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Speech Entrainment to Improve Spontaneous Speech in Broca's Aphasia.

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SPEECH ENTRAINMENT TO IMPROVE SPONTANEOUS SPEECH IN BROCA'S APHASIA.

by

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ABSTRACT

Speech entrainment, a treatment method that requires participants to mimic the speech of an audiovisual model in real time, has been shown to benefit individuals with non-fluent aphasia when they speak about trained topics. It is unclear if it improves spontaneous speech, which does not pertain to trained items, in the same way. In an effort to investigate this matter, the current study examined the effects of speech entrainment on spontaneous speech that does not relate to trained items, it also estimated effect sizes associated with improvements in speech production as a result of this treatment approach, and explored participant characteristics associated with treatment response.

Twenty participants were recruited to participate in this study. Each participant received three weeks of treatment and underwent extensive speech and language testing before and after treatment had concluded, as well as testing of discourse abilities pre-treatment, post-treatment, at three months post treatment and again at six months post-treatment.

We found that speech entrainment treatment does in fact improve spontaneous speech for some people with non-fluent aphasia. The number of words and different words per minute in participants' speech samples did not increase for everybody, but the accuracy of the information content that the participants uttered was found to increase significantly. Notably, there was also a significant positive change in aphasia quotient scores, picture naming, semantic processing and grammatical processing.

Analysis of functional brain activity supported previous findings of the importance of pMTG for speech entrainment and how changes in activity could predict changes in both fluency and informativeness of spontaneous speech output.

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LIST OF ABBREVIATIONS

AAF.....Altered Auditory Feedback

ABA-2..... Apraxia Battery for Adults-2

AF .....Arcuate fasciculus

AOS.....Apraxia of Speech

AQ..... Aphasia Quotient

ASRS..... Apraxia of Speech Rating Scale

ATR.....Anterior Thalamic Radiations

BA .....Brodmann Area

CIU..... Correct Information Unit

CIU/min .....Correct Information Units/minute

%CIUs.....Percent Correct Information Units

DIVA..... Directions into the Velocities of Articulators

dwpm.....Different Words per Minute

HSFC..... Hierarchical State Feedback Control

fMRI.....Functional Magnetic Resonance Imaging

IFG .....Inferior Frontal Gyrus

IFOF .....Inferior Fronto-Occipital Fasciculus

ILF.....Inferior Longitudinal Fasciculus

KDT ..... Kissing and Dancing Test

L ..... Left

MTG ..... Middle Temporal Gyrus

MIT ..... Melodic Intonation Therapy

MRI ..... Magnetic Resonance Imaging

pMTG ..... posterior Middle Temporal Gyrus

pSTG ..... posterior Superior Temporal Gyrus

NAVS ..... Northwestern Assessment of Verbs and Sentences

PNT ..... Philadelphia Naming Test

PPTT ..... Pyramids and Palm Trees Test

PoCG ..... Postcentral Gyrus

PrCG ..... Precentral Gyrus

R ..... Right

ROI ..... Region of Interest

SE ..... Speech entrainment

SFC ..... State Feedback Control

SFG ..... Superior Frontal Gyrus

SLF ..... Superior Longitudinal Fasciculus

SLP ..... Speech-Language Pathologist

SMG ..... Supramarginal Gyrus

SPG ..... Superior Parietal Gyrus

SPGI ..... Superior Precentral Gyrus of the Insula

(Area) Spt ..... Boundary of Parietal & Temporal Areas at Posterior Sylvian Fissure

STG ..... Superior Temporal Gyrus

UF ..... Uncinate Fasciculus

WAB-R ..... Western Aphasia Battery – Revised

WPM ..... Words per Minute

CHAPTER 1

INTRODUCTION

Stroke is a medical condition that is caused by a disruption in blood flow to the brain. It is one of the leading causes of long-term disability and death in the world, and every year, more than 795,000 people in the United States suffer a new or recurrent stroke (Mozaffarian et al., 2015). In 2011, stroke accounted for approximately 1 of every 20 deaths in the United States but the stroke death rate has gradually been declining in all but the southernmost states in the southeastern part of the United States (Mozaffarian et al., 2015). The prospect of improvement after stroke varies with the nature and severity of the initial deficit (Dobkin, 2005) but is mainly predicted by the severity of the initial stroke (extent of brain damage and location) and age at onset of stroke (Donnan, Fisher, Macleod, & Davis, 2008; Cramer, 2008, Pedersen, Jørgensen, Nakayama, Raaschou, & Olsen, 1995). Some people recover relatively well but others make a relatively limited recovery. Studies have shown that only 25 percent of patients return to their previous level of everyday participation and achieve physical functioning comparable to that of community-matched persons who have not had a stroke (Lai, Studenski, Duncan, & Perera, 2002); nearly 50 percent of stroke survivors are left disabled (Warlow, Sudlow, Dennis, Wardlaw, & Sandercock 2003). About 20-30 percent of stroke patients experience speech- and language deficits following their strokes and need speech therapy (Dobkin, 2005; Berthier, 2005). Among the diverse deficits caused by strokes, aphasia is

probably the most devastating (Hilari, 2011; Pollock, St George, Fenton, & Firkins, 2012). Aphasia is defined as a loss or impairment of the complex process of interpreting and formulating language symbols caused by acquired brain damage affecting a widely distributed network of cortical and subcortical structures of the language-dominant hemisphere (McNeil & Pratt, 2001).

Aphasia is a multi-modal disorder that can affect auditory comprehension, reading, expressive language and writing, but it should not be viewed as a domain-specific disorder because other predominantly left-hemisphere cognitive processes (e.g., auditory-verbal short-term memory, attention) necessary for language processing can be affected as well (McNeil & Pratt, 2001).

Most patients with post-stroke aphasia improve to some extent (Inatomi et al., 2008; Berthier, 2005; Wade, Hewer, David, & Enderby, 1986; Pedersen et al., 1995; Ashtary, Janghorbani, Chitsaz, Reisi, & Bahrami, 2006; Laska, Hellblom, Murray, Kahan, & Von Arbin, 2001). Although a significant amount of spontaneous recovery occurs in the acute phase (Maas et al., 2012; Pedersen et al., 1995; Kertesz & McCabe, 1977) a number of studies have shown that speech and language therapy long after stroke is effective: many people with aphasia show benefits from therapy (e.g. Poeck, Huber, & Willmek, 1989; Moss & Nicholas, 2006; Brady, Kelly, Godwin, & Enderby, 2012; Robey, 1994, 1998; Holland, Fromm, DeRuyter, & Stein, 1996; Holland, Fromm, Forbes, & MacWhinney, 2017; Pulvermuller et al., 2001; Fridriksson et al., 2009; Fridriksson et al., 2012; Bonilha, Gleichgerrcht, Nesland, Rorden, & Fridriksson, 2016; Breitenstein et al., 2017). Responses to aphasia therapy vary widely among people, making it very difficult to predict who will benefit from treatment and what kinds of treatments should

be utilized with participants with different patterns of language impairment (e.g., Fridriksson, Bonilha, Baker, Moser, & Rorden, 2010). To date, there is no conclusive evidence that one approach is better than another as regards functional communication outcomes (Brady et al., 2012) and in clinical practice, speech and language therapists commonly use combinations of different therapeutic approaches in an attempt to tailor the language treatment to each patient's clinical profile (Rose, Ferguson, Power, Togher, & Worrall, 2014).

1.1 Speech and Language Therapy for Broca's Aphasia

Broca's aphasia is a common type of aphasia. Individuals with Broca's aphasia typically have impaired speech production, relatively spared auditory comprehension, and, in many cases, agrammatism (Goodglass, 1993). Some persons with Broca's aphasia who undergo speech therapy have been found to recover remarkably well (e.g., Kertesz & McCabe, 1977).For example, Bakheit et al. (2007) found that patients with Broca's aphasia made greater gains in Western Aphasia Battery scores after 6 months than those with Wernicke's or global aphasia. Other studies have found no clear differences in recovery between different aphasia types (e.g., Sarno & Levita, 1979; Demeurisse et al.,1980).

Traditional speech therapy for Broca's aphasia is generally focused on increasing more fluent speech production by using verbal repetition, picture cards and real objects to elicit spoken words and phrases. Two treatment approaches that are commonly used and that have also been shown to have good outcomes are described below. Both treatment

approaches share some important aspects with the relatively recently developed technique, speech entrainment (SE).

1.1.2 Melodic Intonation Therapy. Melodic Intonation Therapy (MIT) is based on the observation that in many cases severely aphasic patients can produce well-articulated, linguistically accurate words while singing but not during normal speech. The MIT program has been reported in considerable detail and has been used in research and clinical practice for a long time (Sparks, Helm & Albert, 1974; Sparks & Holland, 1976; Helm-Estabrooks, Nicholas, & Morgan, 1989; Schlaug, Marchina, & Norton, 2008). MIT uses melody and rhythm to improve expressive language by capitalizing on a presumptively undamaged contralateral hemisphere's preserved function (singing) and engaging language-capable regions there. The ideal candidates for this treatment are patients with moderately well-preserved auditory comprehension and poorly articulated, non-fluent, or severely restricted output (Helm-Estabrooks et al., 1989). Thus, along with individuals with apraxia of speech, it may be an appropriate treatment approach for people with Broca's aphasia.

MIT is a hierarchically structured program that uses intoned (sung) patterns to exaggerate normal melodic content of speech by transforming spoken phrases into melodically intoned patterns (Schlaug et al., 2008). MIT contains two key features that make it a unique treatment compared to other, non-intonation-based therapies: 1) melodic intonation (singing) with continuous voicing, and 2) rhythmic tapping of each syllable with the patient's left hand while phrases are intoned and repeated (Schlaug, Marchina, & Norton, 2009).

A considerable research literature has demonstrated that MIT is an effective treatment for improvement of language function in individuals with chronic, non-fluent aphasia (Schlaug et al., 2008, 2009; Stahl, Kotz, Henseler, Turner, & Geyer, 2011; Wilson, Parsons, & Reutens, 2006; Conklyn, Novak, Boissy, Bethoux, & Chemali, 2012). These studies have resulted in increased speech production, improved speech fluency, and auditory comprehension (Schlaug et al., 2008; Stahl et al., 2011; Wilson et al., 2006; van der Meulen, van de Sandt-Koenderman, & Ribbers, 2012).

MIT was initially thought to engage expressive language areas in the hemisphere contralateral to the stroke hemisphere, (Albert, Sparks, & Helm, 1973; Sparks et al., 1974). However, currently it is hypothesized that MIT engages both hemispheres, either by unmasking existing music/language connections in both hemispheres, or by engaging preserved language regions in either or both hemispheres (Schlaug et al., 2008; Schlaug, 2016). It remains unclear what aspects of MIT are crucial for the therapeutic effect, which specific neural mechanisms are involved, and the extent to which MIT targets aphasia, apraxia, or both (Norton, Zipse, Marchina, & Schlaug, 2009; van der Meulen et al., 2012; Schlaug, 2015). Some components of MIT may not to be crucial, but the rhythmic component, reduction of speed, singing in synchrony and tapping/pacing all seem to be beneficial (van der Meulen et al., 2012). Stahl et al. (2011) also found that rhythm is crucial to speech production, in addition to intoning, for people with non-fluent aphasia and Racette, Bard, and Peretz, (2006) found that MIT was most successful for people with aphasia when rhythm and synchronized singing, not tone, was emphasized by tapping to keep the beat.

1.1.3 Script training. Script training is a functional approach to aphasia therapy. This approach involves sentences that are likely to be used in everyday communication. The purpose of the treatment is to facilitate communication and participation in conversational exchanges specifically related to personal interests. During therapy patients also focus on speech initiation, turn taking and socialization once scripts become automated. To promote automatization of script use, cue-based massed drilling of the entire script is required. According to Lee, Kaye, & Cherney (2009), the standard intervention includes 3 weeks of intervention for each script, but other studies have based intervention duration on script mastery (e.g., Youmans, Youmans, & Hancock, 2011) suggesting that some participants may show mastery of the scripts in as few as eight sessions whereas others require as many as nineteen. The most influential feature of script training seems to be the intensity of intervention sessions and the repetitive nature of the treatment.

Conversational scripts have been used with people with varying levels of aphasia severity. Research has indicated that script knowledge is not seriously compromised by aphasia, at least when the deficit is mild or moderate, thus making individuals with aphasia good candidates for script training (Cherney, Halper, Holland, & Cole, 2008). Holland and colleagues (2002) initially developed and tested a script training approach in which scripts were personalized to meet communication needs of each patient. All six of these participants learned their respective scripts in 4-34 sessions but there was little generalization of treatment effects to traditional measures of language such as Western Aphasia Battery (Kertesz, 2007) or Boston Naming Test (Kaplan, Goodglass, & Weintraub, 2001). More recently, Youmans, Holland, Muñoz, and Bourgeois (2005)

recruited two individuals with predominant apraxia of speech and trained them, using a cueing hierarchy that began with simultaneous production with a clinician and ended with independent production. Following script mastery, scripted speech was practiced in conversation with the clinician and novel conversation partners. Their outcome measure was individual mastery of scripts. The authors did not report pre-post training performance on standardized tests such as the Western Aphasia Battery (Kertesz, 2007) or Boston Naming Test (BNT; Kaplan, et al., 2001). Cherney, Halper, Holland, & Cole (2008) recruited three participants with chronic aphasia to a computer script training program and found that two of them made significant gains on the Western Aphasia Battery (Kertesz, 2007). Further, all three participants improved on all measures of script related outcomes (content, grammatical productivity and rate of production of script related words) on every script they practiced (Cherney, Halper, Holland, & Cole, 2008).

The massed drilling of this treatment approach can be accomplished in a more cost-effective way using computers. Providing therapy, using computers, minimizes therapist time and resources and is very cost-effective as the clinician can program a virtual therapist to take over some of the workload. This has been done in multiple successful studies (e.g. Lee et al., 2009; Cherney, Halper, Holland, & Cole, 2008; Cherney, Patterson, & Raymer, 2011).

1.1.4 Speech entrainment. Speech entrainment (SE) is a relatively new treatment technique that shows promise of increasing fluency in non-fluent aphasia (Fridriksson et al., 2012). It is based on astute clinical observations of Darlene Williamson, who noticed the effect of visual-auditory cueing on speech production, and subsequently developed

VAST (Video Assisted Speech Therapy), a mobile application that focuses on this approach. The treatment technique was developed following Fridriksson et al's (2009) findings of improved speech production in a treatment that involved audio-visual speech perception compared to treatment that involved auditory speech perception without the visual part. Speech entrainment results were also comparable to good treatment results in studies of script training, a treatment approach designed for individuals with chronic aphasia (Cherney, Halper, Holland, & Cole, 2008; Cherney, Patterson, Raymer, Frymark, & Schooling, 2008). SE rests on theories of automaticity and audio-visual speech perception that is incorporated with elements of computerized script training. SE has a visual component that is similar to the modeling seen in apraxia of speech treatment (Rosenbek, Wertz, & Darley, 1973) and also shares some similar treatment aspects of MIT such as slowed down speech and "choral speech".

In SE, an individual with aphasia views a video of a model's mouth while the model speaks. The person with aphasia is asked to mimic the script at the same time as the model. Fridriksson et al. (2012) used computer-based script training but also incorporated the condition of SE to investigate the potential therapeutic outcomes of SE as a treatment for non-fluent aphasia. Fridriksson and colleagues (2012) theorized that SE works by providing a temporal gating for speech as well as visual feedback of articulatory movements to increase fluency of those with non-fluent aphasia and mild apraxia of speech. They found that SE improved speech fluency and that the treatment showed great potential for therapeutic generalization. One unique aspect of SE is that it can be put onto a mobile device such as a mobile smartphone or any other portable device. SE can be used either functionally, as an augmentative/alternative communication

device, or in treatment as a fluency-inducing condition, making it a very versatile and portable option for people with non-fluent aphasia who can use computers independently. Using computers as a medium for delivering conversational script training treatment programs has also been proven to be both feasible and cost effective (Cherney, Halper, Holland, & Cole, 2008).

Table 1.1 Treatment approaches for non-fluent aphasia.

	SE	MIT	ST
Slower pace	YES	YES	YES
Repetition	NO	YES	YES
Fading	NO	YES	YES
Replying to questions	NO	YES	YES
Singing	NO	YES	NO
Hierarchy of Tx levels	NO	YES	NO
Natural prosody	YES	NO	YES
Personalized scripts	NO	YES/NO	YES
Scripts	YES	NO	YES
Computerized	YES	NO	YES/NO
Percussion	NO	YES	NO
Sustained syllables	NO	YES	NO
Cueing hierarchy	NO	YES	YES
Covert rehearsal	NO	YES	NO
Choral speech	YES	YES	YES

Note: SE: Speech entrainment; MIT: Melodic Intonation Therapy; ST: Script Training.

