, Norton, Marchina, Zipse & Wan, 2010, p. 661). Singing and MIT are two treatment approaches that have addressed fluency and speech deficits in individuals with Broca's aphasia. However, these approaches often lack naturalness at the conversational level. In addition to these two approaches, script training has been utilized in this population and provides a more functional approach to increasing speech fluency.

1.4 Script Training in aphasia

Script training has been examined as a means to improve non-fluent speech in individuals with Broca's aphasia (Youmans, Holland, Munoz & Bourgeois, 2005; Youmans, Youmans & Hancock, 2011; Cherney, Halper, Holland & Cole, 2008; Cherney, Halper & Kaye, 2010; Fridriksson, Hubbard, Hudspeth, Holland, Bonilha, Fromm & Rorden, 2012). However, script training has not been implemented in individuals with non-fluent PPA and only a few studies have examined this approach in individuals with prominent apraxia of speech (Youmans, Youmans & Hancock, 2011; Henry et al., 2013).

Script training is a therapy method that trains participants to produce pre-determined, scripted language. Scripts are often written in collaboration with the participant in order to maximize usage in functional communication exchanges. Youmans, Holland, Muñoz and Bourgeois (2005) described script training as a therapy approach that has been used to "re-inject islands of automatic natural language" by having participants practice scripts as monologues and, later, in conversational contexts. To re-establish automaticity, therapy focuses on the whole message rather than specific language component skills such as word finding and grammar. This deflection from specific components of language thus allows language production to emerge with less effort.

Their study (Youmans et al., 2005) utilized a protocol wherein scripts were trained one phrase at a time through a hierarchy that included phrase repetition, choral reading of phrases with the clinician, and independent production. Mastery of a phrase (in order to move onto the next phrase) was determined when the participant independently recited the phrase at least 20 consecutive times. Participants were expected to practice for 15 minutes per day and were given audiotape cassettes of client and clinician-produced versions of the script. Once one entire script was mastered, monologue scripts were practiced in conversation with the therapist as well as with novel conversation partners. Results showed that script performance improved to 97% and 100% accuracy for two persons with non-fluent aphasia using a single-subject, multiple baseline design across three different scripts. A more recent study (Goldberg, Haley and Jacks, 2012) examined how script training can improve non-fluent speech in individuals with Broca’s aphasia to facilitate automatic spoken production of trained scripts. Treatment capitalized on the patient’s spared comprehension and cognitive abilities despite significant expressive speech difficulties. Results showed mastery of scripts, more automatic and natural speech production, an increase in speaking rate, and relatively errorless production.

Script training has more recently been given a technological boost with computer-based approaches that make practice for participants portable. Cherney, Halper and Kaye (2008) used AphasiaScripts©, a computer software program developed for training conversational scripts in clients with aphasia. The program consists of an avatar or animated agent that serves as a virtual therapist. Scripts are developed with the participant and are incorporated into a whole conversation with the virtual therapist. Script treatment for AphasiaScripts© has three phases. First, the participant listens to the whole script silently as it appears on the screen. Next the participant practices each sentence repeatedly through oral reading of the sentences in unison with the avatar. Specific individual words can be practiced separately as well. The final step has the client practice the entire conversation by taking turns with the virtual therapist. Results showed improvement for the three participants with chronic aphasia (i.e., Broca's, Wernicke's and anomic) in the content, grammatical productivity and rate of script production for every script following training with AphasiaScripts©.

More recently, Fridriksson et al., (2012) utilized a somewhat different approach to training scripted material with a technique called "speech entrainment." Their study examined changes in speech fluency brought about by training with audio-visual speech stimuli involving real human models in subjects with non-fluent aphasia caused by stroke. The treatment utilized general (non-personalized) scripts, trained and untrained, that were recorded by a speaker whose mouth could be seen on an iPod screen. Participants attempted to recite the script by simultaneously mimicking the speaker's mouth movements. Three variables were studied: performance with audio and visual feedback, performance with audio-only feedback, and spontaneous speech without speech entrainment. No changes were observed with the audio-only scenario or in spontaneous speech. The audio-visual speech condition was shown, using functional MRI, to activate residual left frontal speech areas in patients with non-fluent speech, resulting in improved speech production. A follow-up study addressed the neural bases for improved speech production via speech entrainment using voxel-based lesion symptom mapping in a group of individuals with stroke-induced aphasia (Fridriksson, Basilakos, Hickok, Bonilha and Rorden, 2015). The lesion analysis showed that speech entrainment facilitated fluency in non-fluent patients with damage to Broca's area (specifically, pars opercularis of the inferior frontal gyrus), which is presumed to support speech syllable programming. The authors proposed that facilitation of speech fluency in speech entrainment may occur via activation of auditory-visual syllable targets in an alternative auditory-motor circuit. The auditory-motor pathway, outlined in the current Hierarchical State Feedback Control Model (Hickok, 2014), typically involves motor syllable programs in the inferior frontal gyrus, auditory syllable targets in superior temporal gyrus/sulcus, and an area at the temporoparietal junction that serves as an auditory-motor interface between the two. Critically, activation of auditory-visual targets using speech entrainment may facilitate processing via an alternate route, one that circumvents damaged motor programs in the inferior frontal gyrus.

The on-line mimicking of audio-visual speech allowed participants with Broca's aphasia to increase their speech output, produce a greater variety of words, and to speak at a rate more closely approximating normal fluency. However, severe apraxia of speech (AOS) was noted as a contraindication for speech entrainment in that study. The authors hypothesized that motor speech processing must be largely preserved for speech entrainment to be beneficial, as results showed improvement for patients with milder forms of apraxia of speech.

1.5 Apraxia of speech and script training

Acquired apraxia of speech (AOS) is a prominent feature of the non-fluent variant of PPA (Gorno-Tempini et al., 2011; Henry et al., 2013). AOS is a motor speech planning disorder that presents with deficits in the ability to select and sequence the motor commands needed to correctly position the articulators during the voluntary production of phonemes (Brookshire, 2007). The disruption of programming and sequencing of the oral patterns for speech causes phonetic and prosodic distortions (Duffy, 2005; Youmans, Youmans & Hancock, 2011). AOS renders production of multisyllabic words difficult, due to increased articulatory complexity (Henry et al., 2013). One study has found script training to be a functional treatment approach in this population because AOS "involves the fundamental loss of automaticity" (Youmans, Youmans & Hancock, 2011). This study evaluated script training efficacy for individuals with AOS concurrent with mild anomic aphasia. Although scripts were not produced without error, all patients were able to successfully master their scripts by meeting the accuracy and intelligibility criterion of 90%. Participants reported increased confidence, speaking ease, and speech naturalness as a result of treatment.

1.6 Potential limitations to the original speech entrainment approach (content and speech rate)

The content of scripts themselves is a potentially critical component of speech entrainment treatment because participants are asked to repeatedly practice their scripts daily as homework. Given the repetitive and intensive nature of the daily homework, motivation to practice scripts is an important aspect of this treatment. In order to facilitate participant motivation, it is imperative that the content of scripts is personally relevant and functional for the participant. Fridriksson et al., (2012) used general scripts (e.g., how to make scrambled eggs) that were not tailored to individual participants, in order to achieve consistency of stimulus features across participants. Other script training studies have emphasized the importance of creating personally motivating scripts in collaboration with the participants, which may be autobiographical or concern topics that are of interest to each individual. Goldberg, Haley and Jacks (2012) used individualized scripts that were developed with the participant, a family member, and a clinician. Script training in this study involved a progression through tasks, including repetition, choral reading and independent production. Positive effects were noted for rate of speech, percent of target script words used, and number of disfluencies.

In addition to script content, a potential variable that may influence the effectiveness of an approach such as speech entrainment is speech rate. In Fridriksson et al., (2012), rate of production in video stimuli was not tailored to the participant's average rate of speech, and no script-based studies with non-fluent stroke have observed the effect of modifying the rate of production on treatment outcomes. Two studies found that singing therapy facilitated fluency in individuals with Broca's aphasia, in part because the slower speech rate during singing gave those with concomitant dysarthria more time to plan their speech and motor movements (Racette et al., 2006; Stahl et al., 2011). Additionally, a slower speech rate is thought to reduce the complexity of the neuromotor processes behind speech production (Wilson, Parsons & Reutens, 2006). Thus, tailoring fluency intervention to an individual's natural speech rate may enhance treatment gains.

1.7 Current study

Participants with Broca's aphasia have shown significant improvements in speech production and fluency with script training and speech entrainment treatments, as seen in previous studies, but research has not been extended to examine these treatment techniques in individuals with non-fluent PPA. The aim of this study was to examine the effect of script training via speech entrainment on speech production/fluency and script accuracy for two individuals with non-fluent PPA. The two participants were treated in different locations, one in the Aphasia Research and Treatment Laboratory at the University of Texas at Austin, and one via Skype©, using protocols that were similar but not identical. Scripts were individualized according to each participant's interests, and rate of speech production was tailored to each participant based on their characteristic speech rate. We hypothesized that individuals with non-fluent PPA would master production of trained, scripted material, with improved intelligibility and grammaticality when speaking on trained topics. Also, we hypothesized that, if script rate could be modified to the participant, AOS would not be a contraindication for this treatment approach. Further, we predicted that individuals would show generalized improvement in fluency and articulation in both untrained scripts as well as connected speech.

Alternatively individuals with non-fluent PPA, may not be responsive to this treatment protocol, suggesting that AOS or some other aspect of their speech language profile is a contraindication for responsiveness to this intervention.

Methods

2.1. PARTICIPANTS AND ASSESSMENT MEASURES

Two individuals with the non-fluent variant of PPA participated in this study. The participants were each evaluated with comprehensive measures of speech, language and cognition (Tables 1, 2 and 3).

Table 1
Demographic Data for Participants

Demographic	SE001	SE002
Age	68	71
Education	18	15
Handedness	Right handed	Right handed
Time post onset	Two years	Three years
Gender	M	F

In addition, they underwent high-resolution structural MRI scanning (T-1 weighted) in order to characterize the location and extent of damage in the brain. For this report, we focus on the behavioral characteristics and imaging findings that confirm the progressive aphasia profile and establish language performance prior to the implementation of treatment.

2.1.1 Participant 1: SE001

SE001 was a 68-year-old right-handed male who was diagnosed with primary progressive aphasia (PPA) in 2013 after experiencing a decline in his ability to communicate that began in 2012. SE001 reported that his first notable symptoms were word-finding difficulty and impaired sentence construction. SE001 attended the University of Wisconsin for an undergraduate degree in electrical engineering and earned a Master of Business Administration degree from New York University. He worked as a manager of an aerospace company, but had retired by the time of his initial evaluation at the University of Texas at Austin for this study. At the time of the initial evaluation, he reported, in addition to his speech production difficulties, short-term memory deterioration and difficulties with reading, writing and math, which were previously enjoyable activities. His conversational speech was halting, with frequent pauses. He spoke primarily in single words and short phrases as he struggled to retrieve and articulate words.

A comprehensive neuropsychological evaluation was completed one year prior to SE001's evaluation in our lab. The report from this evaluation indicated average intellectual functioning, although his current functioning was noted to represent a potential mild decline compared to premorbid status. Despite his reported word-finding difficulty, confrontation naming was not significantly impaired. According to his neuropsychological report, a screen of language functions reported evidence for "central dysarthria, mild dyscalculia, mild spelling dyspraxia, and mild dyslexia." Also, he had difficulty articulating "syllabically complex words." Additional findings revealed below-average to average performance on working memory tasks, slowed visuomotor processing speed, and impaired verbal fluency.

2.1.1.1 Behavioral and imaging characteristics

At the time of his initial evaluation at the University of Texas at Austin, SE001 demonstrated evidence of moderate motor speech impairment. Specifically, his performance on the Motor Speech Exam (Wertz, LaPointe & Rosenbek, 1984) was consistent with moderate deficits for both apraxia and dysarthria (5 out of 8 on a severity rating scale with 0 indicating no impairment and 8 indicating no discernable response; Table 2). He showed reduced speed and accuracy of word repetition, particularly as length of stimuli increased. Phonemic paraphasias were evident in connected speech during picture description tasks. With regard to language, his performance on the *Western Aphasia Battery-Revised* (*WAB-R*; Kertesz, 1982) was consistent with Broca's aphasia (Table 2: Aphasia Quotient (*AQ*)=80.6).

Table 2
Speech, Language, and Cognitive Performance for SE001

Assessment	Pre-TX	Post-TX	3 mo post	Normative Data Mean Score (SD)
Mini Mental State Exam (30)	26	*23*	*27*	28(2.4)[1]
Western Aphasia Battery aphasia quotient (100)	80.6	85.5	71.6	≥93.8
Information content (10)	7	9	7	-
Fluency (10)	5	6	4	-
Comprehension (10)	10	9.75	8.8	-
Repetition (10)	7.6	8.5	7.2	-
Naming (10)	8.7	9.5	8.8	-
Boston Naming Test (60)	55	54		54.9[2] (4.3)
Boston Naming Test (30)			23	

[1] *MMSE* Norms for ages 50-54 from Crum, Anthony, Bassett, and Folstein (1993).
[2] Normative Data for males ages 25-88, from Tombaugh and Hubley (1997).