1.2 Audiovisual vs Audio Only

It has been widely established that auditory speech perception is influenced by visual speech information (Sumby & Pollack, 1954; McGurk & MacDonald, 1976; Callan et al.,

2003). Speech comprehension is possible without watching the speaker, but viewing speech affects language comprehension.

The loss of visual and auditory acuity is observed for both simple and more complex stimuli and is particularly prevalent for speech signals, most notably in the presence of external noise (Humes, 1996; Sommers, Tye-Murray, & Spehar, 2005). Visual cues are known to impact speech perception such that when one can both hear a speaker's utterance and concurrently view articulatory movements speech comprehension is more accurate, and less effortful (Fraser, Gagne, Alepins, & Dubois, 2010), than when only auditory information is available (Ross et al., 2007; Sommers et al., 2005; Sumby & Pollack, 1954).

However, it has not been specifically determined how visual speech is informative. One possibility is that the combination of auditory and visual speech signals leads to a better perception via enhancement of the multisensory signal (Beauchamp, Argall, Bodurka, Duyn, & Martin, 2004; Calvert, Campbell, & Brammer, 2000; Stein & Stanford, 2008). When speech is perceived in noisy environments, auditory cues to place of articulation are compromised whereas such cues tend to be robust in the visual signal (Campbell, 2008). If visual factors supplement auditory/oral speech, people can tolerate greater auditory noise interference than when visual cues are not present (Sumby & Pollack, 1954). It is also plausible that visual speech aids perception by generating predictions about the timing and identity of upcoming speech sounds (Golumbic, Poeppel, & Schroeder, 2012; Grant & Seitz, 2000; Schroeder, Lakatos, Kajikawa, Partan, & Puce, 2008; van Wassenhove, Grant, & Poeppel, 2005). The neurophysiological literature disagrees with these assumptions of prediction and suggests that early effects of

visual speech information and auditory information in speech perception are more likely to be modulatory rather than predictive, given the nature of the anatomical connections between early visual and auditory areas, and the fact that high-level features of visual and auditory speech are represented downstream in the visual and auditory cortical pathways, suggesting that extensive modal processing is required prior to high level audiovisual interaction (Bernstein & Liebenthal, 2014).

1.3 Theoretical Implications – Models of Speech Production

Speech production involves a complex, well-orchestrated sequence of movements, executed to match auditory goals that correspond to the chain of sounds that compose words in a given language (Guenther, 1994; Hickok, 2012; Hickok & Poeppel, 2004; Perkell et al., 2004).

Speech production has been studied from a number of different perspectives, including neuroscience, neuropsychology, linguistics, psycholinguistics and motor control. These different perspectives may seem to have limited interactions since they target different aspects of speech production. Conversely, there is a large overlap of ideas, and recent approaches have suggested a more integrated methodology for studying speech production. A number of models from various disciplines have been proposed to explain the different processes that occur when thoughts are translated into speech. Three contemporary models that have been widely used in studies of normal and impaired speech production are the Directions into the velocities of articulators (DIVA) model and the State Feedback Control (SFC) and Hierarchical State Feedback Control (HSFC) models of speech production.

1.3.1. The Directions Into the Velocities of Articulators (DIVA) model. The focus of the DIVA model (Guenther, 1994; Guenther, 1995; Guenther, 2006; Tourville & Guenther, 2011) is on sensorimotor processes that support speech production. It emphasizes the role of both feedforward and feedback control of articulation (Guenther, 1994; Guenther, 2006; Tourville & Guenther, 2011; Golfinopoulus, Tourville, & Guenther, 2010). Sensory feedback is obviously a critical component of speech production but could not work successfully without internal feedforward control mechanisms due to the rate of speech production and the time it takes for the auditory cortex to process the message. The auditory cortex must process incoming feedback and it has been estimated that in some cases, processing acoustic feedback can require between 30-100ms before the information can be utilized (Houde & Nagarajan, 2011). According to this model, internal feedforward models learn motor commands associated with specific speech sounds (the efference copy) and can initiate speech sound production without reliance on sensorimotor and acoustic input. The internal feedforward models use the efference copy to anticipate the articulatory processes and auditory feedback that correspond to the speech motor movements. If there is a mismatch in the internally predicted outcome and the externally predicted speech targets, the internal feedforward model can send a command to correct the errors before they are realized (Hickok, 2012; Houde & Nagarajan, 2011; Tourville et al., 2008). These internal feedforward commands are fundamental in speech production since they allow the speaker to proceed with little input from sensorimotor and auditory feedback, unless the quality of the message has been adversely affected by something like hearing loss or a bite block (Guenther, 2006; Hickok, 2012; Houde & Nagarajan, 2011; Tourville et al., 2008).

The DIVA model was one of the first models of speech production to explain feedforward and feedback control over the course of speech development, normal speech production and impaired speech production. Other, more recently- developed models have built upon the DIVA model and incorporated principles of limb motor control to motor speech production. These models include the SFC model (Hickok, Houde, & Rong, 2011) and an even more recent version, the HSFC model (Hickok, 2012).

1.3.2 SFC model/HSFC model. Sensory feedback is a critical component of motor control, yet overt feedback is ineffective for online control because it is necessarily delayed, intermittent and often noisy (Kawato, 1999; Shadmehr & Krakauer, 2008). To address this problem, motor-control models incorporate an internal model of the motor effector that allows the system to predict the state of the motor effector as well as the sensory consequences of actions, a so-called "forward model". State feedback control models (SFC models) are good examples of motor control models that use feedback from both the predicted (internal) state as well as the measured state of the effector as input to the controller. According to SFC models, representations at the phonological level, are separated into internal motor targets and auditory consequences. Speech acts initiate a motor speech plan and an exact efference copy of that plan providing sensory targets at the level of proprioception and audition (Hickok et al., 2011). More recently, Hickok (2015), proposed that efference copies may be a part of planning a motor speech act prior to execution, rather than after the initiation of a motor command. This does not change the notion that SFC/HSFC, DIVA and other models of speech production consider efference copies to be important for speech production.

1.3.3 Efference copy and SE. If there is damage to feedforward projections from a speech sound map to an articulator map it will probably affect motor programming required for speech because the correct motor plans cannot be accessed. This mismatch may also impair feedback control because the access to feedforward efference copy has been damaged. Without the efference copies, errors in initiation and production cannot be detected via auditory or somatosensory feedback thus eliminating corrective motor commands (Guenther, 2006). Similarly, SFC models suggest that problems with efference mechanisms would likely impair and impact feedforward and feedback processes required for naturally occurring initiation and monitoring of speech production (Hickok, 2012).

As reported in Fridriksson et al. (2012), some individuals with Broca's aphasia are able to mimic an audio-visual speech model in real time and, thereby, produce more fluent speech. In that study, the authors also demonstrated that mimicking audio-only speech does not have the same positive effect on speech fluency. They proposed that the audio-visual speech model provides an on-line target for speech production. Specifically, on-line monitoring is thought to be a basic principle of the nervous system where each motor action is initiated by a motor plan as well as by the generation of an internal model (efference copy) against which the sensory consequences of motor movement can be compared in real-time (Jeannerod, 2003). On-line comparison between the predicted model (the efference copy) and the actual sensory consequences acts to guide and fine tune movement to achieve the targeted motor act. The role of the efference copy in speech production has received considerable attention, mostly in relation to altered auditory feedback (AAF) and is an important feature in the three contemporary models of

speech production introduced above. As established above, both models include an internally generated copy of the motor plan (efference copy) which is then compared to the actual sensory feedback during speech production. Guenther and colleagues (Guenther et al., 2006; Guenther, 2006; Tourville et al., 2008) have shown that real-time auditory and proprioceptive feedback is crucial for correct speech production. Hickok suggested that incorrect matching between the efference copy and the actual sensory feedback is the central impairment that gives rise to conduction aphasia where patients repeatedly attempt to correct speech errors (Hickok, 2014).

At this time, it is not clear what the efference copy codes as the target for speech production (e.g. phonemic, syllabic, or whole word targets). Nevertheless, strong evidence suggests that real-time AAF results in immediate modification of speech output indicating that a real-time model is needed to guide correct speech production. Recent evidence suggests that the generation of efference speech copy relies on the left inferior frontal gyrus (Wang et al., 2014; Niziolek, Nagarajan, & Houde, 2013). Fridriksson and colleagues, (2012) suggested that some patients with Broca's aphasia fail to produce an efference speech copy to which the speech output can be compared. In addition to the effects of other factors (e.g. impaired lexical retrieval or syntactic processing), impaired production of efference speech copy contributes to non-fluent speech production typically seen in Broca's aphasia (Feenaughty et al., 2017). Fridriksson et al., (2012) proposed that speech entrainment provides individuals with Broca's aphasia with an external target (efference copy) to which the sensory feedback can be compared.

1.4 Neuroimaging and SE

In a pursuit to determine the neural mechanisms that support SE, Fridriksson and colleagues (Fridriksson et al., 2012), scanned ten individuals with Broca's aphasia and twenty control subjects using functional MRI scans while the subjects did tasks in the scanner. They found greater bilateral cortical activation for speech produced during speech entrainment compared to spontaneous speech at the junction of the anterior insula and Brodmann area 47 (BA47), in Brodmann area 37 (BA37), and unilaterally in the left middle temporal gyrus (MTG) and the dorsal portion of Broca's area. In 2015 Fridriksson and colleagues set out to better understand the neural mechanisms of SE and to identify patterns of cortical damage that predict a positive response to SE's fluency inducing effects. They scanned 44 individuals that had all experienced a single event stroke to their left hemisphere. Twelve individuals did not have aphasia but 32 of the participants had a clinical diagnosis of some type of aphasia. Fridriksson and colleagues found that decreases in fluency in spontaneous speech were associated with damage to the posterior superior temporal, inferior parietal, inferior frontal, and insular regions, while brain damage associated with SE related improvements in dwpm was mostly localized within the inferior frontal and middle frontal gyri (Fridriksson et al., 2015).

1.5 Purpose and Project Outline

Prognosis for chronic Broca's aphasia is generally poor. Even though some treatment approaches do improve speech output (Fridriksson et al., 2012; Holland et al., 1996; Robey 1994, 1998), such gains are often very modest, and it is unclear if the treatment effects generalize to real life situations. The large number of individuals who suffer from

chronic Broca's aphasia, as well as the limited treatment success in these individuals, suggests that there is an urgent need to improve treatment that targets speech production in Broca's aphasia.

Fridriksson and colleagues (2012), showed that real time mimicking of audio-visually presented speech (using speech entrainment treatment) may facilitate fluent speech production of trained narratives in individuals with chronic Broca's aphasia. Fridriksson and colleagues (2015), then showed that the positive effects of speech entrainment (significant increase in different words per minute during SE versus spontaneous speech) can be predicted by damage to IFG and that individuals with chronic Broca's aphasia benefit more from speech entrainment than individuals with other types of aphasia.

The aim of the current study was to examine the improvements in spontaneous speech production as a result of SE treatment in a group of individuals with Broca's aphasia, and to explore and predict individuals' characteristics associated with treatment response.

1.6 Specific Aims and Hypotheses

Specific Aim 1: Determine if three weeks of daily speech entrainment treatment (11.25 hours) could increase accurate production of spontaneous speech for individuals with chronic Broca's aphasia.

> ***Hypothesis 1.*** Positive treatment effects of speech entrainment treatment would not only increase accurate production of trained narratives, but also generalize to spontaneous speech output in individuals with Broca's aphasia.

Specific Aim 2: Use a multi-modal neuroimaging approach to identify patterns of regional and network damage that correlate with SE outcome.

Hypothesis 2a. Participants that have lesions that include areas of five anatomic regions associated with apraxia of speech characteristics: precentral gyrus, postcentral gyrus, superior corona radiata, superior longitudinal fasciculus, and supramarginal gyrus (Basilakos, Rorden, Bonilha, Moser, & Fridriksson, 2015) would experience less improvement in spontaneous speech output than participants who do not.

Hypothesis 2b. SE activates auditory-visual syllable targets, perhaps rooted in the posterior middle temporal gyrus (Fridriksson et al., 2012; Venezia, J. H., Fillmore, P., Matchin, W., Isenberg, A. L., Hickok, G., & Fridriksson, J., 2016). Similar to auditory syllable targets that are mapped onto articulation via the area Spt, the same processing route could be assumed for AV syllable targets. In order to see if it was possible to identify areas that correlate with changes in accurate production and fluency of spontaneous speech, SE-task activation in scanner was compared to spontaneous speech task activation in the predetermined areas.

CHAPTER 2

METHOD

2.1 Participants

Twenty individuals between ages 41-79 (mean age 60.14; 4F) who have experienced a single-event left hemisphere stroke were recruited for the study. Study participants were at least 12 months post-stroke and had a diagnosis of Broca's aphasia due to hemorrhagic or ischemic stroke. The presence and type of aphasia was determined using the Western Aphasia Battery-Revised (WAB-R; Kertesz, 2007). Each participant provided informed consent for study participation as approved by the University of South Carolina Institutional Review Board. Prior to the first MRI scan, participants were screened to assure MRI compatibility (e.g. no implanted metal, no implanted medical devices containing metal or electronic components, and no history of claustrophobia). An MRI could not be performed on participant 4 due to a stent, or participant 7 due to a pacemaker. All participants were asked to discontinue group and individual speech therapy intervention for the duration of the research study and follow-up testing (approximately six months).

Hearing and visual acuity were not specifically tested but all participants had adequate hearing and levels of vision for the assessment and treatment tasks based on testing performance: answering questions, pointing to objects when asked, and following instructions.

Table 2.1 Demographic data and Aphasia Quotient (AQ) from the Western Aphasia Battery-R.

Participant	Age	Gender	MPS	AQ
1	53	M	59	56.7
2	54	F	119	80.7
3	57	M	75	76.0
4	60	F	99	27.2
5	71	F	28	67.6
6	41	F	115	56.6
7	68	M	131	58.4
8	50	M	55	15.7
9	79	M	316	20.7
10	56	M	13	30.6
11	70	M	223	45.8
12	65	M	13	33.9
13	49	M	77	47.8
14	57	M	14	22.0
15	64	M	16	21.5
16	45	M	25	72.4
17	72	M	41	17.8
18	56	M	151	59.6
19	77	M	27	22.0
20	58	M	37	66.6
Range	41-79		13-316	17.8-80.7
Mean	60		81.7	45
SD	10.43		79.83	21.86

Note: MPS=months post stroke.

2.2 Standardized Behavioral Assessments

All participants underwent extensive testing of speech and language abilities at baseline as well as after treatment was concluded. The order of speech and language tests was randomized before each testing session and all of the sessions were video-recorded and later scored by a certified speech-language pathologist. The Western Aphasia Battery-Revised (Kertesz, 2007) was administered to all participants at baseline to characterize the participants' overall language abilities. The results of this testing gave an aphasia quotient (AQ), a measure of aphasia severity on the WAB-R where a score higher than 93.8 indicates performance within the normal range. The Pyramids and Palm Trees Test (PPT; Howard & Patterson, 1992) and the Kissing and Dancing Test (KDT; Bak & Hodges, 2003) were administered to assess semantic processing of nouns and verbs,

respectively. The Northwestern Assessment of Verbs and Sentences (NAVS; Cho-Reyes & Thompson, 2012) was administered to assess grammatical processing. A composite score (Z-score) of four subtests was used as a measure of agrammatism (verb naming, verb comprehension, argument structure production, and argument structure priming). The Apraxia of Speech Rating Scale (ASRS; Strand, Duffy, Clark, & Josephs, 2014) was used to determine the presence/absence of and rate-related treatment changes in specific speech characteristics commonly observed in apraxia of speech (AOS). Naming impairment and treatment related changes in naming was assessed using the Philadelphia Naming Test (PNT; Roach, Schwartz, Martin, Grewal, & Brecher, 1996).

2.3 Outcome measures

To evaluate generalization from speech entrainment treatment to spontaneous speech, participants underwent testing of discourse at baseline, in the week after treatment was completed, and three months, and six months after treatment was completed. The measures that were used were originally developed for the AphasiaBank; an NIDCD supported project devoted to collecting discourse data in a large sample of aphasic patients (2011).