Table 2, Continued

Pyramids and Palm Trees: pictures (14)	14	14	-	13.9 (.24)[3]
Motor Speech Evaluation-apraxia rating (0-7)	5	5	7	6.9 (2.7)[4]
Motor Speech Evaluation-dysarthria rating (0-7)	5	5	6	-
Spaghetti List(24)	10	10	-	-
Arizona Phonological Battery				
Phoneme replacement (words)	10	10	-	-
Phoneme replacement (non-words)	9	7	-	-
Phoneme deletion (words)	7	10	-	-
Phoneme deletion (non-words)	6	6	-	-
Phoneme blending (words)	7	6	-	-
Phoneme blending (non-words)	4	3	-	-
Northwestern Anagram Test (short)				-
Subject Wh-Q's (5)	4	5	0	-
Subject Wh-Q's (5)	0	2	5	-
UCSF Syntax Comprehension (48)	44	44	44	-
Short lexical	8	8	7	-
Short active	8	7	8	-
Short passive	7	8	8	-
Long lexical	7	7	7	-
Long easier	8	8	8	-
Long harder	6	6	6	-
Arizona Battery for Reading and Spelling: ABRS reading: words				
Regular high frequency (9)	8	6	-	-
Regular low frequency (9)	7	9	-	-
Irregular high frequency (5)	5	9	-	-
Irregular low frequency (5)	9	4	-	-
ABRS reading list (non-words)	5	8	-	-
ABRS spelling list (words)				
Regular high frequency (5)	4	-	-	-
Regular low frequency (5)	5	-	-	-
Irregular high frequency (5)	5	-	-	-
Irregular low frequency (5)	4	-	-	-

[3] Normative Data for ages 46-80 (Breining et al., 2015).
[4] Normative Data for ages 70-79 (Zec et al., 1992).

Table 2, Continued

ABRS spelling list (non-words) (10)	3	-	-	-
Oral Mechanism Exam	Unremarkable	-	-	-
Pure Tone Screen	Passed	-	-	-

His spontaneous speech was often telegraphic and halting, with some grammatical organization. Confrontation naming on the *Boston Naming Test* (*BNT*: Kaplan, Goodglass & Weintraub, 2001) was only mildly impaired (correctly produced 55 of 60 items). Object naming on the *WAB-R* was also mildly impaired (58/60 points; 19/20 objects named without cues). SE001's semantic knowledge was preserved, as measured by the picture version of the *Pyramids and Palm Trees Test* (100%) *(PPT*; Howard & Patterson, 1992).

SE001 demonstrated a mild impairment for single word reading and a more severe impairment for non-word reading (30/36 correct for words; 5/18 for non-words), and spelling performance was relatively preserved for words but severely impaired for non-words (18/20 for words; 3/10 for non-words). Example errors for non-words included *snide* for *snite* and *morfer* for *mofer*. Due to severe rigidity in his right arm, the patient started the spelling evaluation by spelling out loud, but thought he would be more accurate if he tried writing the word. SE001 demonstrated difficulty writing the word clearly, so the clinician asked him to clarify illegible letters.

SE001's performance on the *Mini Mental State Examination (MMSE;* Folstein, Folstein & McHugh, 1975) was 26/30, with difficulty observed in repetition of a phrase, writing a grammatical sentence (e.g., *I am Austin)* and copying pentagons. On the *UCSF*

Bedside Neuropsychological Screen (Kramer, Jurik, Sha, Rankin, Rosen & Johnson, 2003), he showed deficits on digit span (digits forward: 4; digits backward: 2). Visuospatial ability and memory for the complex figure (9/17) were impaired, however performance was confounded by weakness in the right arm.

A syntax comprehension test and sentence production test were administered to examine the status of SE001's comprehension and production of canonical and non-canonical sentence structures in sentences of varying length. SE001 demonstrated a mild impairment in syntax comprehension on the *UCSF Syntax Comprehension Test* (Wilson, Dronkers, Ogar, Jang, Growdon, Agosta, Henry, Miller & Gorno-Tempini, 2010) with more errors on longer harder (6/9 correct), short passive (7/9 correct) and long lexical structures (7/9 correct) (44/48 correct for all sentence structures). A syntax production impairment was observed on the *Northwestern Anagram Test (NAT;* Thompson, 2011) with good performance for canonical structures and severe impairment on non-canonical structures (4/5 correct for canonical subject wh-questions; 0/5 correct for non-canonical object wh-questions). This pattern of sentence production deficit is common in individuals with the agrammatic variant of PPA (Caplan & Hanna, 1998; Friedmann & Grodzinski, 1997; Schwarts, Saffran, Fink, Myers & Martin, 1994; Thompson, Cho, Wieneke, Weintraub &Mesulam, 2012; Weintraub, Mesulam, Wieneke, Rademaker, Rogalski & Thomspon, 2009).

Phonological processing difficulty was apparent on the *Arizona Phonological Battery* (*APB*; Kay, Lesser & Coltheart, 1992). SE001's performance on minimal pair discrimination was spared for words and non-words (20/20 for words; 20/20 non-words) and relatively strong for non-verbal phoneme replacement in real and non-words (10/10 for words; 9/10 for non-words). However, he showed impairment in phoneme deletion for words and non-words (4/5 for initial and 3/5 for final position in words; 3/5 for initial and 3/5 for final position in non-words). Impairment was also seen in sound blending, particularly with non-words (7/10 for words; 4/10 for non-words).

SE001's high-resolution structural MRI scan revealed significant widespread cortical atrophy, with more prominent atrophy in the left than right hemisphere (Figure 1). The most pronounced atrophy was observed in the left middle and inferior frontal gyri and insula. The atrophy pattern and cognitive-linguistic profile were consistent with the non-fluent/agrammatic variant of PPA. The extent of atrophy and the behavioral profile reflected a relatively advanced stage of the disease process.

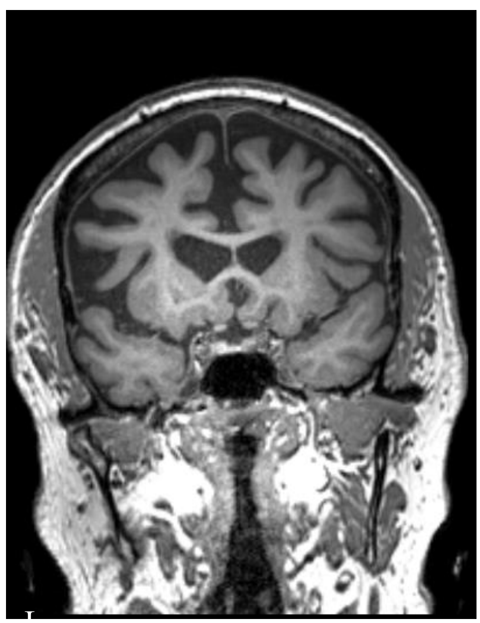

Figure 1. SE001 high-resolution MRI scan was obtained pre-treatment showing bilateral frontal atrophy (L>R).

2.1.2 Participant 2: SE002

SE002 was a 71-year-old right-handed female who was diagnosed with primary progressive aphasia (PPA) in 2012 after experiencing a decline in her ability to communicate that began in early 2011. SE002 reported that her first notable symptoms were difficulty with finding and pronouncing words. SE002 attended the University of Virginia and obtained a nursing degree. She worked as a registered nurse, but had retired by the time of her initial evaluation at the University of Texas at Austin for this study. At the time of the initial evaluation, she reported difficulties with reading and spelling, in addition to her speech production difficulties. Her conversational speech was effortful yet moderately fluent, with frequent pauses, interjections such as "um," and grammatical errors. She demonstrated mild apraxia of speech and no dysarthria.

A comprehensive neuropsychological evaluation was completed six months prior to SE002's evaluation in our lab. The report from this evaluation stated that SE002's speech abilities had deteriorated in the last three years. She reportedly made "grammatical errors when speaking and writing, making phonetic errors during speech, and confuses yes from no." Neuropsychological testing revealed no significant impairment in confrontation naming, but deficits on "repetition, reading and verbal agility." The report noted apraxia of speech and "mild buccofacial apraxia." No motor symptoms were reported.

2.1.2.1 Behavioral and imaging characteristics

At the time of her initial evaluation at the University of Texas at Austin, SE002 demonstrated evidence of mild motor speech impairment. Her performance on the *Motor Speech Exam* (Wertz, LaPointe & Rosenbek, 1984) was consistent with mild-moderate apraxia (3 out of 8 on a severity rating scale with 0 indicating no impairment and 8 indicating no discernable response) and no dysarthria (0 out of 8). She showed reduced speed and accuracy of word repetition, particularly as word length increased. With regard to language, her performance on the *Western Aphasia Battery-Revised* (*WAB-R*; Kertesz, 1982) was consistent with Broca's aphasia (Table 3, Aphasia Quotient=85).

Table 3
Speech, Language, and Cognitive Performance for SE002

Assessment	Pre-TX	Post-TX	3 mo pending	Normative Data Mean Score (SD)
Mini Mental State Exam (30)	29	*29*		28(2.4)[5]
Western Aphasia Battery aphasia quotient (100)	85	85.6		≥93.8
Information content (10)	10	10		-
Fluency (10)	5	5		-
Comprehension (10)	9.2	9.3		-
Repetition (10)	8.9	9		-
Naming (10)	9.4	9.5		-
Boston Naming Test (60)	56	n/a		54.9[6] (4.3)
Boston Naming Test (30)	n/a	25		
Pyramids and Palm Trees: pictures (14)	14	14		13.9 (.24)[7]

[5] *MMSE* Norms for ages 50-54 from Crum, Anthony, Bassett, and Folstein (1993).
[6] Normative Data for males ages 25-88, from Tombaugh and Hubley (1997).
[7] Normative Data for ages 46-80 (Breining et al., 2015).

Table 3, Continued

Motor Speech Evaluation-apraxia rating (0-7)	3	4	6.9 (2.7)[8]
Motor Speech Evaluation-dysarthria rating (0-7)	0	0	-
Spaghetti List(24)	21	23	-
Arizona Phonological Battery			
Phoneme replacement (words) (6)	3	1	-
Phoneme replacement (non-words) (6)	4	3	-
Phoneme deletion (words) (6)	5	6	-
Phoneme deletion (non-words) (6)	5	4	-
Phoneme blending (words) (6)	3	4	-
Phoneme blending (non-words) (6)	3	4	-
Northwestern Anagram Test (short)			-
Active Sentences (5)	5	5	-
Passive Sentences (5)	3	4	-
Subject Wh-Q's (5)	3	5	-
Subject Wh-Q's (5)	2	3	-
Subject Relatives (5)	3	5	-
Object Relatives (5)	0	0	-
Total Canonical (5)	11	15	-
Total Non-canonical (15)	5	7	-
Total Correct (30)	16	22	-
UCSF Syntax Comprehension (48)	41	42	-
Short lexical	8	8	-
Short active	8	7	-
Short passive	8	8	-
Long lexical	8	8	-
Long easier	7	7	-
Long harder	2	3	-
Arizona Battery for Reading and Spelling: ABRS reading: words			-

[8] Normative Data for ages 70-79 (Zec et al., 1992).

Table 3, Continued

Regular high frequency (9)	9	9	-
Regular low frequency (9)	9	9	-
Irregular high frequency (5)	8	7	-
Irregular low frequency (5)	8	8	-
ABRS reading list (non-words)	5	8	-
ABRS spelling list (words)			-
Regular high frequency (5)	5	5	-
Regular low frequency (5)	4	4	-
Irregular high frequency (5)	3	***3***	-
Irregular low frequency (5)	3	*4*	-
ABRS spelling list (non-words) (10)	5	5	-
Oral Mechanism Exam	Unremarkable	-	-
Pure Tone Screen	Passed	-	-

Her spontaneous speech was often telegraphic and halting, with some grammatical organization. Confrontation naming on the *Boston Naming Test* (*BNT*: Kaplan, Goodglass and Weintraub, 2001) was mildly impaired (she correctly produced 56 of 60 items). Her performance on the object naming subtest of the *WAB-R* revealed intact naming for high frequency items (60/60 points; 20/20 objects named without cues). SE002's conceptual knowledge was strong, as measured by the picture version of the *Pyramids and Palm Trees Test* (100%) *(PPT*; Howard & Patterson, 1992).

SE002's single word reading and non-word reading were relatively spared (34/36 correct for words; 17/18 for non-words), and spelling performance was relatively spared for words but moderately impaired for non-words (18/20 for words; 5/10 for non-words). SE002's performance on the *Mini Mental State Examination (MMSE;* Folstein, Folstein & McHugh, 1975) was 29/30, indicating no significant dementia.

A syntax comprehension test and sentence production test were administered to examine the status of SE002's comprehension and production of canonical and non-canonical sentence structures of varying lengths. SE002 demonstrated a moderate impairment in syntax comprehension on the *UCSF Syntax Comprehension Test*, with more errors on long/hard (2/9 correct) and long/easy structures (7/9 correct) (Wilson et al., 2010) (41/48 correct for all sentence structures). Syntax production impairment was observed on the *Northwestern Anagram Test (NAT;* Thompson, 2011) with moderately impaired performance for canonical structures and severe impairment on non-canonical structures (11/15 correct for canonical subject wh-questions; 5/15 correct for non-canonical object wh-questions). This pattern of sentence production deficit is common in individuals with the agrammatic variant of PPA (Caplan & Hanna, 1998; Friedmann & Grodzinski, 1997; Schwarts, Saffran, Fink, Myers & Martin, 1994; Thompson et al., 2012; Weintraub et al., 2009).

Phonological processing difficulty was apparent on the *Arizona Phonological Battery (APB*; Kay, Lesser and Coltheart, 1992). SE002's performance on minimal pair discrimination was spared for words and non-words (20/20 for words; 20/20 non-words) and relatively strong for phoneme deletion of real words and non-words (10/10 for words; 8/10 for non-words). However, she showed impairment in sound blending for words and non-words (4/10 for words; 4/10 for non-words), and verbal phoneme replacement for words and non-words (10/15 for words; 5/15 for non-words).

SE002's pre-treatment high-resolution structural MRI scan revealed significant widespread cortical atrophy, with greater atrophy in the left than right hemisphere (Figure 2). Atrophy was most pronounced in the left middle and inferior frontal and gyri and insula. The atrophy pattern and cognitive linguistic profile were consistent with the agrammatic/non-fluent variant of PPA (Gorno-Tempini et al., 2011). Significant cortical atrophy was observed in the right hemisphere as well.

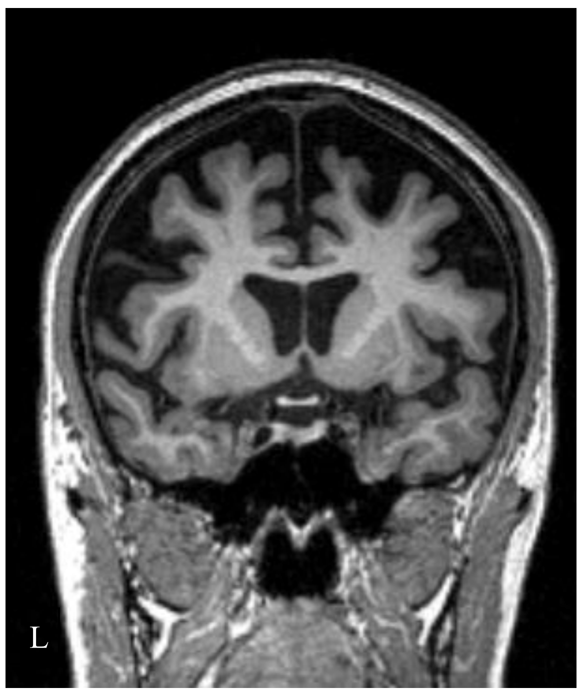

Figure 2. SE002 high resolution MRI scan was obtained pre-treatment showing bilateral frontal atrophy (L>R).

2.2 Treatment

The treatment approach implemented for both participants was designed to facilitate fluent and intelligible speech through training with a visual and auditory speech model. Sound errors were addressed through targeted articulation practice with the aid of a trained clinician in therapy and independently as the participant completed homework. Scripts were tailored to each participant, but employed a common protocol that moved from structured to more functional tasks. In-session treatment provided a sequence of tasks to reinforce homework practice, target articulation for unintelligible words, and move from more structured tasks to more open-ended tasks in order to promote memorization and generalization. Table 4 shows the treatment protocol steps.

Table 4

Treatment protocol for speech entrainment in-session practice

Treatment Steps	
Structured Treatment	a. Choose correct trained script sentences from four foil sentences.*
↓	b. Prompt each sentence in script order (e.g., “Tell me about___.”
	c. Target unintelligible or missing words from the scripted sentences.
	d. Produce the entire script from memory.
Functional Application	e. Elicit the scripted sentences out of order through dynamic conversation.

*****For SE002, treatment protocol differed in that she chose the correct sentence in each script from 3 foil sentences

The hierarchy transitions from more structured tasks targeting accuracy and intelligibility and moving to less structure by using scripted sentences out of order and in conversation with unfamiliar conversational partners.

To assess whether treatment was implemented according to the protocol in Table 4, two trained undergraduate students in communication sciences and disorders independently and randomly scored three (25%) of the nine video-recorded sessions for treatment fidelity for both participants. To eliminate experimenter bias, the two observers were naïve to experimental conditions from which the video recordings were drawn. When the two observers showed a discrepancy in scores greater than 10 points, both observers re-examined the video recording and came to a rating consensus.

Reliability was assessed for the primary outcome measure (percent correct, intelligible words) for 25% of sessions, or three randomly selected treatment sessions. One trained undergraduate transcribed all probes from each session and coded each word as correct/incorrect and intelligible/unintelligible relative to the script. Number of coding discrepancies (between the clinician and independent rater) were divided by the total number of words in each script to derive overall percent agreement.

2.2.1. Script generation and tailored speech rate

Seven total scripts were generated for SE001, and six for SE002. These were tailored to each participant and were developed via a collaborative process involving the participants, their family members, and the clinician. Participants selected script topics and generated sentences, which were then edited and shaped by the clinician. Multisyllabic words were used sparingly, due to participants' articulatory difficulty, and scripts were limited to approximately four sentences. After scripts were generated, a team of two undergraduate students, one graduate student, and one clinical fellow video-recorded each script. The mouth model read the client's script at the approximate rate of each participant's speech (with a metronome used for pacing). To determine the tailored rate for the audio-video stimuli, each participant's words produced per minute (wpm) were derived from both a picture description speech sample, and a reading passage. If a discrepancy was found between a participant's picture description and their reading rate, we chose the participant's faster rate, which was the reading rate for SE002 (47 wpm vs. 32 wpm for picture description), and the picture description rate for SE001 (27 wpm vs. 25 wpm for reading rate). The rationale for choosing the faster speech rate was to ensure that the scripted material was attainable, natural, yet challenging for each participant.

2.2.2 Training criteria, data collection

For SE001, four scripts were trained and three remained untrained. For SE002, four scripts were trained and two remained untrained. Criterion for mastery was set at 90% or greater words produced correctly and intelligibly over two sessions (with a maximum of three sessions per script). If the participant met criterion in the second session, they moved on to a new trained script. If criterion was not met after three sessions, the client moved onto a new trained script. Intelligibility was defined as whether the listener could understand the target word within the context of the script topic. Each word was coded online by the clinician as intelligible or unintelligible, and as present or omitted (relative to each script). Trained undergraduate coders, that were blind to the outcomes of the study, used CHAT and CLAN (MacWhinney & Snow, 1985) to transcribe all probes, and coded unintelligible words. Productions that were deemed unintelligible were transcribed phonetically. A correct production required that the word was a lexical unit from the script and that it was intelligible within the context of the script. If the participant self-corrected, the correction was counted as correct (towards their intelligibility if the self-correction was intelligible, or towards their accuracy if they retraced their production). Percent intelligibility and accuracy of each script were examined pre-treatment, during nine treatment sessions, and post-treatment.

Performance on the trained script and half of all other trained and untrained scripts was probed at the beginning of each treatment session prior to any treatment activities (so that all scripts were probed once per week). Percentage of grammatical errors by word class and overall intelligibility and grammaticality were calculated for trained and untrained scripts for all pre-treatment, treatment and post-treatment sessions. Percentage intelligibility and total grammatical errors were assessed pre- and post-treatment for the *WAB-R* picture description task.

2.2.3 Statistical analysis

To estimate the treatment effect size, the change in the level of performance on the last two maintenance scores for each trained script was compared to the first two pre-treatment probes, and *d*-statistics were calculated for each script. Effect sizes were evaluated relative to benchmarks derived by Robey and colleagues in their review of single-subject research in aphasia. With one extreme outlier removed from the effect sizes derived from 12 studies, the first, second, and third quartiles for the *d* statistic were small: d=2.6, medium: d=3.9, and large: d=5.8 (Robey, Schultz, Sinner and Sinner, 1999; Beeson & Robey, 2006). Wilcoxon signed-rank tests were conducted to compare pre-treatment performance with post-treatment and follow-up performance on grammaticality and intelligibility measures for scripts, as well as performance in different grammatical word classes. McNemar tests were used to compare pre- versus post-treatment scores on select language measures, including the *Boston Naming Test* (Kaplan, Goodglass and Weintraub, 2001), the *Pyramids and Palm Trees Test (PPT*; Howard & Patterson, 1992), *Northwestern Anagram Test (NAT;* Thompson, 2011), and the *UCSF Syntax Comprehension Test* (Wilson et al., 2010).

Results

3.1 Participant 1: SE001

3.1.1 Treatment implementation and outcomes

SE001 participated in nine weeks of treatment, with sessions occurring twice weekly for forty-five minutes, for a total of 13.5 hours of direct contact with the clinician. SE001 also completed at least 30 minutes of homework seven days per week, totaling approximately 31.5 total hours of homework. During treatment sessions, he was guided through the speech entrainment treatment protocol for the set currently being trained.

Multiple baseline data for SE001's performance on spontaneous speech probes for trained and untrained scripts are shown in Figure 3 and Figure 4. His performance was relatively stable over the first two pre-treatment probes, but as treatment was implemented, he showed some improvement in to-be-trained scripts on the primary outcome measure of percent correct, intelligible words from scripts. This upward drift in performance suggested generalization of self-monitoring and articulation strategies used in trained scripts to untrained scripts. As shown in Figure 3, SE001 demonstrated mastery (90% correct, intelligible words or better) of each trained script within three sessions, and maintained good performance for the duration of the training period. To estimate the treatment effect size, the change in the level of performance on the last two maintenance scores for each trained script was compared to the first two pre-treatment probes, and *d*-statistics were calculated for each script.

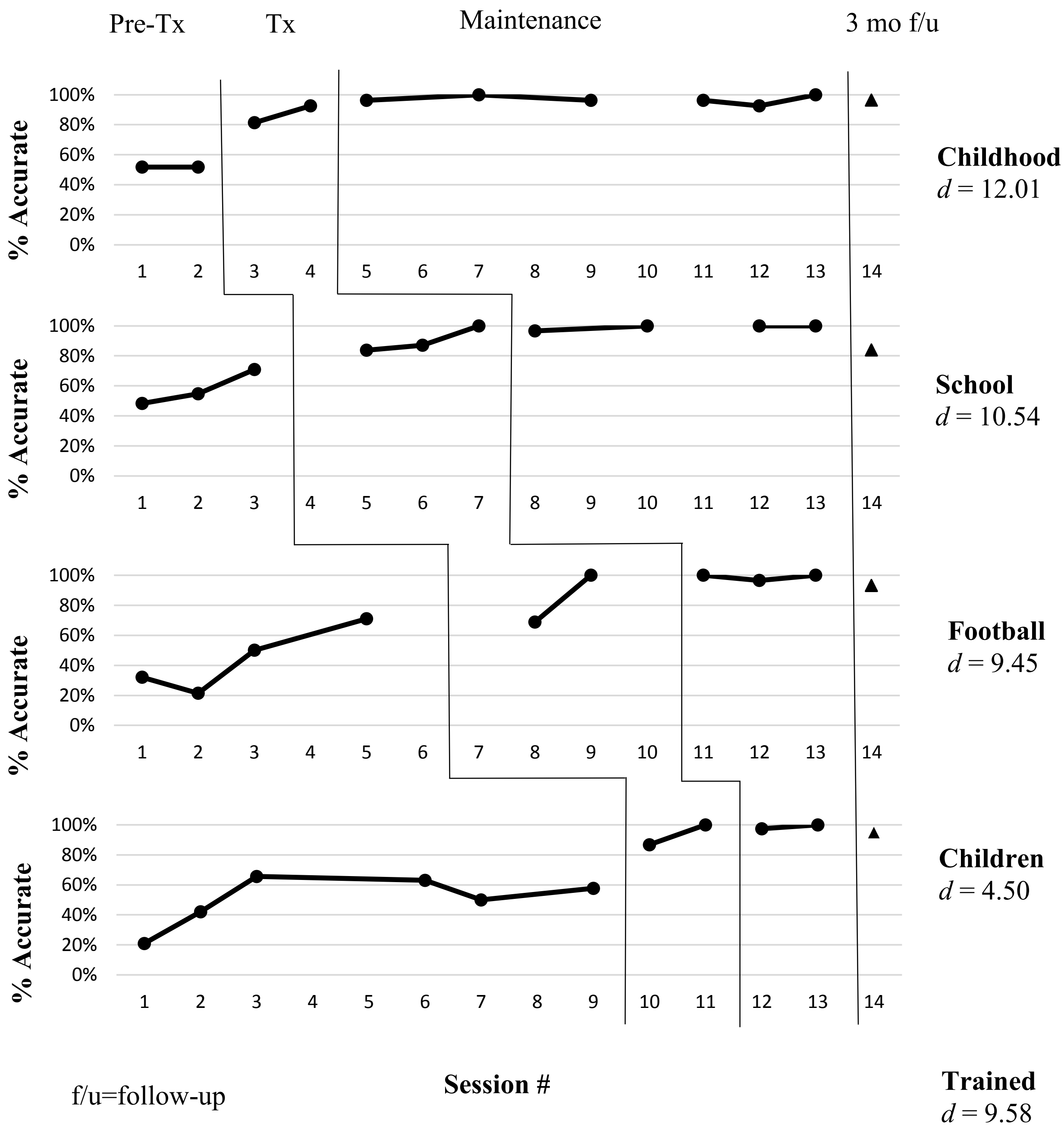

Figure 3. Multiple-baseline data for SE001's performance during and after speech entrainment treatment for percentage of script words produced correctly and intelligibly on each trained script. Phases of treatment are separated by vertical lines, including baseline, treatment sessions, maintenance sessions, and follow-up probes at three months after the completion of this treatment.