The AphasiaBank test battery includes a wide range of standardized measures and tasks of which four discourse elicitation tasks were used: 1. Broken Window – The clinician showed the participant a series of four pictures of a child playing with a soccer ball and breaking a window. The participant was instructed to look at the pictures and then tell a story with a beginning, middle and an end; 2. Cinderella Story, a task commonly used for narrative assessment in participants with aphasia (MacWhinney,

Fromm, Forbes, & Holland, 2011; Fromm, Forbes, Holland, Dalton, Richardson, & MacWhinney, 2017; Holland et al., 2017; Webster, Franklin, & Howard, 2007). The Cinderella story provides listeners with sufficient context but is not so restrictive as to prevent valid assessment of functional communication (Webster et al., 2007) The participant was asked to look through a short story book about Cinderella where the words had been covered up. The clinician then removed the book and asked the participant to tell the Cinderella story using details from the book and any other details they may otherwise remember. In adherence to AphasiaBank instructions, there was no time limit placed on the story telling; 3. Peanut Butter and Jelly Sandwich – The participant was asked to describe the steps involved in making a peanut butter and jelly sandwich; 4. Picture description – The participant was asked to describe the picnic scene picture from the WAB-R (Kertesz, 2007). To establish stable baseline and post-treatment performance, participants completed the four discourse tasks in two separate sessions during the week before treatment initiation and again in two separate sessions at each assessment point following treatment completion. AphasiaBank guidelines for assessment setup and data collection were followed. Each task was video recorded, transcribed, and error coded off-line according to AphasiaBank rules and guidelines. Four discourse measures were included: Measure 1 – Words per minute (WPM). Measure 2 - Consistent with a previous study (Fridriksson et al., 2012), the average number of different words produced per minute (dwpm) for each discourse task across baseline sessions were counted and compared to averages in post-treatment sessions. Although dwpm correlates with the number of total words produced per minute, this measure was chosen as individuals with non-fluent aphasia often repeat the same words without adding

information content. Measure 3 – In addition to dwpm, correct information units produced per minute (CIU/min) were counted. Measure 4 - Percent correct information units (%CIUs) (Nicholas & Brookshire, 1993) were also calculated. Analysis of CIUs (CIUs/min and %CIUs) was selected because it is a widely used method that attempts to assess the informativeness of connected speech of individuals with aphasia (Brookshire & Nicholas, 1994; Doyle, Goda, & Spencer, 1995; Doyle, Tsironas, & Goda, 1996). Although WPM, dwpm, CIU/min and %CIUs are probably not independent measures, it is likely that they contribute unique information; WPM and dwpm are probably more related to overall speech output whereas CIU/min and % CIUs provide data regarding information content.

2.4 Treatment Stimuli

The treatment stimuli consisted of a videotaped narrative produced by a speaker whose face was visible only from the nose down. The videos were displayed on a laptop computer screen using Psychtoolbox (Kleiner, Brainard, Pelli, ingling, Murray, & Broussard, 2007; Brainard & Vision, 1997) and Matlab software (Mathworks, Inc., Natick, MA). Accompanying audio was delivered over headphones at a comfortable listening level, determined by the participant himself on the training items in the first session. Forty different scripts were used (see Appendix A for scripts) and those were recorded by two different speakers, a male and a female. The scripts vary in length between 48 and 58 words and take an average speaker ~1 min to read aloud, using a comfortable speaking rate. The content of the scripts was controlled for number of words, word class, and word frequency using CELEX (Baayen, Piepenbrock, & van Rijn, 1993).

2.5 Procedure

2.5.1 Administration of treatment. The administration of SE is relatively simple: Participants practiced imitating (in real-time) 1-minute narratives presented in the audio and visual (AV) modalities on a laptop computer. The participant was presented with a video showing the mouth of a normal speaker below the nose and heard the audio speech via headphones (see *Figure 1*). The AV speech model involves a relatively slow speech rate and a high-speed video frame rate. For the purpose of our study, the AV speech model represented a video of a speaker's mouth producing a 'narrative' about a given generic topic and was presented using a laptop computer with a high-speed video card. A certified speech-language pathologist (SLP) was present during each session to provide guidance and ensure treatment compliance. At the discretion of the SLP, the speech rate of the AV model was slowed down or sped up to better fit each participant's needs.

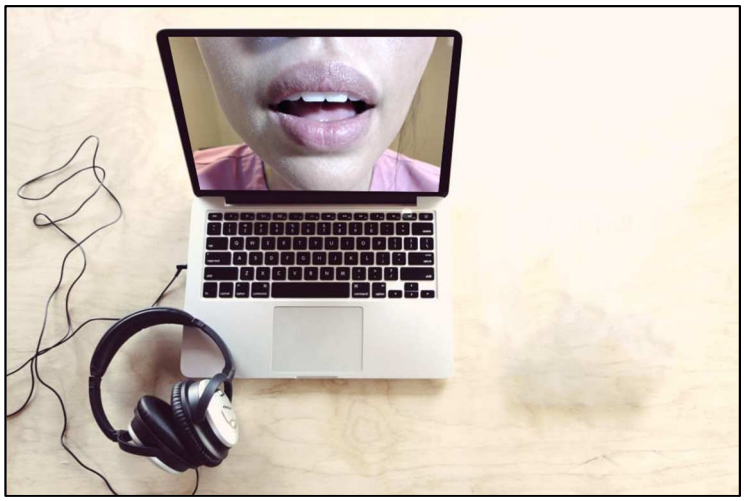

Figure 2.1. An example of a speech entrainment treatment setting.

2.5.2 The treatment session. A certified speech-language pathologist administered all treatment either at the Discovery I building of the University of South Carolina, or in the participant's home. During the first treatment session, the SLP modelled the manner in which the participant should imitate the AV speech model. Once participants understood the approach (as per clinical judgment of the SLP), the speech entrainment training session was started. When treatment began, the participant observed/listened as the narrative was presented in its entirety without mimicking. On successive presentations, the participant mimicked the narrative in real-time. Once a given script (video) had been mimicked three times, a new script was presented and then practiced three times, and so on. Practicing each narrative three times was based on anecdotal experience, suggesting that participants improve considerably from the first to the third practice of a given narrative.

During the treatment session, a new narrative video was selected at random. Each participant cycled through all narratives before repeating any. In-house computer software was used to accomplish stimulus presentation, start and stop the treatment session, speed up/slow down rate of video, and keep track of treatment data (e.g. the average number of narratives trained per session, how many times a given narrative was trained during the course of treatment, how well the participant did on a given narrative). The speech-language pathologist also recorded how many words the participant was able to mimic in each script and fed that information to the computer program to monitor changes in performance on the different scripts between sessions.

2.5.3 Treatment dosage. Each participant received treatment in 45-minute sessions administered 5 days/week over a three-week period for a total of 15 sessions. This treatment dosage is in line with previous literature reviews that suggest that a weekly dosage ranging from 5 to 10 hours, referred to as 'moderately-intensive', is sufficient to ensure significantly improved language performance on standardized aphasia test batteries (Bhogal, Teasell, & Speechley, 2003; Allen, Mehta, Andrew McClure, & Teasell, 2012; Brady, Kelly, Godwin, Enderby, & Campbell, 2016). The number of training trials across participants within each session was determined by the speed of stimulus presentation so some participants went through more scripts than others. The mean number of scripts was 132.85, SD=17.1. The person that got through fewest scripts finished 96 and the person that got through the most finished 150 scripts.

2.6 Neuroimaging Data

Participants were scanned using Siemens Prisma 3T MRI scanner with a 20-channel head coil. The average time between structural and functional MRI acquisition was 9.7 months (SD = 9.1, range 0-28 months).

2.6.1 Functional MRI. Functional MRI scans were used to establish a pre-treatment baseline. The same exact scan sequences were then repeated in a randomized order after the treatment had concluded.

Functional MRI scanning was accomplished using a Siemens 3T scanner equipped with an audio–video presentation system. Different functional MRI runs were collected for each of three conditions: (i) speech entrainment–audiovisual; (ii)

spontaneous speech; and (iii) audio/visual speech perception (without an overt response). During the speech entrainment–audiovisual condition, participants mimicked a speaker producing speech entrainment scripts. To emphasize visual speech perception and simulate the speech entrainment – audiovisual condition that was used during the treatment, only the mouth of the speaker was visible. Functional MRI data collection relied on sparse imaging where whole brain volumes were acquired with a repetition time of 10 seconds and acquisition time of 2 seconds. This allowed for stimulus presentation whereby each script was segmented in such a way that single sentences and phrases were presented during the 8 seconds of silent intervals between actual functional MRI scanning. Participants were instructed to mimic the speech that started immediately after the collection of each volume and ended at least 1 second before the start of the next volume collection. Overt speech was recorded using an MRI compatible microphone for later offline scoring to verify task compliance. During the spontaneous speech condition, participants were instructed to speak about the events of the current day while watching a speaker's mouth movements and listening to backwards speech. This was done to control for low-level perceptual information while minimizing neural activity that would reflect inhibition of real language activation while participants produce spontaneous speech. The final condition, audio/visual speech perception, involved the same stimuli used during the speech entrainment–audiovisual condition, but no overt response was permitted. Audio recording was used to verify that participants were not speaking during the audio/visual speech perception task. Specific parameters for the functional MRI sequence are as follows: repetition time = 10 s; echo time = 35 ms, attenuation time = 2 s, 64 x 64 axial matrix with 33 3.2-mm-thick slices (no gap); field of view = 208 x 208 mm; number of

volumes = 60; total acquisition time = 10 min. The three conditions were counterbalanced in order to avoid introducing an order effect. All of the videos displayed in the scanner were presented at a comfortable listening level determined by the participant themselves. Contrary to the treatment sessions the SLP had no control over the speech rate of videos and they were presented at the same rate, a normal speaking rate, for all participants.

2.6.2 Structural MRI. T1-weighted image was acquired utilizing MP-RAGE sequence with 1 mm isotropic voxels, a 256 x 256 matrix size, and a 9-degree flip angle using parallel imaging (GRAPPA=2, 80 reference lines). A 192-slice sequence with TR=2250 ms, TI=925 ms and TE=4.11 ms for a total acquisition time of 6:17 mins was used. A T2-weighted image was acquired using a sampling perfection with application optimized contrasts using a different flip angle evolution (3DSPACE) sequence. This 3D TSE scan uses a TR = 3200 ms, a TE of 567 ms, variable flip angle and a 256 x 256 matrix scan with 176 slices (1 mm thick) using parallel imaging (GRAPPA=2, 80 reference lines). The total acquisition time was 5:06 mins. The T2-weighted image used the same slice center and angulation as the T1-weighted scan.

Lesion demarcations were accomplished using the T2-MRI in native space, and the T1-MRI images were used for qualitative reference of lesion boundaries.

2.7 Data Analysis

2.7.1. Analysis of discourse tasks. Participants were videotaped while completing each of the four assessment sessions and five graduate students transcribed

the tasks of the outcome measures. The graduate students were all blinded to the timepoint of assessment (pre-treatment, post-treatment, 3 months, 6 months). A doctoral student and certified speech pathologist and a postdoctoral researcher provided the graduate students with transcription training. Transcription was done by watching and listening to the videotape with high quality headphones using the CHAT (Codes for the Human Analysis of Transcripts) format and linked to the digitized audio and video (MacWhinney, 2000). The CHAT format is a transcription format that has been developed over the last 30 years for use in a variety of disciplines and is designed to operate closely with the CLAN (Child Language Analysis) programs (MacWhinney, 2000), which allow for the analysis of a wide range of linguistic and discourse structures. The CHAT format was originally designed for child language research but has been modified for aphasia use and has been used in aphasia research for at least 14 years when work on establishing AphasiaBank was started in 2005 (MacWhinney et al., 2011).

Similarly to previous studies (e.g. Doyle et al., 2000) both the number of words per minute and different words per minute for each task was tallied and recorded to assess speech fluency and verbal productivity. The reason behind focusing on the number of different words as well as the total words uttered is that some participants with Broca's aphasia repeat the same words without necessarily adding communicative value. To measure information content, the number of CIUs per minute was tallied and recorded and the percentage of CIUs were calculated by tallying the total number of correct information units and dividing them by the total number of words. The total speaking duration was calculated as the number of seconds of speech, beginning with the participant's first utterance following the experimenter's prompt to start the task. When

the experimenter spoke or prompted at any point during the recording, this time was subtracted from the overall duration of speaking time of the participant. Each of the transcripts was coded by a trained transcriber and then reviewed in its entirety by a speech-language pathologist with clinical research experience in aphasia and transcription. Inter-rater reliability was calculated for 10% of randomly selected samples and intra-rater reliability was calculated for 10% of randomly selected samples per rater. Reliability was assessed using intraclass correlation coefficient (ICC) in SPSS 25 using two-way mixed model for consistency at 95% confidence level. We will refer to ICC as poor (below 0.40), fair (0.41–0.59), good (0.60–0.74), or excellent (above 0.75) (Cicchetti, 2001; Shrout & Fleiss, 1979). Inter-rater reliability was excellent for all measures of speech fluency used in this study (ICC>.9). Intra-rater reliability for all measures of speech fluency used in this study was also excellent, ranging from ICC of 0.95 to 0.99.

2.7.2 Preprocessing of neuroimaging data.

2.7.2.1 Structural brain lesions were manually drawn on the T2 weighted image by a neurologist who was blinded to the participant's language scores at the time of the lesion drawing. The T2 image was co-registered to the T1 image, and these parameters were used to re-slice the lesion into the native T1 space. The resliced lesion maps were then smoothed with a 3 mm full-width half maximum (FWHM) Gaussian kernel to remove jagged edges associated with manual drawing. After that, an enantiomorphic segmentation-normalization (Nachev, Coulthard, Jäger, Kennard, & Husain, 2008) was performed, using SPM12 and Matlab scripts developed by Rorden and colleagues (2012).

The procedure was as follows: first, a mirrored image of the T1 scan (reflected around the midline) was created, and this mirrored image was co-registered to the native T1 image. Then a chimeric image based on the native T1 scan with the lesioned tissue replaced by tissue from the mirrored scan (using the smoothed lesion map to modulate this blending) was created. SPM12's unified segmentation-normalization (Ashburner & Friston, 2005) was used to warp this chimeric image to standard space, with the resulting spatial transform applied to the native T1 scan as well as the lesion map and the T2 scan (which used the T1 segmentation parameters to mask non-brain signal). The normalized lesion map was then binarized, using a 50% probability threshold. Figure 2.2 shows the overlap of lesions.

2.7.2.2 Image preprocessing of functional neuroimaging data was completed using SPM12 (SPM12, Wellcome Institute of Cognitive Neurology, London, UK). Standard preprocessing steps were implemented including slice time correction, rigid body motion correction, co-registration of functional images to respective T1 structural images, and normalized to the Montreal Neurological Institute (MNI) template. Normalized functional images were then smoothed using a 6mm Gaussian filter. Voxel-wise repeated measure *t*-tests were conducted using the estimated parameters of the regressors (beta weights) to create T-maps for our three conditions: speech entrainment (SE), spontaneous speech (SS), and speech perception. T-maps from speech perception were subtracted from both SE and SS T-maps for all participants to create contrast maps specific to SE and SS, respectively. After that, T-maps from SE at pre-treatment were subtracted from SS T-maps at pre-treatment and T-maps from SE at post-treatment were

subtracted from SS T-maps at post-treatment. Finally, pre-treatment T maps for SS – SE were subtracted from post-treatment T maps for SS-SE. These three group-level contrasts were then used to see if we could find areas that could predict changes in spontaneous speech output.

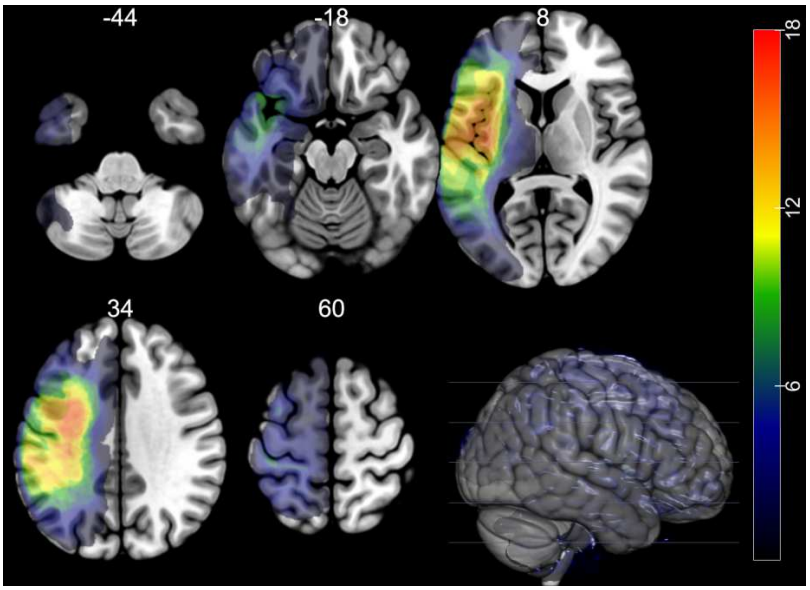

Figure 2.2. Lesion overlay map showing the distribution of damage among the participants (n=18). Note: The greatest lesion overlap was found in the post central gyrus, precentral gyrus, supramarginal gyrus and superior longitudinal fasciculus. The numbers above each axial slice designate the slice labels in standard anatomical space. Warmer colors indicate that more participants had a lesion in that area.