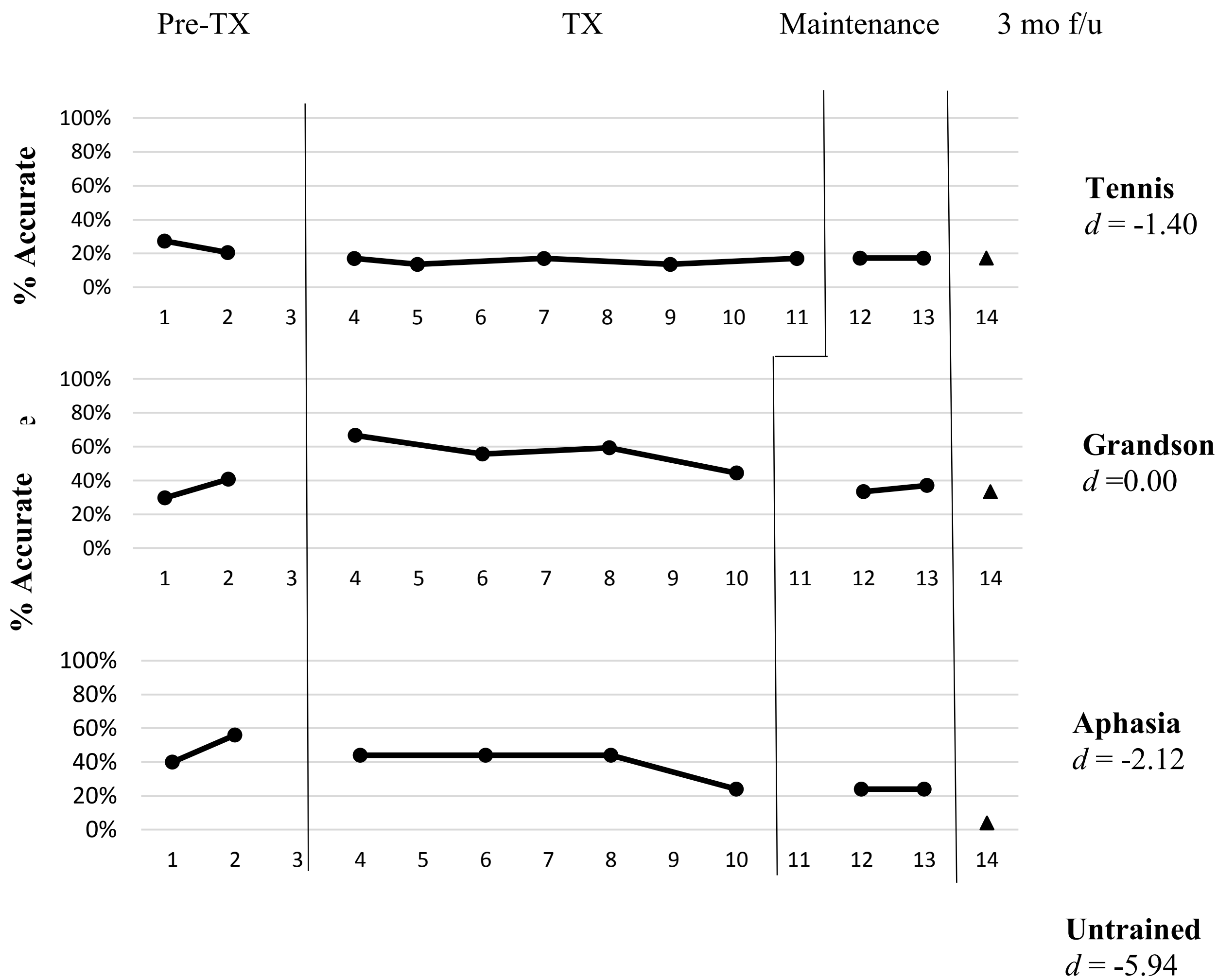

Figure 4. Multiple-baseline data for SE001's performance during and after speech entrainment treatment for percentage of script words produced correctly and intelligibly on each untrained script. Phases of treatment are separated by vertical lines, including baseline, treatment sessions, maintenance sessions, and follow-up probes at 3 months after the completion of this treatment.

The weighted effect size for all trained sets was 9.58, a strong, positive response to treatment indicated by large effect sizes (*d*>5.8) for the trained scripts from baseline to post-treatment (see Robey, 1999, as well as Beeson & Robey, 2006, for calculation details). The weighed effect size for all untrained sets was -5.94, indicating an overall deterioration in speech production and fluency for untrained topics. A *z*-test was conducted to compare the effect sizes from each treatment condition. This test revealed a significant difference between trained and untrained sets (z=5.86, p<0.001 one-tailed).

Number of words produced correctly in each grammatical class was calculated before and after treatment for trained scripts (Figure 5). SE001 showed improvement for all grammatical classes except light verbs (of which there was only one). SE001 produced the one light verb accurately during pre-treatment probes but not post-treatment probes. Functors showed the most significant improvement. Grammatical class accuracy generalized to untrained scripts, which revealed an increase in accuracy for all grammatical classes except for the copula verb (Figure 6). A Wilcoxon signed rank test for trained scripts showed significant improvement for trained scripts (z=-2.14, p=0.015, one-tailed), and improvement in grammatical classes showed generalized effects in untrained scripts (z=-2.37, p=0.008, one-tailed).

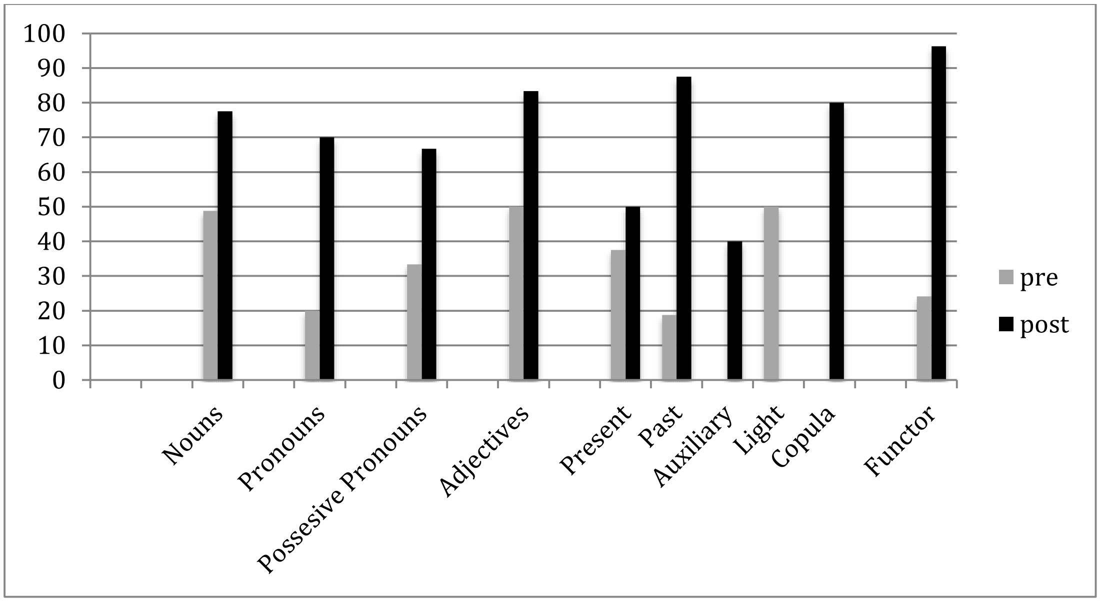

Figure 5. Percent correct words by class for trained scripts for SE001.

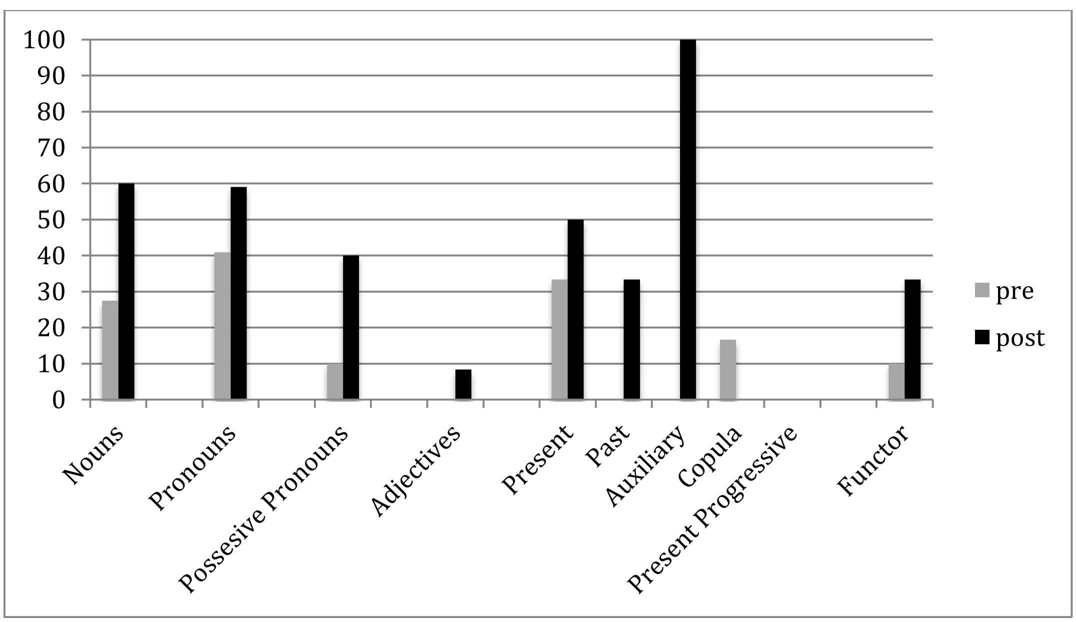

Figure 6. SE001 percent correct words by class for untrained scripts

Figure 7 shows SE001's total grammatical errors for scripted topics. Results showed a decrease in grammatical errors across all scripts except the untrained "Aphasia" script. Overall, these changes were significant, as measured by a Wilcoxon signed rank test for trained scripts, z=1.83, p=0.034, one-tailed, but were not significant for untrained scripts, z=-0.82, p=0.207, one-tailed. Percentage of total intelligible words for scripted topics is shown in Figure 8. SE001 increased his overall intelligibility for every script from pre to post-treatment. Overall, these changes were significant for trained scripts as measured by a Wilcoxon Test, z=-1.83, p=0.034, but not significant for untrained scripts, z=-1.60, p=0.055 one tailed.

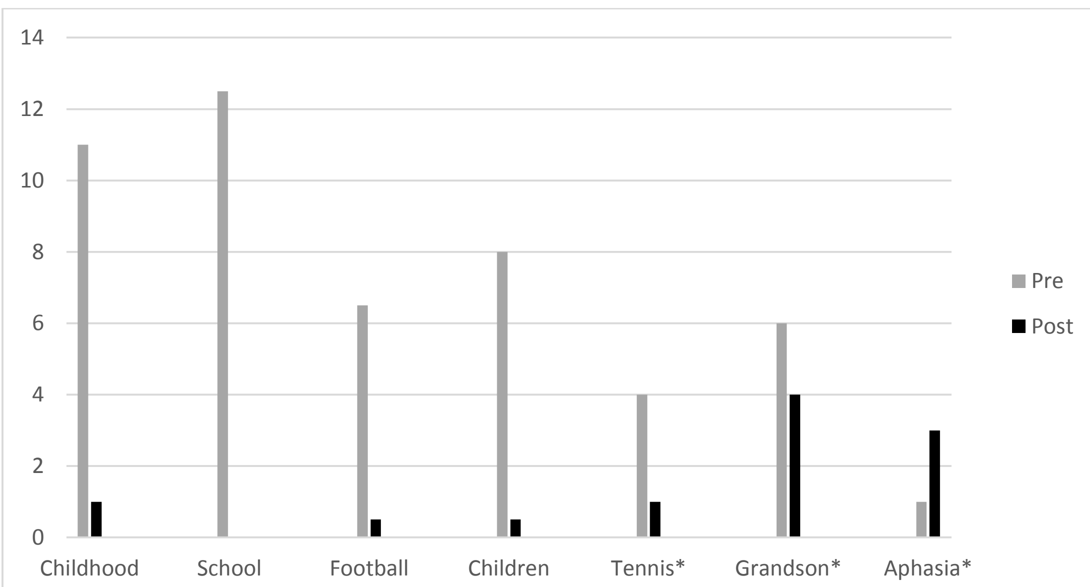

Figure 7. SE001 total grammatical errors during spontaneous speech probes for trained and untrained topics. Asterisks denote untrained scripts.