2.7.3 Analysis of structural neuroimaging data. Regions of interest (ROIs) from the brain parcellation developed by Faria and colleagues (2012) were used in a ROI lesion-based analysis in NiiStat (https://www.nitrc.org/projects/niistat) to see if it was possible to establish which ROIs were associated with improvement in spontaneous speech fluency. The five ROIs we chose were determined by Basilakos and colleagues (2015) to be associated with apraxia of speech characteristics. Those ROIs were the

precentral gyrus, postcentral gyrus, superior corona radiata, superior longitudinal fasciculus, and supramarginal gyrus. We also ran a lesion-based analysis based on Venezia and colleagues' findings (2016) and included the bilateral precentral gyrus, L IFG triangularis, L IFG orbitalis, L IFG opercularis, the L middle temporal gyrus, the L posterior middle temporal gyrus and the L caudate.

Permutation thresholding was used to control for multiple comparisons during the analyses and a one-tailed p-value of .05. The dependent variable in these analyses was the raw change from pre- to post-treatment testing of speech fluency (WPM, dwpm, CIUs/min, %CIUs). The anatomical brain atlas containing the parcellation, developed by Faria and colleagues (2012) was aligned with each individual's T1 image and the T1 image was divided into parcels according to the atlas. After that, we computed the proportion of damage (number of lesioned voxels divided by the size of the parcel) for each parcel (ROI) included in our analysis.

2.7.4 Analysis of functional neuroimaging data. Regions of interest (ROIs) from the brain parcellation developed by Faria and colleagues (2012) were used in a ROI activity-based analysis in NiiStat (https://www.nitrc.org/projects/niistat) to see if it was possible to establish if activity (or change in activity) in predetermined ROIs were associated with improvement in spontaneous speech fluency. The ROIs that were chosen were based on Venezia and colleagues' findings (2016) and included the bilateral precentral gyrus, left IFG triangularis, left IFG orbitalis, left IFG opercularis, the left middle temporal gyrus, left posterior middle temporal gyrus and the left caudate.

CHAPTER 3

RESULTS

The main goal was to measure if speech entrainment - induced improvements in speech production would generalize to untrained speech. The hypothesis was that not only would the positive treatment effects of speech entrainment treatment increase accurate production of trained narratives, but that it would also generalize to spontaneous speech output in individuals with Broca's aphasia. For this purpose, effect sizes for changes in words per minute (WPM), different words per minute (dwmp), correct information units per minute (CIU/min), and percentage of correct information units (%CIUs) for each of the primary outcome tasks were measured. Cohen's r was calculated by dividing Z scores for difference in performance post-treatment minus performance at baseline with the square root of N ($r = Z/\sqrt{N}$. Cohen's r of 0.1 is considered a small effect size, Cohen's r of 0.3 represents a medium effect size and 0.5 represents a large Cohen's r effect size. Effect sizes for the secondary, standardized behavioral measures to compare baseline and post-treatment data were also calculated, as well as improvement scores for each individual. The association of baseline measures to treatment outcome were explored using multiple linear regression. Separate multiple linear regressions were performed with change in dwmp and change in CIUs/min as the response variables. Our hope was that these exploratory analyses of behavioral scores and primary treatment outcomes (WPM, dwpm, CIUs/min, %CIUs) could reveal findings that could be used to further

guide a larger trial (e.g. to identify patients' baseline characteristics that would be more likely to respond to treatment).

3.1 Behavioral Outcome Measures

We collected behavioral data from twenty participants in two sessions on two consecutive days pre-treatment and in two sessions on two consecutive days post-treatment. We also collected follow up data for 14 out of the 20 people at 3 months post-treatment and 13 out of 20 people at 6 months post-treatment. One participant‘s videos at three months post-treatment were corrupt and could not be used. Another participant‘s videos at 6 months follow up testing were also corrupt and could not be used, and one participant passed away before the 6 months follow up testing could be done. At the time of writing this dissertation we had not analyzed follow-up assessment data from the remaining 5 participants. All of the behavioral data were analyzed using SPSS 25.0 (IBM SPSS Statistics for Macintosh, Version 25.0). Since SPSS 25.0 does not allow incomplete datasets, we had 20 complete datasets for baseline and post-testing but only 12 complete datasets for analysis of 3 and 6 months follow up testing sessions.

3.1.1 Analysis of discourse measures before and after treatment (WPM, dwpm, CIUs/min, %CIUs) (N=20).

A Shapiro-Wilk test of normality revealed that the data were not normally distributed so we used non-parametric methods of analysis. Results of Wilcoxon signed-rank test (one-tailed) were as follows: the median increase from baseline to post-test in words per minute (WPM) was 2.035 words (IQR=7.5)($Z=1.344$, $p=.08$). The median increase in different words per minute (dwpm)

was 0.48 words (IQR=3.5)(Z=.261, p=.39). The median increase in correct information units per minute (CIUs/min) was 0.62 units (IQR=2.88)(Z=2.627, p=.004) and the median increase in percent correct information units (%CIUs) was 2% (IQR=12.5%)(Z=1.823, p=.03). Results for each individual's primary treatment outcome measures at baseline, one week post treatment, 3 months and 6 months after treatment completion can be found in Appendix B.

Effect sizes (Cohen's r) for changes between baseline and post-treatment scores were calculated for the group (see Table 3.1.)

Table 3.1 Effect sizes (Cohen's r) for primary outcome measures.

WPM	dwpm	CIUs/min	%CIUs
0.213	0.041	0.415	0.288

Note: Baseline to post-treatment assessment. (WPM = words/min; dwpm=different words/min; CIUs/min=correct information units/min; %CIUs=percent correct information units).

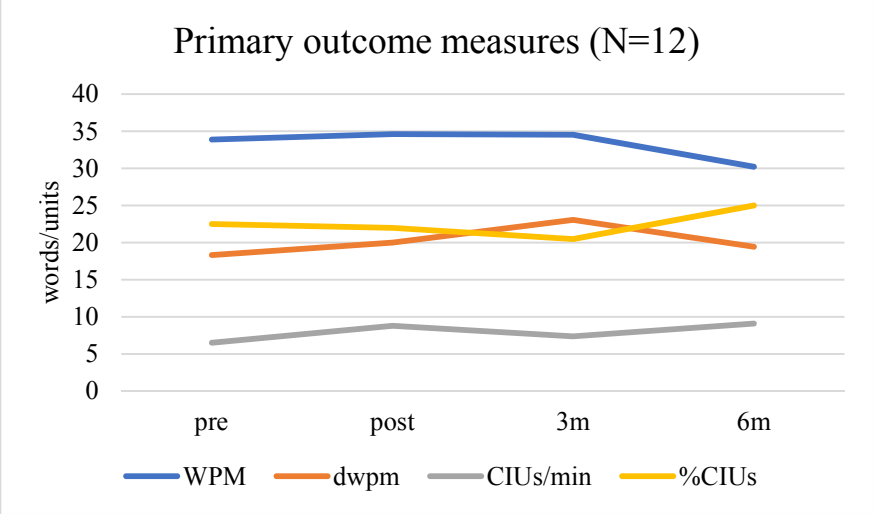

Figure 3.1 Median scores for WPM, dwpm, CIUs/min and %CIUs at four different timepoints.

3.1.2 Differences in distribution of scores at four timepoints (N=12). A Friedman test (N=12) was run to determine if there were differences in distribution of the number of words per minute (WPM), dwpm, CIUs/min and %CIUs at baseline, after treatment, at 3 months and at 6 months after treatment had been concluded. None of the differences reached statistical significance at $p<.05$. Median scores for WPM, dwpm, CIUs/min and %CIUs at four different timepoints can be found in Figure 3.1.

3.1.3 Individual discourse tasks scores (N=20). Results of Wilcoxon signed-rank test (one-tailed) were as follows:

1. Broken window: The median increase from baseline in words per minute (WPM) was 0.87 words (IQR=11.16) (Z=.336, p=.37). The median increase in different words per minute (dwpm) was 0.27 words (IQR=10.38) (Z=.411, p=.34). The median increase in correct information units per minute (CIUs/min) was 0 units (IQR=7.58) (Z=.568, p=.28) and the median increase in percent correct information units (%CIUs) was 0% (IQR=10.66%) (Z=.454, p=.32).

2. Cinderella. The median increase from baseline in words per minute (WPM) was 3.59 words (IQR=9.51) (Z=2.165, p=.015). The mean decrease in different words per minute (dwpm) was 0.37 words (IQR=6.19) (Z=.187, p=.42). The mean increase in correct information units per minute (CIUs/min) was 0.47 units (IQR=2.09) (Z=1.586, p=.056) and the mean increase in percent correct information units (%CIUs) was 2% (IQR=11.95%) (Z=1.775, p=.038).

3. Peanut Butter and Jelly Sandwich. The median increase from baseline in words per minute (WPM) was 0.27 words (IQR=12.39) (Z=.560, p=.287). The median decrease in

different words per minute (dwpm) was 0.07 words (IQR=6.04) (Z=.411, p=.34). The median increase in correct information units per minute (CIUs/min) was 0.86 units (IQR=3.97) (Z=2.817, p=.002) and the median increase in percent correct information units (%CIUs) was 2% (IQR=10.30%) (Z=1.586, p=.056).

4. Picnic. The mean decrease from baseline in words per minute (WPM) was 0.96 words (IQR=9.38) (Z=.075, p=.47). The mean increase in different words per minute (dwpm) was 0.01 word (IQR=4.01) (Z=.149, p=.44). The mean increase in correct information units per minute (CIUs/min) was 0.12 units (IQR=2.53) (Z=1.349, p=.09) and the mean increase in percent correct information units (%CIUs) was 0% (IQR=5.95%) (Z=.402, p=.34). Effect sizes for individual discourse tasks can be found in Table 3.2.

Table 3.2 Effect sizes (Cohen's r) for individual discourse tasks.

BW-WPM	**BW-dwpm**	**BW-CIUs/min**	**BW-%CIUs**
0.053	0.065	0.09	0.072
Cinderella-WPM	**Cinderella-dwpm**	**Cinderella-CIUs/min**	**Cinderella-%CIUs**
0.342	0.03	0.251	0.281
PBJ-WPM	**PBJ-dwpm**	**PBJ-CIUs/min**	**PBJ-%CIUs**
0.089	0.065	0.445	0.251
Picnic-WPM	**Picnic-dwpm**	**Picnic-CIUs/min**	**Picnic-%CIUs**
0.012	0.024	0.213	0.064

Note: small effect = 0.1; medium effect = 0.3; large effect = 0.5.

3.1.4 Differences in distribution of scores within individual tasks (N=12).

1. Broken window. Separate Friedman tests were run to determine if there were differences in the distribution of the numbers of words per minute (WPM), different words per minute (dwpm), CIUs/min and %CIUs at baseline, after treatment, at 3 months

and at 6 months after treatment had been concluded. CIUs/min were the only outcome measures that were found to be statistically significantly different at the different time points during the study time, $\chi^2(3) = 7.831$, $p = .05$. Post hoc Friedman test analysis revealed statistically significant increase in CIUs/min from pre- to 3 months ($p = .04$) and pre- to 6 months ($p = .018$). These were not corrected for multiple comparisons.

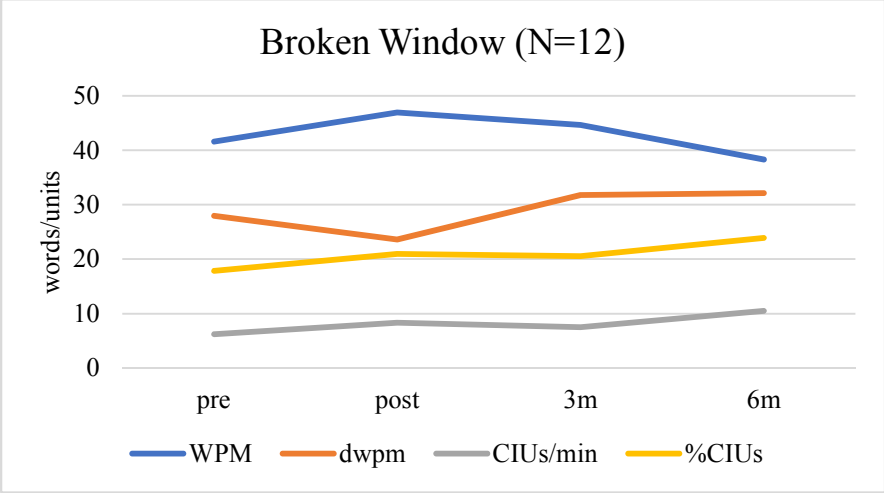

Figure 3.2 Median scores for Broken Window picture description task at four different timepoints.

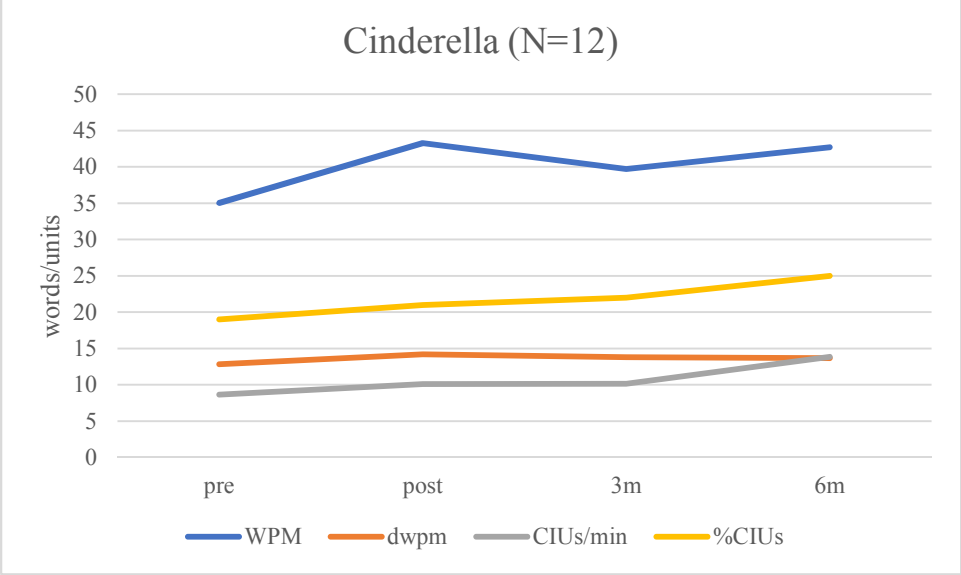

Figure 3.3 Median scores for Cinderella task at four different timepoints.

2. Cinderella. Separate Friedman tests were run to determine if there were differences in the distribution of numbers of WPM, dwpm, CIUs/min or %CIUs at baseline, after treatment, at 3 months and at 6 months after treatment had been completed. None of them were found to be significantly different at $p<.05$. Median scores for Cinderella task at four different timepoints can be found in Figure 3.3.

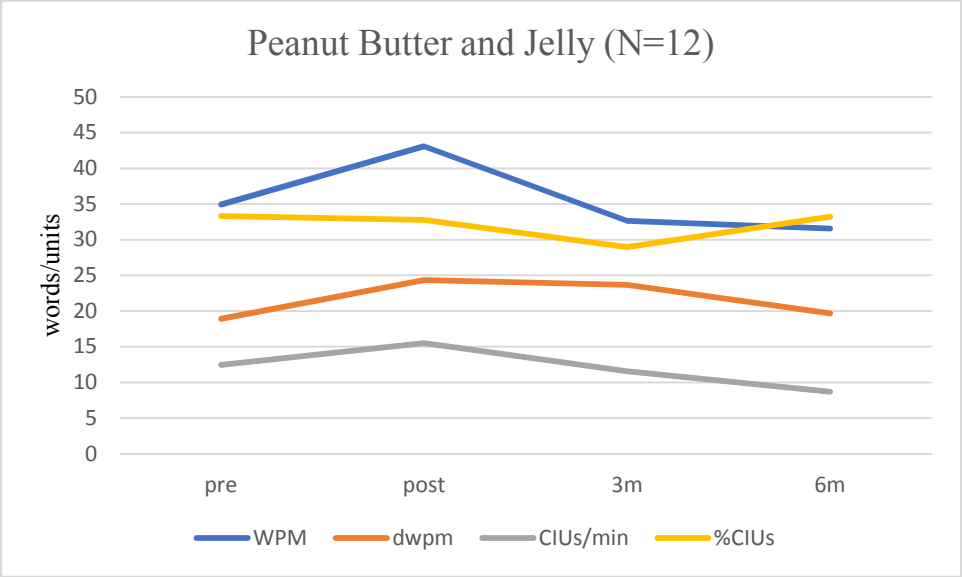

Figure 3.4 Median scores for Peanut Butter and Jelly task at four different timepoints.

3. Peanut butter and Jelly Sandwich. Separate Friedman tests were run to determine if there were differences in the distribution of numbers of WPM, dwpm, CIUs/min and %CIUs at baseline, after treatment, at 3 months and at 6 months after treatment had concluded. Differences in the distribution of numbers of dwpm and %CIUs were not significant. The number of WPM was statistically significantly different at the different time points during the study time, $\chi^2(3) = 10.6$, $p = .014$. Post hoc Friedman Test analysis revealed statistically significant differences in WPM from pre- to 6 months ($p = .027$) and post- to 6 months ($p = .002$) other differences did not reach statistical significance.

The number of CIUs/min was also found to be statistically significantly different at the different time points during the study time, $\chi^2(3) = 9.7$, $p = .021$. Post hoc Friedman Test analysis revealed statistically significant differences in CIUs/min from pre- to post- ($p = .018$) from post- to 6 months ($p = .011$) and post- to 3 months ($p = .007$). Median scores for Peanut Butter and Jelly task at four different timepoints can be found in Figure 3.4.

4. Picnic. Separate Friedman tests were run to determine if there were differences in the distribution of WPM, dwpm, CIUs/min and %CIUs at baseline, after treatment, at 3 months and at 6 months after treatment had concluded. None of the differences in distribution of scores were found to be statistically significant. Median scores for Picnic task at four different timepoints can be found in Figure 3.5.

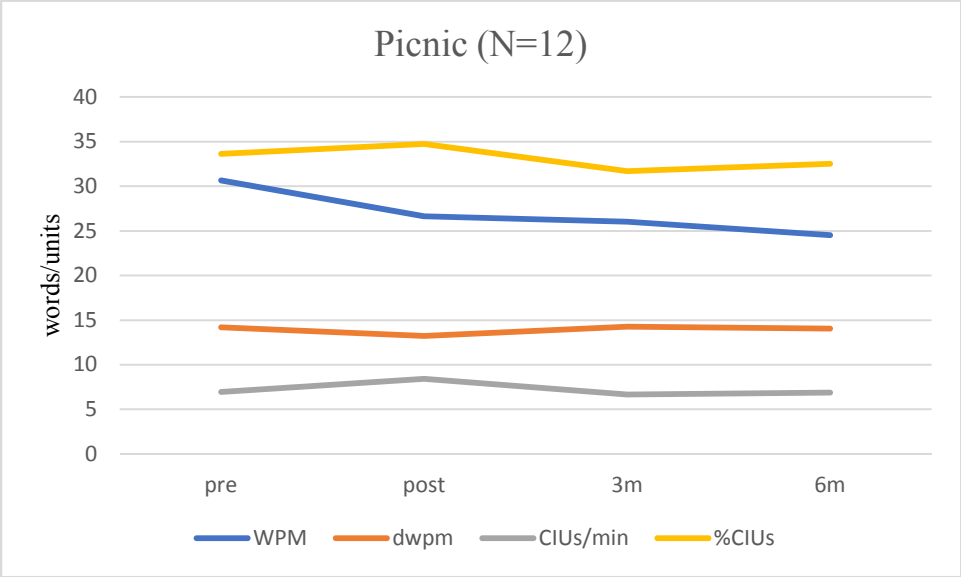

Figure 3.5 Median scores for Picnic picture description task at four different timepoints.

3.2 Results of Analysis of Standardized Behavioral Measures (N=20)

A Wilcoxon signed-rank test (one tailed) revealed a statistically significant increase between baseline testing and post-treatment testing on all secondary measures but the ASRS (*Z*= 0 p=1.0) and the Pyramids and Palmtrees Test (PPTT)(*Z*= 1.372 p=.08). The mean increase in WAB AQ was 2.83 points (*Z*= 3.062, p=.001). The mean increase in correctly named items on the Philadelphia Naming test (PNT) was 4.2 items (*Z*= 2.750, p=.003). The mean increase in correct responses on Kissing and Dancing Test (KDT) was 1.8 points (*Z*= 2.216 p=.013) and there was an 0.03 point increase in the composite score for the Northwestern (NAVS) (*Z*= 1.924 p=.027).

Effect sizes (Cohen's r) for changes between baseline and post-treatment secondary outcome scores were calculated for the group (see Table 3.3)

Table 3.3. Effect sizes (Cohen's r) for standardized behavioral measures.

PPTT	K&D	PNT-C	NAVS-Comp	WAB AQ
0.217	0.350	0.435	0.316	0.484

Note: Baseline to post-treatment assessment. Note: (WAB AQ= WAB Aphasia Quotient; PPTT=Pyramids and Palm trees Test; Kissing and Dancing Test; PNT-C= Philadelphia Naming Test-Correct scores; NAVS-Comp= Northwestern Assessment of Verbs and Sentences-Composite Score. There were no changes in scores on the Apraxia of Speech Rating Scale (ASRS), therefore no effect sizes were calculated for that test.

3.3 Proportional change in discourse and baseline measures

Proportional change in discourse outcome measures and the standardized behavioral measures was calculated by subtracting baseline scores from post-treatment scores and dividing those by baseline scores. Individual scores can be found in Table 3.4 and Table 3.5.

3.4 Exploratory analysis of behavioral data

An exploratory analysis evaluated behavioral variables as predictors of treatment outcome. A stepwise linear regression was calculated in order to identify significant predictors of the four measures of treatment outcome; WPM, dwpm, CIUs/min and %CIUs, based on baseline behavioral test scores. No significant variables were identified for WPM or %CIUs but two were identified for dwpm and CIUs, one for each.

Table 3.4 Proportional change in primary outcome measures.

Participant	WPM	dwpm	CIUs/min	%CIUs
1	22.07%	-2.24%	-10.60%	-27.80%
2	4.73%	2.34%	7.03%	2.22%
3	22.53%	17.20%	-0.21%	-19.80%
4	43.76%	16.08%	-24.98%	-16.99%
5	14.49%	8.45%	39.97%	24.05%
6	8.62%	-13.71%	4.82%	-8.39%
7	35.97%	53.79%	103.97%	35.91%
8	119.21%	94.20%	0.00%	0.00%
9	40.48%	75.36%	0.00%	0.00%
10	-17.05%	-6.19%	14.67%	41.59%
11	-0.50%	-23.23%	147.19%	186.64%
12	40.77%	-12.75%	24.80%	-11.56%
13	12.17%	9.92%	12.01%	21.08%
14	-14.10%	-38.70%	-26.47%	96.95%
15	2.95%	18.89%	132.93%	259.05%
16	-12.03%	-4.88%	10.29%	18.35%
17	-42.23%	-38.05%	0.00%	0.00%
18	6.37%	1.60%	14.19%	8.39%
19	-45.15%	-16.53%	-37.23%	189.74%
20	-8.36%	20.56%	16.19%	25.56%
Mean	11.73%	8.11%	21.43%	41.25%
SD	35.53%	33.89%	49.74%	79.50%
Range	-45.15 - 119.2%	-38.7 - 94.2%	-37.23 - 147.19%	-27.8 - 259.05%

Note: WPM=words/minute; dwpm=different words/minute;
CIUs/min= correct information units/minute;
%CIUs= percent correct information units.

3.4.1 Analysis I: change in dwpm. The scores for dwpm were skewed so we applied a square root transformation to them. The only significant predictor for dwpm_sqrt was ASRS scores pre-treatment ($F(1,18) = 5.605$, $p=.029$), with an R^2 of .237. The prediction equation was change in different words per minute = 2.048 - .025 x points on ASRS at baseline. Every extra point on ASRS leads to a 0.025 decrease in different words per minute (dwpm). This indicated that greater apraxia severity resulted in less improvement in dwpm.

Table 3.5 Proportional change in standardized behavioral test scores.

Participant	WAB AQ	PPTT	KDT	PNT	NAVS
1	7.58%	-1.96%	2.00%	7.41%	-6.35%
2	-4.83%	2.00%	8.51%	3.23%	7.04%
3	3.29%	4.26%	2.08%	1.23%	-1.22%
4	-1.47%	0.00%	6.67%	0.00%	-5.00%
5	5.47%	-5.77%	-1.96%	16.67%	2.33%
6	6.71%	-2.04%	4.26%	-20.00%	1.59%
7	4.62%	-2.17%	-6.12%	12.16%	-5.36%
8	-6.37%	-2.00%	-10.20%	0.00%	5.56%
9	14.01%	2.70%	5.13%	0.00%	28.57%
10	25.82%	17.95%	9.09%	71.43%	6.67%
11	6.33%	-2.13%	14.63%	37.50%	71.43%
12	19.76%	15.38%	-2.33%	-75.00%	21.43%
13	-2.93%	2.22%	2.00%	5.17%	72.41%
14	9.09%	8.33%	9.09%	100.00%	50.00%
15	9.77%	-10.53%	56.25%	14.29%	6.67%
16	6.63%	2.17%	0.00%	14.81%	-6.38%
17	25.84%	10.87%	6.52%	0.00%	0.00%
18	9.73%	4.08%	0.00%	20.21%	4.69%
19	32.27%	11.90%	2.50%	0.00%	7.14%
20	-0.75%	-1.92%	2.04%	2.82%	17.54%
Mean	8.53%	2.67%	5.51%	5.6%	13.94%
SD	10.52%	7.15%	13.21%	41.84%	23.99%
Range	-6.37 – 25.84%	-10.53 – 17.95%	-10.2 – 56.25%	-75 – 100%	-6.38 – 72.41%

Note: Scores include changes in aphasia quotient from Western Aphasia Battery – Revised (WAB), changes in number of correct items named on Philadelphia Naming Test (PNT), number of correct answers on Pyramids and Palm Trees Test (PPTT) and Kissing and Dancing Test (KDT) and changes in composite score on the Northwestern Assessment of Verbs and Sentences (NAVS).*There was no change in scores on ASRS.

3.4.2 Analysis II: change in CIUs/min. The scores for CIUs/min were also skewed so we applied a square root transformation to them. The only significant predictor for CIUs/min was WAB AQ scores pre-treatment ($F(1,18) = 8.852$, $p=.008$), with an R^2 of .330. The prediction equation was change in correct information units per minute= -0.003 + .025 x points on the WAB-R AQ at baseline. Every extra point on WAB AQ leads to a 0.025 increase on CIUs/min. Indicating that people that received a higher AQ on the WAB-R could say more CIUs/min during the discourse tasks.

3.5 Brain Imaging

The second aim of the study was to use a neuroimaging approach to identify patterns of regional and network damage that correlate with SE outcome.

3.5.1 The first hypothesis. The first hypothesis related to this aim was that participants who have lesions that include areas of five anatomic regions associated with apraxia of speech characteristics: precentral gyrus, postcentral gyrus, superior corona radiata, superior longitudinal fasciculus, and supramarginal gyrus (Basilakos, Rorden, Bonilha, Moser, & Fridriksson, 2015) would experience less improvement in spontaneous speech output than participants who do not. None of the five regions survived a $p < 0.05$ threshold, after correcting for multiple comparisons, but superior longitudinal fasciculus survived at a $p<0.1$ threshold for predicting CIUs/min.

None of the seven ROIs based on Venezia and colleagues' findings survived a $p<.05$ threshold, after correcting for multiple comparisons either.

3.5.2 The second hypothesis related to this aim was based on previous findings that SE activates auditory-visual syllable targets, perhaps rooted in the posterior middle temporal gyrus (Fridriksson et al., 2012; Venezia et al., 2016). In order to possibly identify areas that are associated with changes in accurate production and fluency of spontaneous speech, the functional brain activation related to the SE task was compared to the activation related to the spontaneous speech (SS) task. We ran analyses that related the four outcome measures (WPM, dwpm, CIUs/min and %CIUs) to fMRI data in *a priori* ROIs at three different timepoints: 1) SS-SE (i.e. *spontaneous speech* contrasted with *speech entrainment*) at baseline; 2) SS-SE at post treatment testing; and 3) change in contrast of T maps for SS and SE from baseline to post treatment testing For the first analysis, the magnitude of differential activation in no ROI was statistically significantly associated with the outcome measures. For post-treatment SS-SE, two regions survived $p < 0.05$ threshold for significance. More negative values of the contrast SS-SE in the left caudate nucleus post-treatment was found to be associated with change in dwpm and more negative values of the contrast SS-SE in left posterior MTG (pMTG) was associated with increase in both CIUs/min and %CIUs. When comparing post-pre, SS-SE, more negative values for the contrast SS-SE in left pMTG was found to predict increase in CIUs/min.

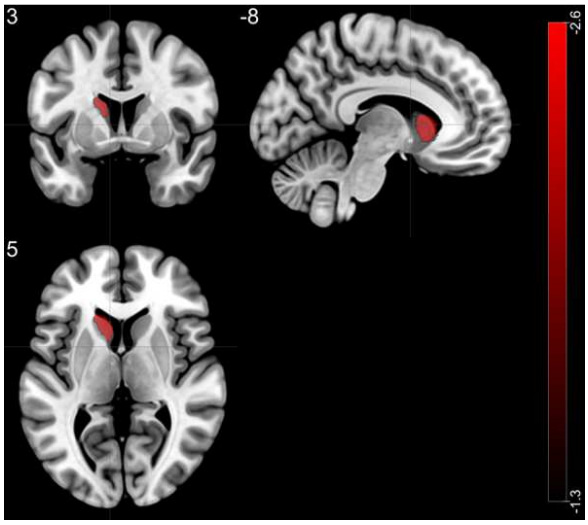

Figure 3.6 More negative values of the contrast SS-SE in L caudate nucleus at post-testing predicted change in dwpm.

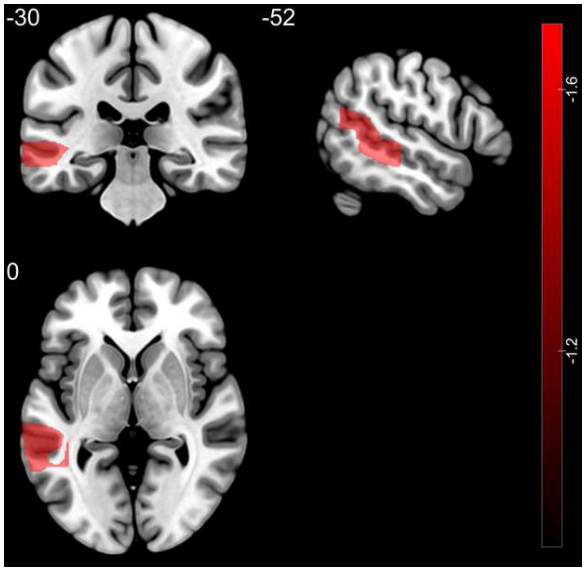

Figure 3.7 More negative values for the contrast SS-SE in L pMTG at post-testing was associated with increase in CIUs/min and %CIUs. More negative values of the contrast SS-SE, post-pre in L pMTG was associated with increase in CIUs/min.

3.6 Exploratory Analysis of Neuroimaging Data

None of the five regions previously suggested by Basilakos et al., 2015 to be associated with apraxia of speech survived a $p < 0.05$ threshold, after correcting for multiple comparisons, but superior longitudinal fasciculus (SLF) survived at a $p < 0.1$ threshold for CIUs/min. This led us to take a further look at what we had already found to be significant. We performed multiple different linear regression analyses to predict outcome based on lesions and/or regional brain activity. The model that had the greatest predictive power included proportional damage to left SLF, proportional damage to the left middle temporal gyrus (MTG), and not pMTG, as well as change in activity (post treatment-pre-treatment) in left MTG as predictors ($F(3,14)= 3.723$, $p=0.037$) with an $R^2=.44$. This result indicates that people who respond better to SE treatment seem to have smaller lesions in left SLF, larger lesions in left MTG and less activation in left MTG post treatment. Running linear regression on any combination of two out of three predictors yielded worse results, suggesting that all three predictors provide substantial information to the model.

CHAPTER 4

DISCUSSION

The purpose of this study was to examine the improvements in spontaneous speech production as a result of SE treatment in a group of individuals with Broca's aphasia, and to explore and predict individuals' behavioral and brain related characteristics associated with treatment response. A total of 20 participants were recruited and received Speech entrainment treatment for three consecutive weeks. All of the participants had received a diagnosis of non-fluent, Broca's aphasia, but still exhibited very wide variability in aphasia severity (AQ=17.8-80.7). This study examined three hypotheses and two exploratory analyses to determine if previously confirmed improvement in speech production (Fridriksson et al., 2012) could generalize to untrained, spontaneous speech and if we could identify patterns of regional and network damage that might correlate with treatment outcome. The following discussion focuses on how the current findings relate to each of the research aims stated in the introduction, as well as the current literature.

4.1 Speech Entrainment - Induced Improvements in Speech Production

1) Determine if three weeks of daily speech entrainment treatment (total of 11.25 hours) can increase accurate production of spontaneous speech for individuals with chronic Broca's aphasia.