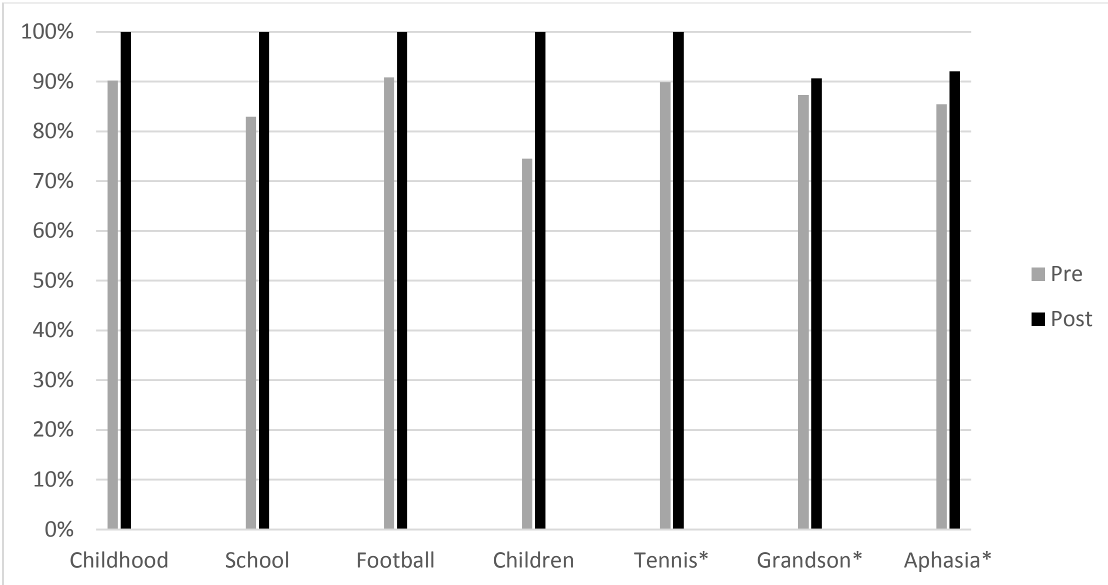

Figure 8. SE001 percent intelligibility during spontaneous speech probes for trained and untrained topics. Asterisks denote untrained scripts.

3.1.2 Post-treatment and follow-up assessments and generalization effects

SE001's performance on the *WAB-R* showed a clinically significant change after the course of treatment (AQ 80.6-85.5) (Kertesz, 1982). Improvement was noted on the spontaneous speech subtest (from 14 to 15 points out of 20), and on the naming subtests (from 87 to 95 points out of 100). The spontaneous speech sample on the *WAB-R* picture description showed a 50% reduction in grammatical errors (from 8 total errors to 4). A slight increase in speech intelligibility was observed in the spontaneous speech measure on the *WAB-R* picture description showing 90% intelligibility at pre-treatment and 92% intelligibility at post-treatment. A measure of reading performance showed relative stability for words (28/36 from 30/36 pre-treatment), with a slight improvement on non-words (8/18 from 5/18 pre-treatment).

His performance on the *BNT* stayed relatively stable, with a score of 54/60 (from 55/60 pre-treatment). Phonological awareness maintained relative stability as well. Performance on syntax production on the *NAT* improved from pre- to post-treatment from a score of 4 (pre-treatment) to 7 out of 10; however, these changes were not significant overall. Syntax comprehension remained stable at all three time points, with a score of 44 out of 48. No significant changes in severity level of apraxia or dysarthria were observed on the multisyllabic word repetition list or in the *Motor Speech Evaluation* from pre- to post-treatment. Semantic comprehension also remained stable from pre-to post-treatment, as measured by the *Pyramids and Palm Trees* test*.*

At three months post-treatment, SE001 was able to recall three of four scripts with above 93% accuracy and one script at 83.87% accuracy (Figure 3). Other speech and language measures at the three-month follow up are shown in Table 2. SE001's performance on the *WAB-R* decreased to 71.6, with fluency showing the most significant decrease from a 6 post-treatment to a 4 at three-months post-treatment. Performance on syntax output on the *NAT* dropped to 5 out of 10 at three-months post-treatment from a 7 at post-treatment. Performance on the *Pyramids and Palm Trees* test remained unchanged. *MSE* rating suggested a significant increase in the severity level of SE001's apraxia from post-treatment (rating of 5, or moderate) to three-months post-treatment (rating of 7, or severe). An *MSE* rating increase was also noted for dysarthria (from 5 to 6, both moderate).

In summary, on generalization measures, SE001 showed improvement in fluency and grammatical competence in a spontaneous speech task as well as in syntax production in sentences from pre- to post- treatment. A slight decline in performance was seen at three-months post-treatment across many assessments, with the exception of syntax comprehension.

3.1.3 Self-assessment of change

In order to evaluate SE001's perspective on changes in his communication skills following treatment, he completed a self-assessment questionnaire using a quantitative rating scale one week after treatment ended (Table 5). SE001's reading and comprehension skills were sufficient to comprehend survey items. He rated his communication skills as "Better" for his ability to both detect and correct his own speech errors when they occur. He gave a rating of "Somewhat Better" for ability to speak more fluently without errors within practiced scripts and during normal conversation. He also rated his articulation in practiced scripts and in normal conversation as "Somewhat Better" as well as his ability to use functors or "little" words within scripts and in normal conversation. He rated his overall speaking ability as "Unchanged" as well as his ability to speak smoothly and overall number of hesitations and pauses. At baseline, SE001 did not report feeling stressed or frustrated and felt confident about his communication skills with familiar and unfamiliar people; thus, these ratings did not change after treatment.

Table 5

SE001 Post-treatment Survey Results

Survey Questions	A lot worse	Worse	Some-what worse	Unchanged	Some-what better	Better	A lot better
Ability to detect error in your speech?						X	
Ability to correct your own speech errors when they occur?						X	
Ability to speak smoothly and without errors in practiced scripts?					X		
Ability to speak smoothly and without errors during normal conversation?					X		
Ability to speak in complete sentences, using all the “little” grammatical words in practiced scripts?					X		
Ability to speak in complete sentences, using all the “little” grammatical words in normal conversation?					X		
Articulation during practiced scripts (ability to say the sounds within a word)?					X		
Ability to speak in time with video model during speech entrainment?					X		
Ability to speak smoothly in phrases or sentences?				X			
Amount of hesitation or pauses while speaking?				X			
Overall speaking ability? (*not stressed at all*				X			

Table 5, Continued

Stress level during conversation?	X
Confidence in communication with your primary communication partner?	X
Confidence in communication with familiar people?	X
Confidence in communication with unfamiliar people?	X
Frustration level during communication exchanges with primary communication partner?	X
Frustration level during communication exchanges with familiar people?	X
Frustration level during communication exchanges with unfamiliar people?	X
Overall comfort level while speaking?	X

Directions: Since completing treatment, how would you rate your… (*this individual's*, caregiver survey*)*:

X = participant response

Table 6

SE001 Additional post-treatment survey items

I use practice words, phrases or sentences (from my scripts) in conversation	X
I am more likely to try to use complete sentences when talking	
I am less likely to give up if I can't say something correct the first time	X

Directions: Please select ways in which your approach to communication is different now relative to when you started treatment (*choose as many as necessary)*

X = participant response

3.2 Participant 2: SE002

3.2.1 Treatment Effects in SE002

SE002 was treated using the same speech entrainment protocol as SE001, with a few modifications. Because SE002 lived across the country in Oregon, all treatment sessions were conducted using videoconferencing software (Skype©), which allows one to alternate between face-to-face viewing and sharing of the clinician's computer screen. SE002 participated in nine weeks of treatment with sessions occurring twice weekly for forty-five minutes, for a total of 13.5 hours of direct contact with the clinician. SE002 was also assigned 30 minutes of homework per day. Actual completion of homework was less reliable due to traveling, and totaled approximately 17.7 hours. As with SE001, during treatment sessions, SE002 was guided through the speech entrainment treatment protocol for one script (per session). Some additional modifications were made to the protocol. Instead of having one foil sentence for every sentence in the trained script as was done with SE001, the task for SE002 was modified, so that she chose each correct sentence from the script with three foils sentences per each sentence in the script (in order to increase task difficulty). Also, dynamic conversation with a novel listener was less structured. The novel communication partner followed a general script that included questions to ask the participant, with room for conversational exchange that allowed the naïve partner to comment and share their own anecdotes that related to the script topic.

SE002's performance was relatively stable over the first two pre-treatment probes and continued to remain stable after treatment was implemented (Figure 9). Criterion for script accuracy was met in two sessions for three of the scripts, and in three sessions for one. Performance was maintained for the duration of the training period. The weighted effect size for all trained sets was 11.74, a strong, positive response to treatment indicated by large effect sizes (d>5.8) for the trained scripts from baseline to post-treatment (see Robey, 1999, as well as Beeson & Robey, 2006, for calculation details). The weighed effect size for all untrained sets was 3.58, a small positive response to treatment indicated by a small effect size (d=2.6). A z-test was conducted to compare the effect sizes from each treatment condition. This test revealed a significant difference between trained and untrained sets (z=2.97, p=0.001, one-tailed).

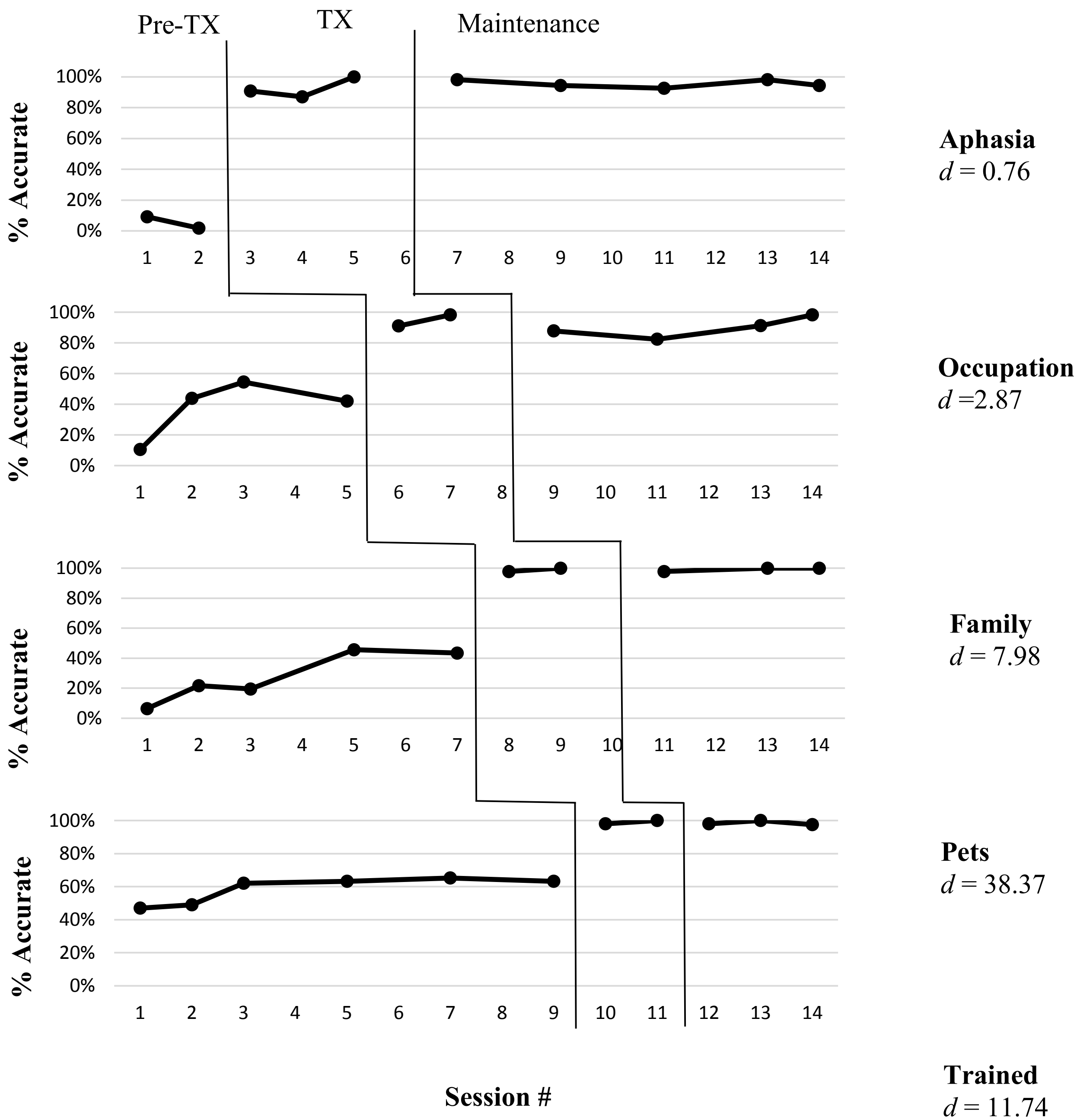

Figure 9. Multiple-baseline data for SE002's performance during and after speech entrainment treatment for percentage of script words produced correctly and intelligibly on each trained script. Phases of treatment are separated by vertical lines, including baseline, treatment sessions, and maintenance sessions. Follow-up probes at three months after the completion of this treatment were pending at this time point in the study.