Fridriksson and colleagues (2012), showed that real time mimicking of audio-visually presented speech (using speech entrainment treatment) can facilitate fluent speech production of narratives in individuals with chronic Broca's aphasia. In their study, participants were able to produce a greater variety of words both with and without speech entrainment at 1 and 6 weeks after training completion.

Participants in the current study exhibited an overall median increase on all of the primary outcome measures (WPM, dwpm, CIUs/min and %CIUs) of the four discourse tasks. The median performance from baseline to post-treatment all improved to various extents, but the increase was not uniformly statistically significant at $p<0.05$. Effect sizes for changes in primary outcome measures were small to medium (Cohen´s r range 0.041-0.415). Analysis of differences in distribution of median scores between the four timepoints of assessments (baseline, post-treatment, 3 months follow up, 6 months follow up) did not reach statistical significance ($p<.05$) for the primary outcome measures of the discourse tasks (WPM, dwpm, CIUs/min, %CIUs). Even though this is perhaps not what we had expected it is very important to keep in mind that the variability in individual scores between participants was extensive, demonstrated by the large interquartile ranges (IQRs).

Median scores between baseline and post-testing for the four individual discourse tasks (BW, Cinderella, PBJ, Picnic) also varied considerably. None of the outcome measures (WPM, dwpm, CIUs/min, %CIUs) for Broken Window (BW) were statistically significant. For Cinderella the median increase in WPM and %CIUs were significant (WPM, $p=0.015$; %CIUs, $p=0.038$) but the decrease for dwpm did not reach a significant threshold ($p=0.42$) and the increase for CIUs/min was trending towards statistical

significance (p=.056). For PBJ the overall increase for WPM and decrease in dwpm was not statistically significant but the increase in CIUs/min was significant (p=.002) and %CIUs was trending towards statistical significance (p=.056). Finally, the decrease in WPM, and increase in dwpm, CIUs/min and %CIUs were not significant for the Picnic Scene picture description task. Effect sizes for changes in individual test outcomes were small to medium (Cohen´s r range 0.01-0.445, see table 3.2).

Analysis of differences in distribution of median scores within individual tasks at baseline, in the week after treatment completion, at 3 months after treatment completion and at 6 months after treatment completion, highlighted even further the variability in this cohort. For Broken Window, CIUs/min were the only outcome measure that reached significance at different timepoints during the study. None of the differences in distribution of median scores for Cinderella were significant at $p<.05$. For Peanut Butter and Jelly, median WPM and median number of CIUs/min were found to be significantly different at different timepoints. Post- to 6 months follow-up testing scores for WPM were found to be significantly different (p=.009) and post- to 3 months follow up testing scores for CIUs/min. None of the differences in distribution of median scores for the Picnic picture description task were found to be statistically significantly different at $p<.05$.

The lack of differences in distribution of median number of words, number of different words, number of correct information units and percent correct information units can suggest that the long-term effects of the treatment were minimal, but we are more inclined to say that the large variance played a dominant role in these results. Participants exhibited a very wide range of scores and large standard deviations.

When looking at the individual improvement scores and the proportional change in primary outcome measures some of the numbers look a little peculiar. Some of the improvement scores and proportional changes were very much inflated by the fact that some of the participants only said a handful of words, sometimes in only a few seconds so when that was calculated into minutes their score was very much overstated. For example, participant number 8 said 0.93 WPM at baseline and 2.05 WPM during post testing which is a 119.21% increase; same participant said 0.93 dwpm at baseline and 1.81 dwpm during post-testing which is a 94.20% increase between timepoints. Participant number 11 said 3.73 CIUs/min at baseline but 9.22 WPM during post-testing, an increase of 147.19% and participant 15 said 0.69 CIUs/min at baseline and 1.6 CIUs/min at post-testing and 0.04 %CIUs at baseline and 0.15 %CIUs at post-testing, a change of 132.93% and 259.05%, respectively. Proportional changes for individual participants can be found in Tables 3.4.

4.1.1 Discourse measures. A variety of discourse measures are used to elicit spoken language in aphasia research (Bryant et al., 2016). The most common is probably a picture description where a participant is provided with a picture or picture sequences and asked to describe what is happening in the picture(s). Another common task to elicit spoken language is narrative discourse, or story retelling. For this type of discourse task, the person is asked to recount a personal story or to retell a well-known story (e.g. the Cinderella story) without any visual support. The participant is allowed to review a picture book to refresh their memory but then the book is taken away and the subject narrates the story without any visual help. Because this type of task relies on memory and

macrolinguistic structures like grammar and coherence, it may elicit more complex language compared to picture description tasks (MacWhinney et al., 2010). However, it does not come without problems. Because of the lack of visual support and the macrolinguistic requirements it is inherently more difficult, especially for people with more severe aphasia.

A third, common type of discourse task is procedural discourse where the participant is asked to describe a procedure of some kind (e.g. how to make a peanut butter and jelly sandwich). This type of discourse task is thought to elicit more action words and gestural communication (Pritchard, Dipper, Morgan, & Cocks, 2015).

Stark (2019) did a retrospective study on discourse measures for 90 people with different types of aphasia comparing them to data from a control group of 84 individuals. She used most of the same discourse measures as we did in the current study, BW, Cinderella, PBJ but then she used a picture description task she called the Cat Rescue Story where participants were asked to describe a single picture of a cat being rescued from a tree by firemen. This task is similar to the Picnic picture from the WAB-R which we used in the current study. Stark found that Broken Window (BW) picture sequence elicited more WPM while picture description elicited language that was denser (more words of different types, e.g. verbs, adjectives, adverbs etc.) and had a higher noun-verb ratio (indicating more syntactic complexity). She also found that narrative discourse (Cinderella) produced speech highest in propositional density but lowest number of WPM. In our study we included the same measures of fluency (WPM) but in addition to that we looked at dwpm since people with Broca's aphasia often repeat the same words without adding any information. Instead of examining linguistic complexity we chose to

look at the informativeness of the participants' speech. When analyzing the WPM, we found some similar results. The mean number of WPM was higher for BW at baseline than the other picture description task, in the same way it was for Stark, but the Cinderella task was not the one that induced the smallest number of words. Instead, the Picnic picture description task had the smallest mean number of words. These results should be taken with a grain of salt since variability between participants was great and the mean standard deviation for the group was extensive, as can be seen in Appendix B.

4.1.2 Problems with discourse tasks for people with Broca's aphasia. People with aphasia struggle with discourse tasks. Discourse tasks vary in complexity as discussed above but they can be very taxing, especially for people with non-fluent aphasia. Individuals that have Broca's aphasia will sometimes be tempted (and often encouraged by clinicians) to use other methods of communication to get their message across. Common examples of such alternative ways of communication are gestures or any kind of body movements. Enactment is a phenomenon wherein a speaker employs gestures, body movements, direct reported speech and/or prosody to portray to recipients' aspects of a scene or an event (Streeck & Knapp, 1992, Wilkinson, Beeke, & Maxim, 2010). In regular conversation or story (re)telling, enactment can be used to refer to what someone previously did or said. The occurrence of enactment is not restricted to people with aphasia. In typical interactions involving non-brain-damaged speakers, the occurrence of enactment is common. It is used in diverse contexts (Hengst, Frame, Neuman-Stritzel, & Gannaway, 2005) and is often used in stories, jokes or other genres of discourse (Groenewold & Armstrong, 2018). The occurrence of enactment in our study

was evident and it turned out to be impossible to get participants to only use words. The words the participants uttered were of course all documented and tallied but when most of the information was presented with a gesture or a body movement the participant didn't get scored for any words or information content (CIUs/min, %CIUs) for obvious reasons. Enactment was especially common in the Cinderella story retelling task but also in the procedural task (PBJ; how to make a peanut butter and jelly sandwich) where some participants would act out how to make the sandwich, often without words despite constant reminders to use words.

4.1.3 Standardized behavioral measures. Notably, there was a statistically significant change on four out of six secondary behavioral outcome measures. The only two behavioral measures that participants did not experience a significant increase on was the ASRS and the PPTT. We used the ASRS to determine the presence/absence of and rate-related treatment changes in specific speech characteristics commonly observed in apraxia of speech (AOS). Three weeks of speech entrainment treatment did not seem to influence mean scores on the ASRS as we found no change between participants' scores at baseline and after the treatment had been completed. The lack of change on the scores on this rating scale was not very surprising since previous studies (Fridriksson et al., 2012) have shown that apraxia of speech has a negative effect on speech entrainment outcome. Fridriksson and colleagues (2012) found that scores on ABA-2, a test battery for assessment of apraxia of speech predicted changes in dwpm. Similarly, our exploratory analysis also indicated that scores on a rating scale of apraxia of speech

(ASRS) at baseline could predict changes in dwpm between baseline and after the treatment had been completed.

The PPTT is a test of semantic processing of nouns and again, it is not especially surprising that speech entrainment did not induce a significant mean change in semantic processing abilities since it is a treatment of speech production. A more interesting finding was the fact that the speech entrainment treatment facilitated a significant increase in change of scores on the other four baseline assessments; WAB-R, PNT, KDT, NAVS. These findings raise the question of how that came about. Does SE perhaps have a "language therapy" factor to it, or does the simple fact that they're working on something help their overall outcome? It is tempting to say that speech entrainment can help with both speech and language but without a replication of these findings we should be careful in suggesting one or the other.

4.1.4 Treatment intensity. The role of treatment intensity is also worth considering. Several studies have shown a relation between treatment intensity and treatment effect: higher intensity yields larger treatment effects (Bhogal et al., 2003; Brady et al., 2016; Robey, 1998; Bakheit et al., 2007). For the current study a 'moderately intensive' treatment dosage (11.25 hours) was chosen as previous literature has suggested that this is sufficient to ensure significantly improved language performance on standardized aphasia test batteries (Bhogal et al., 2003; Allen et al., 2012; Brady et al., 2016). However, it is possible that with higher treatment intensity a larger treatment effect and generalization to daily life communication would have been observed.

4.2 Patterns of Regional and Network Damage that Correlate with Outcome

2 a) Use a multi-modal neuroimaging approach to identify patterns of regional and network damage that correlate with treatment outcome. Our first hypothesis stated that participants that have lesions that include areas of five anatomic regions associated with apraxia of speech characteristics: precentral gyrus, postcentral gyrus, superior corona radiata, superior longitudinal fasciculus, and supramarginal gyrus, would experience less improvement in spontaneous speech output than participants who do not.

Fridriksson and colleagues (2012) found that people that had higher scores on the Apraxia battery for Adults (ABA-2; Dabul, 2000), and were therefore more severely apraxic, experienced less improvement in spontaneous speech output than participants that were not diagnosed with apraxia of speech. More severe apraxia of speech was inversely related to how many more words patients were able to produce during the speech entrainment–audio visual condition compared with the spontaneous speech condition.

For the above reason, in the current study we wanted to see if there was a relationship between brain lesions in anatomic regions found to be associated with apraxia of speech characteristics (precentral gyrus, postcentral gyrus, superior corona radiata, superior longitudinal fasciculus, and supramarginal gyrus) and SE treatment outcome. For our lesion-based analysis, none of the five regions of interest survived the $p < .05$ threshold, after correcting for multiple comparisons. However, lesion in superior longitudinal fasciculus survived at a $p<0.1$ threshold for CIUs/min. Our smaller sample size can probably be blamed for the lack of significant correlations with treatment outcome.

2 b) Our second hypothesis was that activation in previously proposed brain areas, bilateral precentral gyrus, L inferior frontal gyrus, L middle temporal gyrus, L posterior middle temporal gyrus and L caudate could be associated with changes in spontaneous speech fluency and accuracy.

In 2015, Fridriksson and colleagues suggested two possible mechanisms by which SE may aid speech production in non-fluent aphasia. Their first suggestion was that SE works at the lower level of processing by providing non-fluent patients surrogate, multisensory targets to guide speech production. As they mention, this mechanism does not seem probable, as enhanced activation at the level of the somatosensory motor circuit doesn't necessarily compensate for damage to IFG pars opercularis, which is not included as a part of this circuit. The second mechanism that they suggest is that SE works at the higher-level cortical auditory-motor circuit of processing. SE activates auditory-visual syllable targets perhaps rooted in the posterior middle temporal gyrus (pMTG) (Venezia et al., 2016). Similar to auditory syllable targets that are mapped onto articulation via the area Spt, the same processing route could be assumed for AV syllable targets. Venezia and colleagues (2016) found that bilateral pre-central sulci, left central sulcus, caudate nucleus, IFG and MTG showed increased activation following visual speech input and responded exclusively to Visual (V), Audio Visual (AV) or both. This finding supports the conclusion that visual speech representations must have access to a distinct pathway to the motor-system that, when engaged in conjunction with auditory–motor networks by an audio-visual stimulus, produces increased activation of speech motor programs (Venezia et al., 2016). Their results suggested that the pMTG was a crucial part of a

distinct sensorimotor pathway for visual speech. Fridriksson and colleagues (2012) also found that pMTG was a crucial part of the system supporting speech entrainment.

In the current study, we used a simple subtraction design to identify areas that correlate with changes in accurate production and fluency of spontaneous speech. When we compared post-treatment activation for SS and SE tasks, we found that activation in the left caudate was associated with change in dwpm and activity in pMTG was associated with changes in CIUs/min and %CIUs. When we compared SS-SE activity post treatment to pre-treatment activity for the same tasks, one region survived the $p < 0.05$ threshold for activation. Activity in pMTG was found to be associated with change in CIUs/min.

Stahl and colleagues (2011) found that providing external rhythm promotes an increase in speech output. The basal ganglia are thought to play a crucial role in the timing of motor activity and when damaged could affect the timing of motor speech (Fridriksson et al., 2005; Stahl et al., 2011; Giraud et al., 2008). Based on these previous findings Fridriksson and colleagues suggested that damage to the basal ganglia could be a crucial predictor of speech production. In their study (Fridriksson et al., 2012) they found that bilateral basal ganglia were particularly active in both the speech entrainment and spontaneous speech conditions, suggesting that speech entrainment may provide patients with crucial speech rhythm that was affected by stroke. However, they also found that the basal ganglia were at least partially preserved in all of the patients included in their research suggesting that speech entrainment probably does not compensate for an impaired basal ganglia function. We found that activation in the left caudate nucleus, a structure which is a component of the basal ganglia, predicted changes in dwpm. The

caudate nucleus contributes to behavior through the excitation of correct action schemas and the selection of appropriate sub-goals based on evaluation of action outcomes; both process fundamental to successful goal-directed action (Grahn, Parkinson, Owen, 2008).

As mentioned above, when we compared SS-SE activity post treatment to pre-treatment activity for the same tasks, activity change in pMTG predicted change in CIUs/min. This was not a surprise as Venezia and colleagues' findings (2016) suggested a distinct pathway to the motor-system that, when engaged in conjunction with auditory–motor networks by an audio-visual stimulus, produces increased activation of speech motor programs. Their findings suggested that the pMTG was a crucial part of this sensorimotor pathway for visual speech and suggested that SE activates auditory-visual syllable targets plausibly rooted in the posterior middle temporal gyrus (pMTG). Fridriksson and colleagues (2012) also found that activity in pMTG is vital for the process that supports SE. Our current findings are supported by these previous findings and we conclude that this change in activation in the left pMTG, is caused by SE treatment and can predict changes in informativeness of speech (CIUs/min and %CIUs) for people with Broca's aphasia.

None of the other cortical areas included in our analyses turned out to have activations that predicted treatment outcome. Certainly, the small sample size might be the culprit for this outcome. There is also a possibility that there may have been some brain areas that had important but short-lived activations where the signal was simply not robust enough to reach a significant threshold. Functional magnetic resonance imaging or functional MRI (fMRI) measures brain activity by detecting changes associated with blood flow. This technique relies on the fact that cerebral blood flow and neuronal

activation are coupled. When an area of the brain is specifically activated, blood flow to that region increases. This technique is widely used, especially in research; however, like any other brain imaging method, it has its pros and cons. FMRI has excellent spatial resolution down to a few millimeters but rather poor temporal resolution. A limitation of hemodynamic methods like fMRI is that across studies they will tend to identify only the most robust and temporally sustained effects, perhaps missing key contributions from other regions that have activations that are subthreshold or more variable localization from one participant to the next (Matchin & Hickok, 2019). Another important reason is the fact that all of our participants had lesions in the pre-central sulcus, left central sulcus and the IFG and therefore probably had limited activation in these areas.

4.3 Exploratory analysis

None of the five regions of interest previously suggested by Basilakos et al., 2015 to be associated with apraxia of speech survived the lesion-based analysis at a $p < 0.05$ threshold, after correcting for multiple comparisons. However, lesion in superior longitudinal fasciculus (SLF) survived at a $p < 0.1$ threshold for CIUs/min. This finding led us to take a further look at what we had already found to be significant. We ran multiple linear regressions to predict outcome based on lesions and/or regional brain activity. The model that had the best predictive powers was one that included lesions in superior longitudinal fasciculus (SLF), lesions in middle temporal gyrus (MTG) and change in activity in MTG as predictors ($F(3,14)= 3.723$, $p=0.037$) with an R^2 of .44. Our results revealed that people who respond better to SE treatment appear to have smaller lesions in SLF, larger lesions in MTG and less activation in MTG post treatment.

Based on these findings we allow ourselves to cautiously deduce that MTG can be damaged but if there is still activation in MTG and SLF has not been affected too much, people can experience positive treatment effects.

4.4 Summary of Findings

All participants fit the reported criteria for treatment inclusion, that is, diagnosis of chronic non-fluent aphasia after left hemisphere lesion. Nevertheless, large individual differences with respect to different baseline scores and different treatment success were observed. There was an overall change in all of the outcome measures but not all of them were statistically significant. To implement SE more effectively in clinical practice, we examined potential determinants influencing therapy outcome such as standardized behavioral test scores at baseline and found that ASRS could predict a negative change in dwpm and WAB AQ could predict positive change in CIUs/min. Every extra point on ASRS leads to a 0.025 decrease in different words per minute (dwpm). Every extra point on WAB AQ leads to a 0.025 unit increase on CIUs/min.

Lesion symptom mapping based on areas found to be related to AOS were not significant, but analysis of functional activity supported previous findings of the importance of pMTG in SE. The fMRI analysis also showed how changes in differential activity can predict changes in informativeness of spontaneous speech output.

Experimental analysis of brain imaging data revealed that people who respond better to SE treatment seem to have smaller lesions in SLF, larger lesions in left MTG and less activation in left MTG post treatment. As previously mentioned, we cautiously postulate that our findings suggest that the L MTG can be damaged but if there is still

activation in L MTG and L SLF has not been affected too much, people can experience positive treatment effects.

4.5 Limitations and Future Directions

We did not test hearing or visual acuity. All of the participants exhibited adequate understanding of the tasks, as determined by them responding appropriately to questions and instructions. Still, hearing and visual acuity should be something that would be beneficial to assess in future studies. For this study we also did not record the participants while they underwent the treatment. If we had, an analysis of response delay by time-locking the responses to the auditory stimulus could have been completed. Response delay could possibly be a sensitive measure of performance improvements across training (could just record responses to the first trial of each session as a measure of retained performance). Another idea would be to look at response delay with recordings during fMRI session. It would also be interesting to see if putting a time constraint on the tasks would change our findings.

Future studies will want to look into treatment dosage as well; 11.25 hours may not be enough to show generalization to untrained tasks. People with Broca‘s aphasia may also need the AV support to successfully talk about untrained scripts like they did in Fridriksson et al., 2012. It would also be interesting to try a different set of outcome measures that could perhaps have even more functional value.

As far as brain imaging goes, future studies may want to include both functional and structural connectivity measures. Damage to white matter underlying the left posterior superior and middle temporal gyri (pSTG and pMTG) has been consistently

implicated as a source of deficits in multiple language domains, including comprehension, naming and repetition (Yourganov et al., 2016, Fridriksson et al., 2013). Lesions affecting the posterior temporal white matter and disrupting connectivity in posterior temporal areas also predict poor responses to language therapies (Fridriksson, 2010; Bonilha et al., 2016). The reason for these negative impacts on different features of language outcome has not been determined. It could perhaps be explained by the fact that portions of the white matter under the pSTG/pMTG contain projections associated with multiple long-range fiber pathways (Turken & Dronkers, 2011), including dorsal and ventral language pathways (Kümmerer et al., 2013; Saur et al., 2008). Fibers associated with at least three language-relevant tracts cross through this region–the arcuate fasciculus (AF), inferior longitudinal fasciculus (ILF), and inferior fronto-occipital fasciculus (IFOF) (Catani & Mesulam, 2008; Turken & Dronkers, 2011). Thus, it has been proposed that the white matter in this area corresponds to a cross-road region and a structural weak point where multiple language-relevant pathways are vulnerable to simultaneous disruption by focal damage (Turken & Dronkers, 2011). Fibers associated with the anterior thalamic radiations (ATR), uncinate fasciculus (UF), and inferior fronto-occipital fasciculus (IFOF) form a cross-road region in the prefrontal white matter near areas where damage is associated with chronic deficits in both semantic deficits and verbal fluency (Griffis, Nenert, Allendorfer, & Szaflarski, 2017). This finding supports the proposal that damage to these cross-road regions may play a role in chronic language deficits after stroke (Mirman et al., 2015). This proposal is certainly also in consensus with recent evidence suggesting that lesions affecting areas of high tract overlap are associated with post-stroke deficits in multiple cognitive domains (Corbetta et al., 2015).

4.6 Conclusion

Three weeks (11.25 hours) of speech entrainment treatment can potentially induce statistically significant improvement in spontaneous speech production. The treatment can also facilitate significant changes in other behavioral measures of speech and language widely used in aphasia research. The effect sizes for the changes in behavioral scores for our group may not have been large, but they were statistically significant. The findings of the current study also concur with previous studies that have suggested the importance of the left posterior middle temporal gyrus for audio-visual information integration and perhaps the idea of a visual pathway and an AV pathway that together produce increased activation of speech programs.

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APPENDIX A

SPEECH ENTRAINMENT SCRIPTS

Narrative 1: Christmas
Christmas is a popular holiday all over the world. People have many different traditions to celebrate this holiday. Many people travel far to see their family on this holiday. A common Christmas tradition is decorating a pine tree with ornaments and lights and placing gifts under the tree for loved ones.

Narrative 2: Brushing Teeth
I brush my teeth in the morning after I eat breakfast. To brush my teeth, I wet a toothbrush and place a small amount of toothpaste on top of the brush. Then I move the toothbrush back and forth across my teeth. Once I am done brushing, I rinse the toothbrush and my mouth with water.

Narrative 3: South Carolina
South Carolina is a state located in the Southeast of the United States. The capital of the state is Columbia. The state dance of South Carolina is the Shag and the state bird is the Carolina Wren. South Carolina is also known for its beautiful beaches, lakes and mountains.

Narrative 4: Days of the Week
A week has seven days in it. Each week begins on Monday and ends on Sunday. There are fifty-two weeks in each year. The most popular days of the week are Saturday and Sunday because many people do not work on these days. The least popular day is Monday since it is the beginning of the week.

Narrative 5: Pizza
Pizza is a popular Italian food. It consists of a baked thin crust with a tomato sauce on top. Pizza also has melted cheese on top. There are many different pizza toppings. Many people put vegetables, extra cheese, or different types of meat on their pizza. Pizza is a favorite food for many people.

Narrative 6: 4th of July
The 4th of July is an American holiday that is celebrated every year. This holiday celebrates when Americans declared their independence from the British a long time ago. Many people celebrate the 4th of July by having a cookout with friends and family. Another common 4th of July activity is watching fireworks.

Narrative 7: The Beatles
The Beatles were a popular English rock band that formed in 1960. The Beatles came to America by plane and landed in New York City in 1964. The Beatles won many music awards and people still listen to their music today. Two of the original members of The Beatles are still living today.

Narrative 8: Grand Canyon
The Grand Canyon is a large canyon found in Arizona in the United States. It is contained within Grand Canyon National Park. The weather at The Grand Canyon is usually dry. The Grand Canyon can reach a depth over a mile. Many people visit The Grand Canyon to enjoy the scenery, raft in the rivers, hike, and run.

Narrative 9: The President
The President of the United States is the head of the government and enforces the laws of the land. The President is elected every four years and the president's term also lasts four years. The White House in Washington, D.C., is the official home and workplace of the president.

Narrative 10: The Beach
Beaches are a type of land found along the ocean or the sea. Many beaches have sand, which are very small pieces of rock. Many people visit beaches in the summertime. Common beach activities are swimming, making a sandcastle, or walking along the shore. People also like to search for seashells along the beach.

Narrative 11: Swimming
Swimming is a fun outdoor activity during the summer, and it is also great exercise. Make sure you have a good kick. Your kick is like a motor on a boat. Keep the kicks small and fast with straight legs. Remember to lay flat to make it easier to move forward.

Narrative 12: Peanut Butter Cookies
Here is a simple recipe for peanut butter cookies. Mix one cup of peanut butter and one cup of sugar together. Put spoonfuls of the mix on a cookie sheet. I like to put a Hershey's kiss on top. After baking, make sure to let the chocolate cool completely so it keeps its shape.

Narrative 13: Gardening
I enjoy gardening. Every spring I buy new flowers, herbs, and trees to plant all around the house. I enjoy picking and eating all the fruits and vegetables from the backyard. This year I am going to plant tomatoes so I can have fresh ones in my salsa.

Narrative 14: Traveling
Most people like to travel. Whether it is within the United States or to a different country, it is nice to get away from work. Some people prefer to relax on vacation. Others like to make an adventure out of their trip and explore somewhere new. Where do you like to travel?

Narrative 15: Gold Rush
During the California gold rush, families traveled by covered wagons and ships to California. The forty-niners spent long days panning for gold. They filled pans with sand and water from streams and shook them in a circular motion. The gold sank to the bottom of the pan while dirt fell out.

Narrative 16: Knitting
Knitting is a hobby enjoyed by many people. It takes some practice at first, but many knitters become very good. It can be useful to make your own scarves, hats, and even sweaters for winter. Craft stores carry many different kinds of yarn to choose from.

Narrative 17: Piano
The piano is one of the most played instruments. A piano has 88 keys, 52 white keys and 36 black keys. Three types of pianos are the grand piano, the upright piano, and the electric keyboard. Many famous composers have created beautiful piano music that is well-known around the world.

Narrative 18: University of South Carolina
The University of South Carolina is a large school in Columbia, South Carolina. The mascot of the school is a gamecock. The school colors are garnet and black. A major landmark of the school is the Horseshoe, which contains many historic buildings from as early as 1805.

Narrative 19: Cats
Cats are a four-legged animal that many people have as a pet. Cats can be many different colors such as white, gray, brown, or black. Some cats have spots on their fur or are more than one color. Some people have more than one cat, because they are an easy pet to take care of.

Narrative 20: Hiking
Hiking is a common leisure activity. People wear hiking boots and will go to a local trail to walk and enjoy the scenery. The scenery people enjoy the most while hiking are trees, waterfalls, or tops of mountains. Many people will pack a lunch in a backpack to take with them while hiking to eat and enjoy the scenery.

Narrative 21: Morning Routine
My alarm wakes me up at 7 AM. I get up, take a shower, brush my teeth, and put on clothes for work. Then, I make breakfast and eat. Next, I feed the dog and let it outside to use the restroom. I make sure to pack my laptop, phone, wallet, and keys.

Narrative 22: I Love Lucy
I Love Lucy was a popular TV show in the 1950s. This sitcom was set in Lucy's apartment in New York City where she lived with her singer husband, Ricky Ricardo, and their son, Little Ricky. Lucy is very ambitious and wants to get into show business, but usually ends up getting in trouble.

Narrative 23: Mars
Mars is the fourth planet from the sun. It is small and has a reddish tint. No astronaut has ever visited Mars, but NASA has sent rovers to explore the planet. Because there are polar ice caps that contain water on Mars, some people believe that there may have been life on the planet.

Narrative 24: Giraffes
The giraffe is a mammal native to Africa. Their long legs and necks allow them to eat the leaves off of tall trees that other animals cannot reach. At the Columbia Riverbanks Zoo, you can feed the giraffes. Many children and adults enjoy taking pictures with these gentle animals.

Narrative 25: Three Little Pigs
There is a famous story of three little pigs. One built his house out of straw. The other built his house out of wood. The last pig built his house out of bricks. The big, bad wolf huffed and puffed and blew the first two houses down but could not destroy the brick house.

Narrative 26: Shakespeare
William Shakespeare was a famous poet, playwright, and actor in England during the late 1500s. His most famous play is probably *Romeo and Juliet*. This tragic story is about two young lovers from enemy families. They try to be together against their families' wishes but ultimately die trying.

Narrative 27: Statue of Liberty
The Statue of Liberty is a symbol of freedom that welcomes immigrants into the country. It was originally a gift from France and now stands in New York. The statue is made of copper, but because of a reaction with water and air, it looks green today.

Narrative 28: Home
I live in a house. There is a big kitchen perfect for cooking meals. The dining room is just big enough for my family to sit down and eat together. I like to unwind in the comfy living room. And after a long day at work, I like sleeping in my soft bed.

Narrative 29: Kentucky Derby
The Kentucky Derby is a famous horse race. The race is held on the first Saturday of May each year. The race is often called "the most exciting two minutes in sports". Many women wear a nice dress and a fancy hat and men wear a suit. A famous drink served at the race is the Mint Julep.

Narrative 30: Shoes
There are many different kinds of shoes. In the summer, most people like to wear sandals or flip flops. In the winter, many people wear boots or sneakers. When running or walking for long distances, it is best to wear shoes with good arch support. When dressing up, many women like to wear high heels.

Narrative 31: The Olympics
The Olympics is a worldwide event that hosts both summer and winter sports competitions. The Olympic games started in Athens, Greece. Today, over 200 countries participate in the games. Thousands of athletes train and compete in the games. Some of the more popular events are track, swimming, skiing, snowboarding, and ice skating.

Narrative 32: American Idol
American Idol is a popular singing competition and a TV show. People can try out in cities across the country and four judges decide who gets to go to Los Angeles to compete. Every week, contestants perform a song. Viewers can text to vote for their favorite singer. Contestants are eliminated every week until there is one winner.

Narrative 33: Weather
The weather in the Southern United States is usually very pleasant. During the spring, it is warm and sunny. During the summer, it is very hot with frequent thunderstorms. During the fall it is cool, and the leaves change colors. The winter is usually cold and dry, and it rarely snows.

Narrative 34: Advocacy
I have Aphasia. This means I have difficulty with language. Aphasia affects my language, not my intelligence. It is hard for me to understand what people are saying and to find the words to speak my thoughts. Please speak directly to me and give me time to communicate.

Narrative 35: Eggs
I like to eat scrambled eggs for breakfast. I like them because they are fast and easy. To make eggs I get out a pan and melt some butter over medium heat. I crack the eggs into the pan and stir. I like scrambled eggs best, so I stir until they are done.

Narrative 36: Smoky Mountain
Have you been to the Smoky Mountain National Park? It is a great place for a family vacation. When it is warm, people like to camp and hike. In the fall, the leaves change colors and it is the perfect time for bird watching. The Smoky Mountain National Park is the most visited national park.

Narrative 37: Elvis
Elvis Presley is known as the King of Rock and Roll. He lived at Graceland in Memphis Tennessee. Elvis spent more weeks at the top of the charts than any other artist. He also made more than thirty movies. The King died in 1977, but some say he still lives at Graceland.

Narrative 38: MLK
Martin Luther King Jr. was a leader in the Civil Rights Movement. He was active during bus boycotts that ended segregation on public buses. King led the March on Washington where he delivered his famous “I Have a Dream” speech. In 1964, he received the Nobel Peace Prize. He is honored every January.

Narrative 39: Stroke
Stroke is a serious medical condition. A stroke is when blood flow to the brain is disrupted. Blood carries oxygen and nutrients all over the body. Without blood to parts of the brain the tissue dies. Stroke is the leading cause of adult disability in the United States.

Narrative 40: Thanksgiving
Thanksgiving is a popular American holiday. At the end of November many families come together for a big meal and to give thanks. People travel all over the world to see family at Thanksgiving. The most common Thanksgiving dishes are turkey and dressing, cranberry sauce, green bean casserole, and pumpkin pie.

APPENDIX B

INDIVIDUAL SCORES FOR INDIVIDUAL TASKS

Table B.1 Individual scores for Broken Window at baseline and post-treatment.