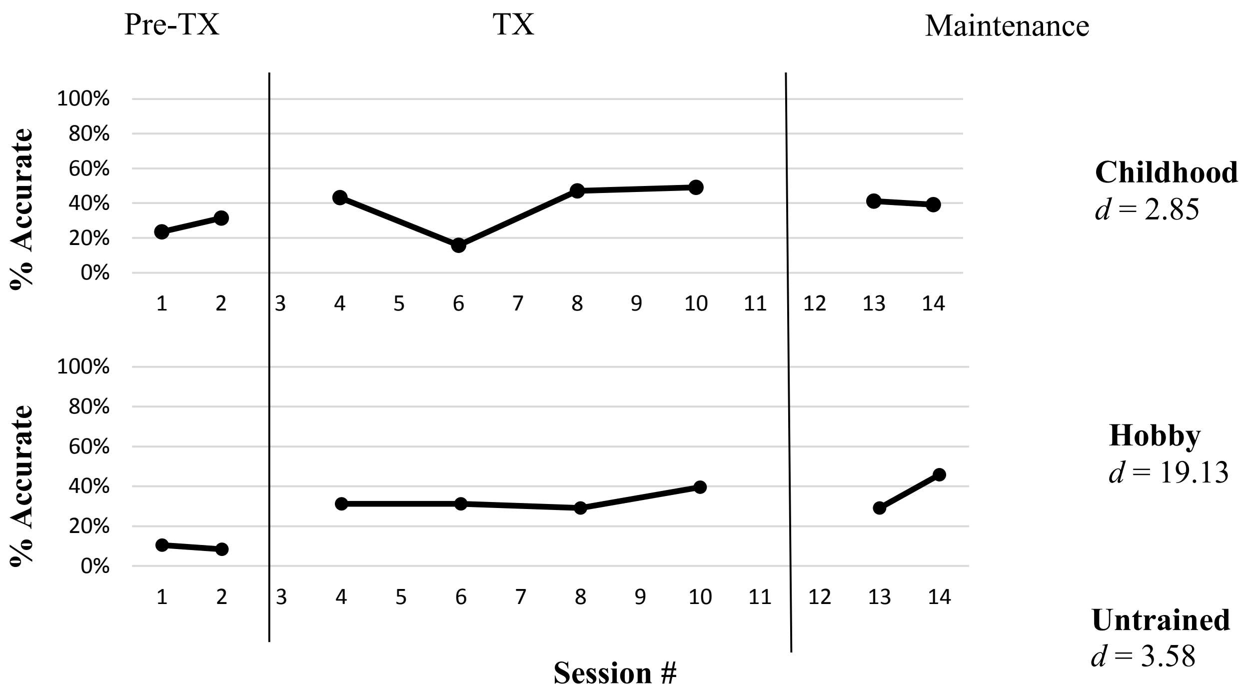

Figure 10**.** Multiple-baseline data for SE002's performance during and after speech entrainment treatment for percentage of script words produced correctly and intelligibly on each untrained script. Phases of treatment are separated by vertical lines, including baseline, treatment sessions, and maintenance sessions. Follow-up probes at three months after the completion of this treatment were pending at this time point in the study.

Number of words correct by grammatical class was assessed pre- and post-treatment. Figure 11 shows an increase in all grammatical classes from pre- to post-treatment. Nouns and auxiliary and copula verbs showed the greatest overall improvement. A Wilcoxon signed rank test for trained scripts showed significant improvement for trained scripts (z=-2.80, p=0.001, one-tailed). Grammatical class accuracy generalized as slight gains were observed to untrained scripts, revealing an increase in accuracy for all grammatical classes except for adverbs, which remained the same pre and post treatment

(Figure 12). This change in production of words across grammatical classes was significant (z=-2.52, p=0.004, one-tailed).

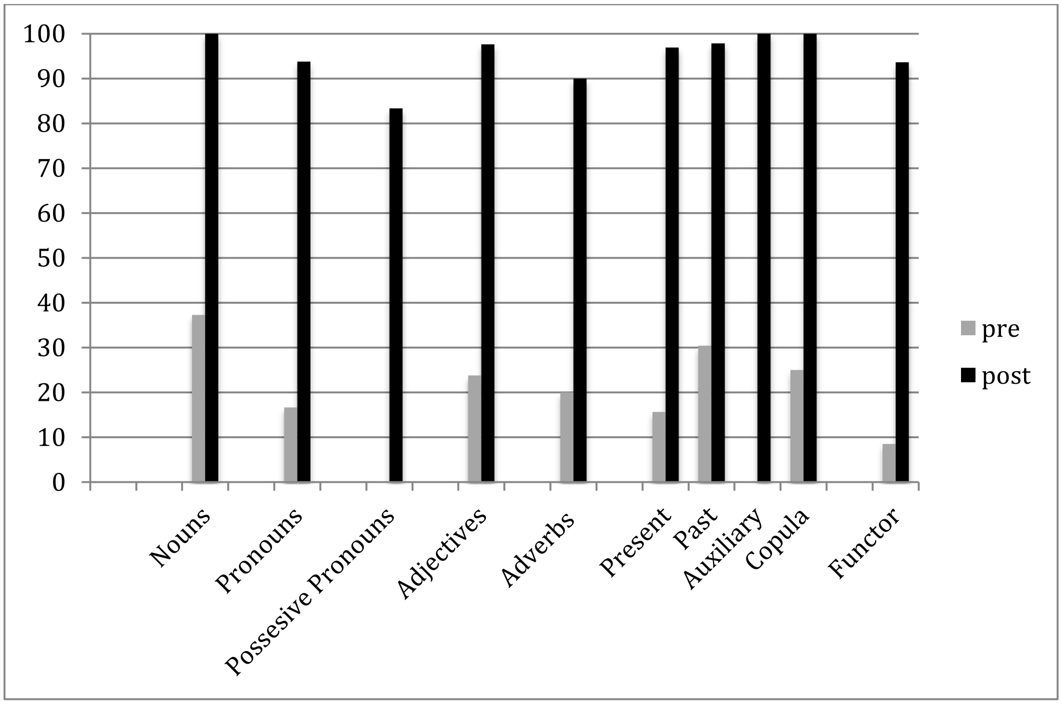

Figure 11. SE002 percentage of grammatical class correct in trained scripts

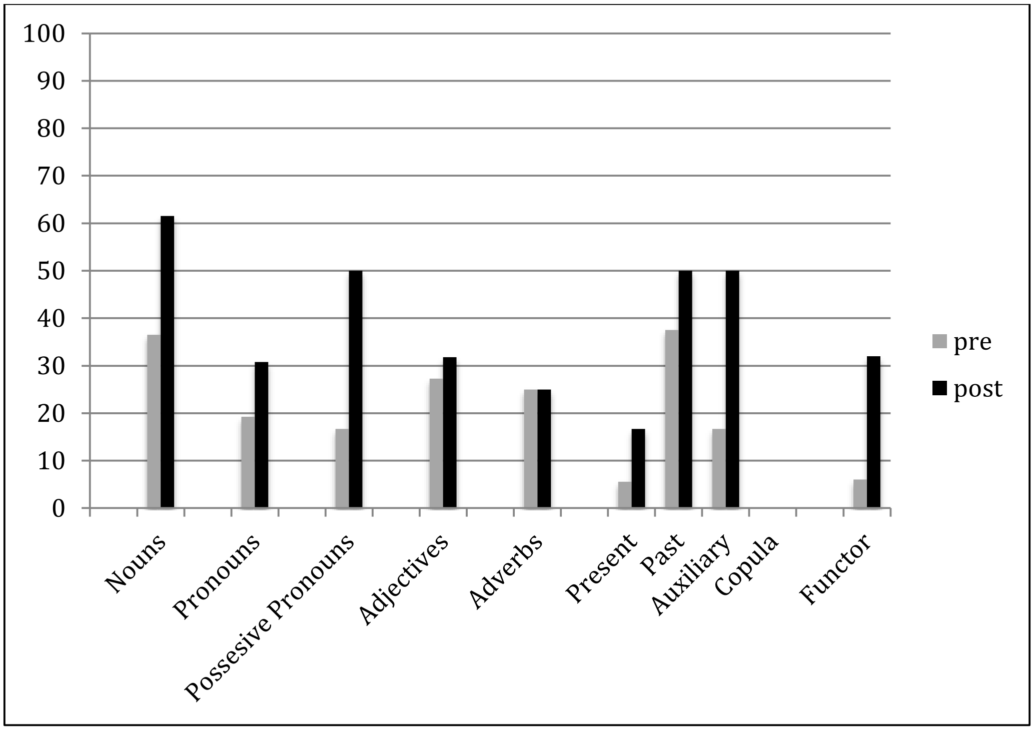

Figure 12. SE002 percentage of grammatical class correct in untrained scripts

Additionally, Figure 13 shows SE002's total grammatical errors in response to spontaneous speech probes. Results showed a decrease in grammatical errors for all script topics from pre- to post-treatment, with the greatest reduction in grammatical errors observed across the four trained scripts. Overall, these changes were significant, as measured by a Wilcoxon signed rank test for trained scripts, z=1.83, p=0.034, one-tailed, but not for untrained scripts, z=-1.34, p=0.09, one-tailed. Percentage of total intelligible words for scripted topics is shown in Figure 14. Intelligibility was not a significant deficit for SE002 (Figure 14). Her total intelligibility remained 100% from pre- to post-treatment. Overall, these changes were not significant for trained scripts, as measured by a Wilcoxon Test, *z*=-0.00, *p*=0.5, one-tailed, or untrained scripts, *z*=-0.00, *p*=0.5, one-tailed.

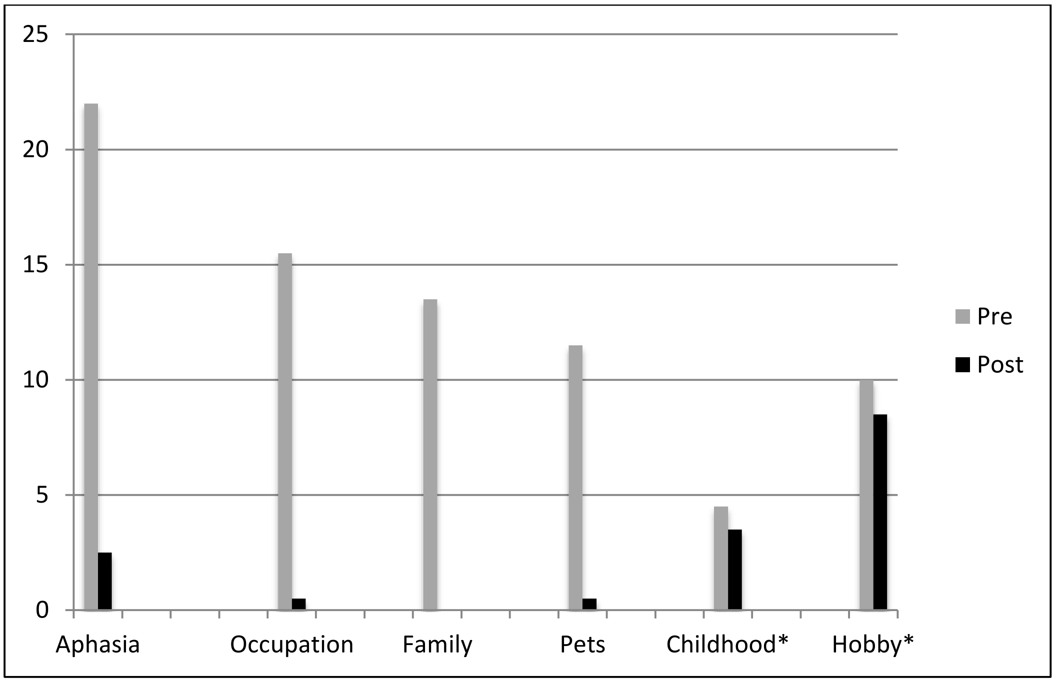

Figure 13. Total grammatical errors for trained and untrained scripts. Asterisks denote untrained scripts.

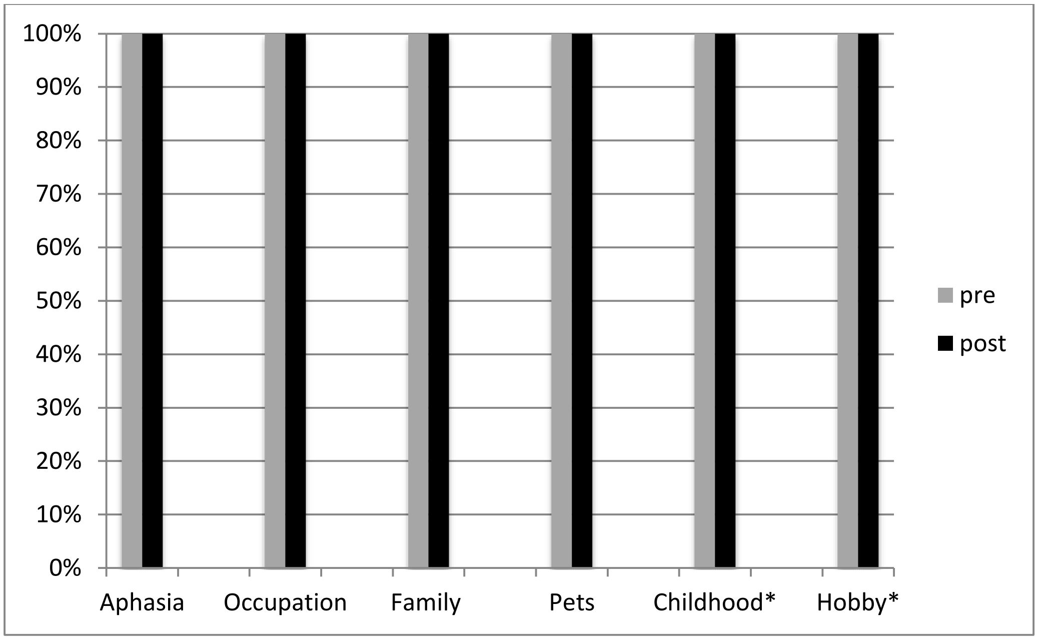

Figure 14. SE002 total percent intelligibility for trained and untrained scripts.

3.2.1 Post-treatment assessments and generalization effects.

SE002's performance on the *WAB-R* remained stable from pre- to post-treatment (*AQ*: 85-85.6), with slight improvement noted on comprehension (from 9.2 to 9.3), repetition (8.9 to 9) and naming (from 9.4 to 9.5) at post-treatment. Total grammatical errors within a spontaneous speech sample on the *WAB-R* picture description increased from 8 total errors to 12 total errors. Errors that she made post-treatment on this measure were primarily omissions of the verb *to be* as part of the progressive tense or substitution of an incorrect verb (i.e., "Man has reading."). Spontaneous speech intelligibility was stable for the picture description task of the *WAB-R,* which showed 100% intelligibility at both pre- and post-treatment. Reading and spelling performance remained relatively stable from pre- to post-treatment, with only slight declines on irregular and non-word scores. On the *Arizona Phonological Battery* and *BNT*, SE002's performance remained relatively stable. Performance on syntax production on the *NAT* improved from 16 to 22 out of 30 (a significant change, as confirmed by pairwise McNemar tests, p=0.035), and remained stable on the syntax comprehension measure (from 41 to 42 out of 48). No significant changes in severity level of apraxia or dysarthria were observed on the multisyllabic word repetition list or the *MSE* at post-treatment. Semantic knowledge, as measured on the *Pyramids and Palm Trees* test, remained stable from pre- to post-treatment.

3.2.2 Self-assessment of change.

In order to evaluate SE002 and her spouse's perspectives on changes in her communication skills following treatment, they completed questionnaires using a quantitative rating scale 1 week after treatment ended (Tables 7 and 8).

Table 7
SE002 Post-treatment Survey and Spouse Survey

	A lot worse	Worse	Some-what worse	Unchanged	Some-what better	Better	A lot better
Ability to speak in time with video model during speech entrainment?						√	X
Ability to detect errors in your speech?					√		X
Ability to correct your own speech errors when they occur?					√		X
Ability to speak smoothly and without errors in practiced scripts?						X	√

Table 7, Continued

Ability to speak in complete sentences, using all the “little” grammatical words in normal conversation?			√	X	
Overall number of hesitations or pauses while producing scripts?		√		X	
Articulation during practiced scripts (ability to say the sounds within a word)?				X	√
Ability to speak smoothly and without errors during normal conversation?		X	√		
Ability to speak in complete sentences, using all the “little” grammatical words in practiced scripts?		X			√
Articulation during normal conversation (ability to clearly say the sounds within a word)?		X	√		
Overall number of hesitations or pauses in normal conversation?		X √			
Ability to communicate your thoughts?		X		√	
Overall speaking ability?		X		√	
Stress level during conversation?		X √			
Overall comfort level while speaking?		X √			
Confidence in communication with your primary communication partner?	√	X			
Confidence in communication with familiar people?		X √			
Confidence in communication with unfamiliar people?		X	√		

Table 7, Continued

Frustration level during communication exchanges with primary communication partner?	√	X		
Frustration level during communication exchanges with familiar people?		X		√
Frustration level during communication exchanges with unfamiliar people?		X		√

Directions: Since completing treatment, how would you rate your… (*this individual's,* caregiver survey*)*:

X = participant response
√ = caregiver response

Table 8
SE002 Additional post-treatment survey items

I use practice words, phrases or sentences (from my scripts) in conversation	X √
I am more likely to try to use complete sentences when talking	√
I am less likely to give up if I can't say something correct the first time	X √

Directions: Please select ways in which your approach to communication is different now relative to when you started treatment (*choose as many as necessary)*

X = participant response
√ = caregiver response

SE002's reading and comprehension skills were sufficient to comprehend survey items. She rated all communication skills for scripted material as "A lot better," "Better," and "Somewhat better" than before treatment. She rated her overall speaking ability as "Unchanged" as well as her ability to speak smoothly and overall number of hesitations and pauses. At baseline, SE002 did not report feeling stressed, and this was "Unchanged" after treatment. A post-treatment survey was also given to SE002's spouse asking for his perspective on change within his wife's speech for scripts and outside scripts. He rated all communication skills within scripts as "A lot better", "Better", and "Somewhat Better." For overall speaking, he rated her ability to detect and correct speech errors when they occur in speech as "Somewhat Better." He rated her overall speaking ability to be "Better." For her confidence in communication with her primary communication partner, or her spouse, he rated her as "Somewhat worse."

3.2.3 Treatment Fidelity and Reliability

Fidelity results for SE001 were an average of 98% treatment steps completed correctly. For SE002, fidelity results were 100% treatment steps completed correctly. These results indicate there was a high degree of fidelity of treatment implementation.

Reliability was assessed for the primary outcome measure (percent correct, intelligible words) for 25% of sessions, or three randomly selected treatment sessions. Number of coding discrepancies were divided by the total number of words in each script. Inter-rater reliability was 87.2% agreement for SE001, and 93.38% for SE002. These results indicate that there was relatively high inter-rater agreement.

Discussion

We have presented treatment outcomes for a modified speech entrainment protocol designed to improve speech production and fluency for functional, scripted material in two individuals with the non-fluent variant of PPA. The treatment approach, which utilized personalized scripts, was designed to re-establish automaticity via repeated practice of text level material, as opposed to focusing on specific language sub-components such as articulation, word-finding and grammar (Youmans et al., 2010). We sought to replicate findings from previous work in speech entrainment in stroke-induced aphasia (Fridriksson et al, 2012), to establish its utility in individuals with non-fluent PPA, and to modify the protocol to include personally-relevant scripts. Another unique aspect of this treatment relative to Fridriksson et al, (2012) included the design of the treatment session, which targeted memorization of the script. Additionally, the inclusion of novel conversational partners within treatment sessions was intended to support generalized use of the script in conversation. The video scripts were also individualized to the person's maximum rate of speech in order to facilitate acquisition of scripts in individuals with concomitant apraxia and dysarthria. Finally, targeted articulation practice was added to the treatment protocol to address decreased intelligibility due to apraxia of speech and/or dysarthria (Henry et al., 2013).

The two participants treated in this study presented with different severity and duration of PPA, as well as partially distinct speech-language profiles. SE001 was two years post-onset of initial symptoms, with evidence of a slight impairment on a cognitive screening measure (*MMSE* =26/30). SE002 was three years post-onset of initial symptoms, with a *MMSE* score of 29 at the time treatment was initiated. Despite the fact that SE002 had reported symptoms for longer, her language deficits were less prominent. She had less severe apraxia and no dysarthria as evidenced by *MSE* ratings. Imaging findings based on a subjective interpretation of the MRI scan indicated a greater degree of atrophy in regions critical for speech production and grammar in SE001's brain, relative to SE002.

Treatment outcomes revealed large effect sizes for both participants in script accuracy/intelligibility (the primary outcome measure) for trained scripts from pre- to post-treatment. Both participants met 90% criterion for trained scripts within three treatment sessions, with good maintenance of gains over time (up to three months post-treatment in SE001). Further, production of words across grammatical classes showed improvement, as well as overall intelligibility and grammatical competence for trained topics. Generalized improvement on syntax production measures and stability over time on syntax comprehension tests in both participants suggest that the treatment protocol was beneficial for syntactic processing overall.

SE001 showed increased frequency and generalized use of error self-correction via strategies explicitly taught to him in treatment sessions. This was most notable in his increase in grammaticality in scripted material and also in spontaneous speech, as measured by the *WAB-R* picture description (from 8 total errors pre-treatment to 4 total grammatical errors post-treatment). A slight increase in speech intelligibility was shown in a spontaneous speech measure on the *WAB-R* picture description showing 90% intelligibility at pre-treatment to 92% intelligibility at post-treatment. The responsiveness of the participant to this treatment, as measured by improved speech production and overall intelligibility, stands in contrast to previous work suggesting that motor commands for speech must be preserved and that participants who have moderate apraxia of speech would be unable to produce online speech with relative fluency and clarity as a result of speech entrainment practice (Fridriksson et al., 2012). SE001's ability to use fluent speech in trained scripts is likely due to one key change relative to the original study. Given that SE001 was assessed to have moderate apraxia of speech, we were able to modify the speech rate of his scripts by choosing his fastest rate of speech from either his reading or spontaneous speaking rate. In this case, his spontaneous speech rate was faster. By practicing with videos at this individually tailored rate, SE001 was able to practice choral speech with the video without lagging behind. Since the homework component of speech entrainment is an essential aspect of this treatment, clients' ability to properly practice with the videos by matching the mouth movements and speech rate of the mouth model is important to achieve fluency gains. With this individually tailored speech rate, SE001 was able to practice speech entrainment properly despite having moderate apraxia.

SE002 showed a positive response to treatment for trained scripts in the primary outcome measure of script intelligibility and accuracy. Though less generalized improvement was seen in untrained scripts for intelligibility and accuracy, she showed improved production of grammatical classes in both trained and untrained scripts. She differed from SE001 in that her apraxia was mild and she was not dysarthric. Unlike SE001, intelligibility was not significantly compromised, with high intelligibility ratings for both trained and untrained material pre- and post-treatment. She also had more verbal output, faster rate of speech, and higher overall intelligibility than SE001 at pre-treatment. Because of this, the scripts for SE002 were slightly longer and more difficult, with more multisyllabic words. Even though SE002 logged fewer homework practice hours than SE001, she was still able to meet criterion in two sessions, except for one script, which took her three sessions. She showed accurate, intelligible script production as well as improved overall grammaticality and intelligibility for scripted topics. In contrast to SE001, who showed an increase in intelligibility as a result of treatment, intelligibility was observed to be stable before and after treatment for SE002 for trained and untrained scripts. Spontaneous speech intelligibility was also stable for picture description task for the *WAB-R*, which showed 100% intelligibility at both pre- and post-treatment.

Daily homework is an essential component of this treatment program. Thirty minutes of homework that focused on speech entrainment was required of each participant daily. Participants reported that the repetitive nature of homework was tedious and not always easy to complete. SE001 conscientiously completed homework over the course of treatment. Relative to SE001, SE002 completed only a little more than half of the homework. Notably, she still showed significant gains that were comparable to those of

SE001. One possibility for this may be that SE002 may have had more residual speech-language ability, which required her to do less homework in order to make significant progress.

All intervention sessions with SE002 occurred through videoconferencing using Skype©. The medium of videoconferencing did not seem to influence the rate at which the participant reached criterion. Remote sessions allowed the participant the opportunity to take part in this study despite her living in Oregon and the primary research site being in Texas. Videoconferencing also conserved time by allowing greater flexibility, with the capacity to maintain the treatment schedule as SE002 traveled out of state during the course of the study.

Videoconferencing did, however, have unique challenges. In particular, choral speaking with the clinician was difficult due to asynchrony between the audio and visual signal (Youmans et al., 2010). When a participant is having difficulty pronouncing certain words, or when words are unintelligible due to apraxia and/or dysarthria, articulation practice with the clinician required choral production. Choral production continued to be attempted, and the participant eventually produced clearer words with repetition and exaggerated articulation of words in addition to choral production. It is unknown whether clearer production was due to the attempted choral production or repetition of words performed independently without the clinician. Overall, it appears that videoconferencing may be an efficient, economical, and viable method of delivering speech entrainment intervention, but due to the limited sample this may not be generalizable to all populations, especially individuals with more severe motor speech or auditory comprehension deficits.

A strength of this study is its verification of the utility of this treatment protocol in a population with a different etiology (i.e., progressive disease), demonstrating that speech entrainment can benefit non-fluent PPA populations in addition to non-fluent stroke populations. Although a positive effect size was observed in each participant, this study had a small number of participants, and these results cannot be generalizable to all individuals with non-fluent PPA.

Future research is needed to understand whether speech entrainment treatment can be effective in PPA patients with more severe concomitant apraxia of speech. Future research can address criteria for candidacy for speech entrainment treatment (e.g., degree of motor speech and grammatical deficits). Also, future studies should address how modifications in treatment can best address motor speech deficits. For example, this study modified rate of speech based on the patient's rate of reading and spontaneous speech and choosing the fastest rate from the two. All scripts were recorded in that fixed rate. It would be interesting to see if increasing the rate of speech over the course of treatment would result in greater improvement of speech rate and possibly greater fluency for trained and untrained topics.

In summary, the results of this study support the hypothesis that speech entrainment is an effective method for improving spoken fluency for scripted material in two individuals with a non-fluent variant of PPA. Their positive responses to treatment provide additional evidence in support of efforts to rehabilitate speech and language deficits in this population. This study also suggests that videoconferencing may be a successful medium for therapy, but further research is necessary to determine if this medium will be successful for all participants, especially those with more severe impairments. The cases reported here illustrate treatment methods that have potential to improve speech and language fluency at the beginning and middle stages of disease. As the disease progresses to later stages, scripts may be implemented using augmentative and alternative communication (AAC) devices, allowing choral production or simply video display, or can be presented as text in memory/communication books. Further, fluently produced scripts (post-treatment) can be recorded and played back at later stages of the disease, in a modified voice-banking format. Thus, generation of functional scripts has potential benefits at later stages of the disease, when spoken language becomes less viable for patients with non-fluent PPA.

References

Albert, M., Sparks R., Helm, N. (1973). Melodic intonation therapy for aphasia. *Archives of Neurology, 29*, 130-131.

Beeson, P.M., Rising, K., Kim, E.S., & Rapcsak, S.X. (2010). A treatment sequence for phonological alexia/agraphia. *Journal of Speech, Language and Hearing Research, 53*(2), 450-468.

Beeson, M., Robey, R.R. (2006). Evaluating single-subject treatment research: Lessons learned from the aphasia literature. *Neuropsychology Review, 16*: 161-169.

Belin, P., Van Eeckhout P., Zilbovicius, M., Remy, P., Francois, C., Guillaume, S., et al. (1996). Recovery from nonfluent aphasia after melodic intonation therapy: A PET study. *Neurology, 47,* 1504-1511.

Breier, J. I., Randle, S., Maher, L. M., & Papanicolaou, A.C. (2010). Changes in maps of language activation following melodic intonation therapy using magnetoencephalography: Two case studies. *Journal of Clinical and Experimental Neuropsychology, 32*, 309-314.

Broca. P., (1861). Loss of speech, chronic softening and partial destruction of the anterior left lobe of the brain. *Bulletin de la Societe Antrhopologique*, 2, 235-238.

Brookshire, R. (2007). *Introduction to neurogenic communication disorders* (7th ed.). St. Louis, Missouri: Mosby.

Caplan, D., & Hanna, J. (1998). Sentence production by aphasic patients in a constrained task. *Brain and Language*, 63, 184-218.

Cherney, L.R., Halper, A.S., Holland, A. L., & Cole, R. (2008) Computerized script training for aphasia: Preliminary results. *American Journal of Speech-Language Pathology*, 17, 19-34.

Cherney, L. R., Halper, A.S., & Kaye, R.C. (2011). Computer-based script training for aphasia: Emerging themes from post-treatment interviews. *Journal of Communication Disorders, 44(*4), 493-501.

Conklyn, D., Novak, E., Boissy, A., Bethoux, F., & Chemali, K. (2012). The effects of modified melodic intonation therapy on nonfluent aphasia: a pilot study. *Journal of Speech, Language and Hearing Research, 55*(5), 1463.

Croot K., Nickels L., Laurence F., & Manning M., Impairment-and activity /participation-directed interventions in progressive language impairment: Clinical and theoretical issues, *Aphasiology,* 23(2) (2009), 236-265.

Crum, R.M., Anthony, J.C., Bassett, S.S., & Folstein, M.F. (1993). Population-based norms for the Mini-Mental State Examination by age and educational level. *JAMA*, 269(18), 2386-2391.

Dronkers, N. (1996). A new brain region for coordinating speech articulation. *Nature*, 384, 159.

Duffy, J. (2005). *Motor speech disorders: Substrates, differential diagnosis and management (*2nd ed.). St. Louis, MO: Mosby.

Folstein, M.F., Folstein, S.E., & McHugh, P.R. (1975). "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research 12(*3*)*, 189-198.

Freed, D.B., & Code, C. (2012) The clinical scientist. *Aphasiology*, *26*(5), 615-617.

Fridriksson, J., Basilakos, A., Hickok, G., Bonilha, L., & Rorden, C. (in press). Speech Entrainment Compensates for Broca's Area Damage. *Cortex.*

Fridriksson, J., Hubbard, H.E., Hudspeth, S.G., Holland, A.L., Bonilha, L., Fromm, D., & Rorden, C. (2012). Speech entrainment enables patients with Broca's aphasia to produce fluent speech. *Brain,* 135(12), 3815-3829.

Friedmann, N., & Grodzinsky, Y. (1997). Tense and agreement in agrammatic production pruning the syntactic tree. *Brain and Language,* 85, 409-426.

Geschwind, N. (1965). Disconnexion syndromes in animals and man. *Brain,* 88, 237-294.

Gorno-Tempini, M. l., Hillis, A. E., Weintraub, S., Kertesz, A., Mendez, M., Cappa, S.F., et al. (2011). Classification of primary progressive aphasia and its variants. *Neurology*, *76*(11), 1006-1014.

Henry M.L., Meese M.V., Truong S., Babiak, M.C., Miller, B.L., & Gorno-Tempini, M.L. (2013). Treatment for apraxia of speech in nonfluent variant primary progressive aphasia. *Behavioural Neurology*, *26(*1–2),77–88.

Henry M.L. (2010). Treatment for Progressive Impairment of Language, *Perspectives on Neurophysiology and Neurogenic Speech and Language Disorders*, *20*(1), 13-20.

Hickok, G. (2014). Towards an integrated psycholinguistic, neurolinguistic, sensorimotor framework for speech production. *Language, Cognition and Neuroscience, 29*(1), 52-59.

Howard, D., & Patterson, K.E. (1992). *The Pyramids and Palm Trees Test: A test of Semantic Access from Words and Pictures.* Thames Valley Test Company.

Jokel, R., Cupit, J., Rochon E., & Leonard, C., Relearning lost vocabulary in nonfluent progressive aphasia with MossTalkWords, *Aphasiology* 23(2) (2009), 175-191.

Kaplan, E., Goodglass, H., & Weintraub, S. (2001). *Boston Naming Test.* Pro-ed.

Kay, J., Lesser, R., & Coltheart, M. (1992). PALPA: Psycholinguistic assessments of language processing in aphasia. Hove: Lawrence Erlbaum Associated Ltd..

Kertesz, A. (1982). *Western aphasia battery test manual*. Psychological Corp.

Kramer, J.H., Jurik, J., Sha S.J., Rankin, K.P., Rosen H.J., Johnson J.K., (2003). Distinctive neuropsychological patterns in frontotemporal dementia, semantic dementia, and Alzheimer disease. *Cognitive and Behavioral Neurology*, 16(4): 211-218.

Louis M., Espesser, R., Rey V., Daffaure V., Cristo A.D., & Habib M. (2001). Intensive training of phonological skills in progressive aphasia: a model of brain plasticity in neurodegenerative disease. *Brain and Cognition*, *46*(1-2), 197-201.

MacWhinney, B. & Snow, C. (1985) The Child Language Data Exchange System. *Journal of Child Language*, *12*, 271-296.

Mesulam, M. (2001). Primary progressive aphasia. *Annals of Neurology,* 49(4), 425-432.

Morrow-Odom, K., and Swann, A. (2013). Effectiveness of melodic intonation therapy in a case of aphasia following right hemisphere stroke, *Aphasiology*, 27:11, 1322 1338.

Racette, A., Bard, C., & Peretz, I. (2006). Making non-fluent aphasics speak: sing along! *Brain*, *129*, 2571-2584. doi:10.1093/brain/aw1250

Robey, R. R., Schultz, A. B., Sinner, C., & Sinner, C. A. (1999). Review: Single-subject clinical-outcome research: designs, data, effect sizes, and analyses, *Aphasiology, 13*(6), 445-473.

Schlaug, G., Marchina, S., and Norton A. (2008). From singing to speaking: Why singing may lead to recovery of expressive language function in patients with Broca's aphasia. In *Music Perception: An Interdisciplinary Journal*, *25*, 315-323.

Schlaug, G., Norton, A., Marchina, S., Zipse, L., and Wan, C. (2010). From singing to speaking: Facilitating recovery from nonfluent aphasia. *Future Neurology*, 5(5) 657-665.

Schwartz, M.F., Saffran, E.M., Fink, R.B., Myers, J.L., & Martin, N. (1994). Mapping therapy: A treatment programme for agrammatism. *Aphasiology, 8*, 19-54.

Sparks, R. (2008) Melodic intonation therapy. In Chapey, R. (2008). *Aphasia intervention strategies in aphasia and related neurogenic communication disorders* (5th ed.). Philadelphia, PA: Lippincott Williams & Wilkins.

Sparks, R., Holland A. (1976). Method: melodic intonation therapy for aphasia. *Journal of Speech and Hearing Disorders, 41*, 287-297.

Schneider, S.L., and Thompson, C.K., Verb production in agrammatic aphasia: The influence for semantic class and argument structure properties on generalisation, *Aphasiology, 17*(3) (2003), 213-241.

Stahl, B., Kotz, S. A., Henseler, I., Turner, R., & Geyer, S. (2011). Rhythm in disguise: why singing may not hold the key to recovery from aphasia. *Brain, 134*, 3083-3093. doi:10.1093/brain/awr240

Stahl, B., Henseler, I., Turner, R., Geyer, S., & Kotz, S. A. (2013). How to engage the right brain hemisphere in aphasics without even singing: evidence for two paths of speech recovery. *Frontiers in Human Neuroscience,* 7. doi:10.3389/fnhum.2013.00035

Thompson, C.K. (2011) *Northwestern Assessment of Verbs and Sentences.* Evanston, IL: Minuteman Press.

Thomspon, C.K., Cho, S., Wieneke, C., Weintraub, S. & Mesulam, M.M (2012). Dissociations between fluency and agrammatism in primary progressive aphasia. *Aphasiology, 26*(1), 20-43.

Tomaino, C.M. (2012). Effective music therapy techniques in the treatment of nonfluent aphasia. *Annals of the New York Academy of Sciences, 1252,*312.

Tombaugh, Tom T. N., & Hubiey, A.M. (1997). The 60-item Boston Naming Test: Norms for cognitively intact adults aged 25 to 88 years. *Journal of Clinical and Experimental Neuropsychology, 19*(6), 922-932.

Weintraub, S., Mesulam, M.M., Wieneke, C., Rademaker, A., Rogalski, E.J., Thompson, C.K. (2009). The Northwestern Anagram Test: Measuring sentence production in Primary Progressive Aphasia. *American Journal of Alzheimer's Disease and other Dementias, 24*, 408-416.

Wertz, R.T., LaPointe, L.L., & Rosenbek, J.C. (1984). *Apraxia of speech in adults: The disorder and its management.* Orlando, FL: Grune & Stratton.

Wilson, S.M., Dronkers, N.F., Ogar, J.M., Jang, J., Growdon, M.E., Agosta, F., Henry, M.L., Miller, B.L., & Gorno-Tempini, M.L. (2010). Neural correlates of syntactic processing in the nonfluent variant of primary progressive aphasia. *The Journal of Neuroscience*, *30*(50), 16845-16854.

Wilson, S. J., Parsons, K., & Reutens, D.C., (2006). Preserved singing in aphasia: A case study of the efficacy of melodic intonation therapy. *Music Perception: An Interdisciplinary Journal, 24*(1), 23-36.

Yamaguchi, S., Akanuma, K., Hatayama, Y., Otera, M., & Meguro, K. (2011). Singing therapy can be effective for a patient with severe nonfluent aphasia. *International Journal of Rehabilitation Research, 35,* 78-81.

Youmans, G., Holland, A., Munoz, M.L., & Bourgeois, M. (2005). Script training and automaticity in two individuals with aphasia. *Aphasiology, 19, 435-450.*

Youmans, G., Youmans, S.R., & Hancock, A.B. (2011). Script training treatment for adults with apraxia of speech. *American Journal of Speech-Language Pathology, 20*, 23-37.