Broken Window

	pre_WPM	pre_dwpm	pre_CIUs/min	pre_%CIUs	post_WPM	post_dwpm	post_CIUs/min	post_%CIUs
1	34.64	16.46	14.91	43.21%	35.28	10.54	10.85	30.48%
2	54.74	33.96	29.39	53.24%	67.29	41.29	40.29	58.91%
3	50.90	27.35	39.36	77.54%	72.18	32.09	30.03	38.76%
4	10.36	9.49	0.64	5.56%	14.00	9.70	0.47	4.05%
5	46.66	24.03	27.65	59.43%	48.18	28.59	36.62	76.19%
6	34.33	31.67	6.00	15.26%	35.43	21.72	3.06	9.08%
7	33.19	18.19	6.75	20.46%	39.50	25.50	23.50	57.35%
8	0.00	0.00	0.00	0.00%	2.37	1.97	0.00	0.00%
9	5.47	5.47	0.00	0.00%	15.63	15.63	0.00	0.00%
10	98.35	41.29	0.00	0.00%	64.79	37.08	0.00	0.00%
11	77.78	41.18	1.11	1.16%	59.77	35.62	12.13	22.89%
12	35.65	28.59	6.41	22.62%	37.09	15.47	5.81	11.54%
13	36.49	17.98	5.30	14.31%	28.18	16.18	5.36	19.09%
14	60.78	33.51	0.00	0.00%	24.75	9.29	0.00	0.00%
15	11.47	6.22	0.00	0.00%	25.63	10.74	1.54	5.56%
16	55.60	40.71	41.79	74.84%	54.76	42.06	50.40	92.46%
17	7.70	26.90	0.00	0.00%	7.68	7.28	0.00	0.00%
18	24.57	15.44	14.87	60.61%	22.44	12.00	14.08	62.88%
19	4.00	2.05	0.59	7.94%	3.81	2.38	0.00	0.00%
20	30.48	13.46	12.54	42.33%	23.83	17.27	9.81	40.75%

Table B.2 Individual scores for Broken Window at 3 months and 6 months post-treatment.

Broken Window

	3m_WPM	3m_dwpm	3m_CIUs/min	3m_%CIUs	6m_WPM	6m_dwpm	6m_CIUs/min	6m_%CIUs
1	41.84	14.47	10.98	26.94%	28.29	10.26	8.47	30.10%
2	69.43	42.00	55.29	79.65%	80.97	53.44	56.45	68.92%
3	60.83	33.83	39.94	66.05%	62.69	30.96	43.282	69.04%
4	19.81	13.03	0.47	2.27%	NA	NA	NA	NA
5	52.31	37.54	41.38	79.04%	55.26	36.29	46.15	83.24%
6	40.48	36.51	9.54	24.29%	43.10	37.90	11.12	27.02%
7	60.13	39.36	27.44	50.00%	36.45	33.29	19.47	53.57%
8	3.57	2.21	0.00	0.00%	NA	NA	NA	NA
9	NA	NA	NA	NA	2.80	2.80	0.65	25.00%
10	90.95	36.29	0.86	0.91%	61.98	36.36	28.31	2.59%
11	52.07	29.75	5.48	10.52%	78.37	35.07	3.90	4.96%
12	29.86	21.00	1.76	6.25%	46.15	21.44	9.85	20.81%
13	33.32	15.38	3.01	9.45%	36.44	19.73	4.83	13.25%
14	38.33	25.11	4.11	10.17%	26.74	20.08	1.07	3.57%
15	17.85	10.60	2.66	16.79%	16.51	10.44	2.22	17.94%

Table B.3 Individual scores for Cinderella at baseline and post-treatment.

Cinderella

	pre_WPM	pre_dwpm	pre_CIUs/min	pre_%CIUs	post_WPM	post_dwpm	post_CIUs	post_%CIUs
1	26.86	7.50	10.97	40.64%	31.17	6.92	8.40	26.85%
2	93.30	24.16	49.86	53.40%	89.72	21.01	50.08	55.79%
3	45.67	12.74	23.95	52.27%	54.75	15.67	21.86	39.70%
4	9.84	7.41	0.64	3.57%	12.33	8.14	0.00	0.00%
5	32.34	15.80	15.38	47.39%	36.13	14.50	25.25	68.30%
6	41.61	13.35	6.31	15.21%	39.42	11.62	4.91	12.88%
7	18.37	10.91	9.60	48.42%	29.07	17.07	16.83	59.20%
8	1.67	1.67	0.00	0.00%	1.45	1.08	0.00	0.00%
9	10.40	7.30	0.00	0.00%	14.54	12.43	0.00	0.00%
10	71.91	22.87	3.75	4.73%	75.32	20.76	4.22	5.65%
11	64.55	24.72	2.63	3.74%	97.91	20.33	8.35	8.60%
12	19.48	6.88	2.54	8.11%	27.39	11.86	3.97	17.31%
13	44.90	15.71	4.35	9.89%	75.99	24.64	5.00	8.32%
14	21.34	11.72	0.00	0.00%	39.10	11.81	1.24	4.63%
15	23.55	9.83	0.00	0.00%	24.47	15.19	1.64	10.53%
16	52.00	18.75	29.54	56.72%	34.88	12.01	28.34	86.15%
17	13.32	5.64	0.00	0.00%	3.95	3.95	0.00	0.00%
18	20.66	8.86	11.42	54.69%	23.69	8.68	12.94	54.46%
19	3.11	2.57	0.36	2.78%	2.22	1.38	0.82	40.00%
20	21.94	10.13	6.36	28.53%	25.71	11.06	10.64	42.81%

Table B.4 Individual scores for Cinderella at 3 months and 6 months post-treatment.

Cinderella

	3m_WPM	3m_dwpm	3m_CIUs/min	3m_%CIUs	6m_WPM	6m_dwpm	6m_CIUs/min	6m_%CIUs
1	27.62	7.35	8.09	29.31%	25.97	5.95	7.40	28.66%
2	91.05	25.07	47.63	52.47%	93.44	23.34	56.32	60.45%
3	45.93	11.28	20.48	44.68%	58.79	13.94	23.04	39.19%
4	21.60	13.20	0.00	0.00%	NA	NA	NA	NA
5	36.87	17.68	25.78	69.88%	37.38	17.62	30.03	80.14%
6	36.17	12.64	3.58	9.93%	41.10	12.13	4.90	11.95%
7	26.56	19.83	21.83	82.21%	24.83	16.60	14.54	58.57%
8	4.08	3.11	0.00	0.00%	NA	NA	NA	NA
9	NA	NA	NA	NA	18.38	14.19	0	0.00%
10	78.32	16.96	4.01	5.08%	57.03	19.73	29.50	2.59%
11	80.68	19.83	7.50	9.32%	81.42	19.76	4.84	5.89%
12	21.23	8.91	0.00	0.00%	25.20	10.25	3.18	15.91%
13	44.48	17.21	2.12	4.65%	38.56	10.74	2.41	6.11%
14	24.74	11.68	0.47	1.61%	30.99	6.92	1.97	6.52%
15	16.47	8.48	0.45	3.13%	21.76	6.73	2.122	9.58%

Table B.5 Individual scores for Peanut Butter and Jelly (PBJ) at baseline and post-treatment.

Peanut Butter and Jelly Sandwich

	pre_WPM	pre_dwpm	pre_CIUs/min	pre_%CIUs	post_WPM	post_dwpm	post_CIUs	post_%CIUs
1	22.46	15.18	14.79	62.80%	30.00	18.89	15.56	51.85%
2	82.46	45.49	60.68	73.65%	88.64	47.22	63.20	71.22%
3	64.13	36.51	42.22	62.80%	77.65	40.88	51.96	66.27%
4	11.08	9.31	2.50	12.50%	12.92	8.62	2.31	16.67%
5	35.52	19.94	20.38	56.93%	54.00	25.92	40.29	74.94%
6	34.32	24.09	12.61	40.81%	40.57	22.74	15.90	38.02%
7	17.86	13.93	12.50	70.00%	37.50	33.00	34.50	91.88%
8	0.00	0.00	0.00	0.00%	2.69	2.69	0.00	0.00%
9	18.54	10.61	0.00	0.00%	2.95	1.82	0.00	0.00%
10	72.46	33.94	12.46	16.47%	57.00	37.58	15.49	27.48%
11	100.67	54.67	8.00	9.09%	93.73	34.93	8.72	9.03%
12	26.30	14.21	7.09	25.79%	42.36	14.76	8.69	19.15%
13	29.31	14.30	3.68	12.54%	27.69	12.15	4.63	12.85%
14	47.93	17.85	3.10	4.69%	43.82	13.86	1.85	10.00%
15	24.05	11.09	1.13	3.33%	12.76	7.79	1.37	12.24%
16	47.98	20.07	27.59	58.33%	42.86	17.65	27.74	61.61%
17	1.30	1.30	0.00	0.00%	0.00	0.00	0.00	0.00%
18	21.97	8.29	9.90	46.32%	26.87	13.62	14.47	53.41%
19	7.50	3.26	3.48	16.00%	2.31	2.31	2.31	0.00%
20	26.72	17.68	13.17	48.01%	23.36	19.47	17.37	74.42%

Table B.6 Individual scores for Peanut Butter and Jelly at 3 months and 6 months post-treatment.

Peanut Butter and Jelly Sandwich

	3m_WPM	3m_dwpm	3m_CIUs	3m_%CIUs	6m_WPM	6m_dwpm	6m_CIUs/min	6m_%CIUs
1	23.95	11.81	8.77	37.04%	21.06	11.16	7.32	34.78%
2	77.52	37.62	53.69	69.29%	85.36	45.63	51.78	60.60%
3	70.48	39.09	48.46	67.94%	56.78	28.76	30.45	53.59%
4	12.00	10.50	3.00	25.00%	NA	NA	NA	NA
5	58.75	31.52	39.24	68.38%	47.73	20.43	32.41	68.29%
6	36.98	26.93	17.21	46.11%	32.13	18.93	12.13	38.20%
7	27.06	20.39	18.73	79.17%	11.70	7.94	8.02	69.05%
8	10.99	10.99	0.00	0.00%	NA	NA	NA	NA
9	NA	NA	NA	NA	10.45	7.29	0	0.00%
10	67.29	38.14	14.36	20.85%	53.57	36.43	6.42	12.00%
11	80.11	34.29	5.11	6.63%	71.79	36.53	9.74	14.06%
12	21.98	9.91	0.00	0.00%	31.01	11.57	9.00	28.39%
13	21.46	9.46	2.35	9.33%	26.11	20.56	8.33	31.67%
14	28.30	12.73	0.76	3.49%	25.45	11.26	1.139	5.36%
15	20.02	5.95	0.47	4.76%	17.81	7.56	1.835	10.12%

Table B.7 Individual scores for Picnic at baseline and post-treatment.

Picnic

	pre_WPM	pre_dwpm	pre_CIUs/min	pre_%CIUs	post_WPM	post_dwpm	post_CIUs	post_%CIUs
1	18.00	9.30	8.35	48.88%	28.01	11.00	9.01	31.98%
2	58.14	33.14	38.29	65.62%	56.65	30.43	37.17	65.46%
3	58.20	22.27	39.80	68.44%	63.65	27.22	41.17	64.65%
4	3.38	3.02	0.49	14.29%	6.16	3.92	0.43	9.09%
5	39.81	25.15	30.32	75.16%	38.38	23.08	29.03	76.94%
6	17.30	10.58	6.89	39.77%	23.14	12.68	9.47	41.75%
7	27.19	16.36	14.11	51.74%	25.28	15.75	12.79	50.64%
8	2.07	2.07	0.00	0.00%	1.68	1.50	0.00	0.00%
9	2.51	2.21	0.00	0.00%	18.75	15.00	0.00	0.00%
10	73.58	25.87	0.98	2.20%	65.27	20.86	0.00	0.00%
11	65.39	23.21	3.18	5.48%	55.43	19.50	7.68	15.30%
12	10.74	5.22	0.86	12.50%	22.91	5.81	2.61	13.04%
13	24.96	11.81	7.02	27.48%	20.30	12.75	7.81	37.50%
14	34.15	12.02	1.57	3.38%	25.09	6.00	0.35	1.27%
15	9.67	6.45	1.62	13.26%	5.81	4.61	1.85	31.25%
16	32.84	21.55	27.96	85.02%	38.99	24.43	33.44	85.13%
17	3.47	2.14	0.00	0.00%	4.56	2.79	0.00	0.00%
18	15.92	7.21	9.03	55.82%	15.43	6.14	10.14	64.93%
19	4.25	1.42	0.57	4.35%	2.37	0.79	0.00	0.00%
20	30.99	15.63	14.39	51.19%	28.04	20.80	16.16	55.56%

Table B.8 Individual scores for Picnic at 3 months and 6 months post-treatment.

Picnic

	3m_WPM	3m_dwpm	3m_CIUs/min	3m_%CIUs	6m_WPM	6m_dwpm	6m_CIUs/min	6m_%CIUs
1	27.44	11.79	9.57	36.18%	24.90	11.83	9.64	38.14%
2	53.85	31.25	37.98	70.29%	69.49	39.24	44.48	63.04%
3	49.59	18.54	28.67	57.83%	61.38	18.14	34.20	55.80%
4	10.64	7.73	1.75	17.63%	NA	NA	NA	NA
5	38.75	22.55	31.18	80.36%	40.12	20.66	30.98	78.96%
6	24.60	13.22	8.30	33.43%	24.15	14.92	11.63	48.26%
7	24.53	15.57	15.57	63.06%	18.90	13.76	12.05	64.95%
8	3.59	2.36	0.50	16.25%	NA	NA	NA	NA
9	NA	NA	NA	NA	3.89	3.58	0.00	0.00%
10	68.11	22.57	1.05	1.72%	47.10	16.20	1.34	2.87%
11	47.33	13.22	3.50	7.92%	58.87	14.34	3.22	5.91%
12	18.12	8.49	2.80	15.48%	18.60	6.17	2.06	11.29%
13	16.92	9.71	5.03	29.97%	15.29	8.20	4.10	26.92%
14	21.88	5.90	1.02	4.67%	23.11	5.76	1.32	5.84%
15	11.14	3.68	1.40	12.88%	7.76	3.88	0.83	20.14%

Table B.9 Individual scores for primary outcome measures at baseline and post-treatment.

Primary Outcome Measures

	pre_WPM	pre_dwpm	pre_CIUs/min	pre_%CIUs	post_WPM	post_dwpm	post_CIUs/min	post_%CIUs
1	25.49	12.11	12.25	48.88%	31.12	11.84	10.95	35.29%
2	72.16	34.19	44.55	61.48%	75.57	34.99	47.69	62.84%
3	54.72	24.72	36.33	65.26%	67.06	28.97	36.25	52.34%
4	7.90	6.54	1.07	8.98%	11.35	7.60	0.80	7.45%
5	38.58	21.23	23.43	59.73%	44.17	23.02	32.80	74.09%
6	31.89	19.92	7.95	27.76%	34.64	17.19	8.34	25.43%
7	24.15	14.85	10.74	47.66%	32.84	22.83	21.90	64.77%
8	0.93	0.93	0.00	0.00%	2.05	1.81	0.00	0.00%
9	9.23	6.40	0.00	0.00%	12.97	11.22	0.00	0.00%
10	79.07	30.99	4.30	5.85%	65.59	29.07	4.93	8.28%
11	77.10	35.94	3.73	4.87%	76.71	27.59	9.22	13.95%
12	23.04	13.72	4.22	17.25%	32.44	11.98	5.27	15.26%
13	33.91	14.95	5.09	16.06%	38.04	16.43	5.70	19.44%
14	38.64	16.71	1.17	2.02%	33.19	10.24	0.86	3.97%
15	16.68	8.06	0.69	4.15%	17.17	9.58	1.60	14.89%
16	48.74	25.27	31.72	68.73%	42.87	24.04	34.98	81.34%
17	7.00	4.38	0.00	0.00%	4.05	2.72	0.00	0.00%
18	20.78	9.95	11.30	54.36%	22.11	10.11	12.91	58.92%
19	4.88	2.05	1.25	7.77%	2.68	1.72	0.78	22.50%
20	27.54	14.22	11.62	42.52%	25.23	17.15	13.50	53.38%

Table B.10 Individual scores for primary outcome measures at 3months and 6 months post-treatment.

Primary Outcome Measures

	3m_WPM	3m_dwpm	3m_CIUs/min	3m_%CIUs	6m_WPM	6m_dwpm	6m_CIUs/min	6m_%CIUs
1	30.21	11.36	9.35	32.37%	25.06	9.80	8.21	32.92%
2	72.96	33.98	48.65	67.92%	82.31	40.41	52.26	63.25%
3	56.71	25.68	34.39	59.13%	59.91	22.95	32.74	54.41%
4	16.01	11.11	1.30	11.23%	NA	NA	NA	NA
5	46.67	27.32	34.39	74.42%	45.12	23.75	34.90	77.66%
6	34.56	22.32	9.66	28.44%	35.12	20.97	9.95	31.36%
7	34.57	23.79	20.89	68.61%	22.97	17.90	13.52	61.53%
8	5.56	4.67	0.12	4.06%	NA	NA	NA	NA%
9	NA	NA	NA	NA	8.88	6.97	0.16	6.25%
10	76.17	28.49	5.07	7.14%	54.92	27.18	16.39	5.01%
11	65.05	24.27	5.40	8.6%	72.61	26.42	5.43	7.71%
12	22.80	12.08	1.14	5.43%	30.24	12.36	6.02	19.10%
13	29.04	12.94	3.13	13.35%	29.10	14.81	4.92	19.48%
14	28.31	13.85	1.59	4.98%	26.57	11.00	1.38	5.32%
15	16.37	7.18	1.25	9.39%	15.96	7.15	1.75	14.45%

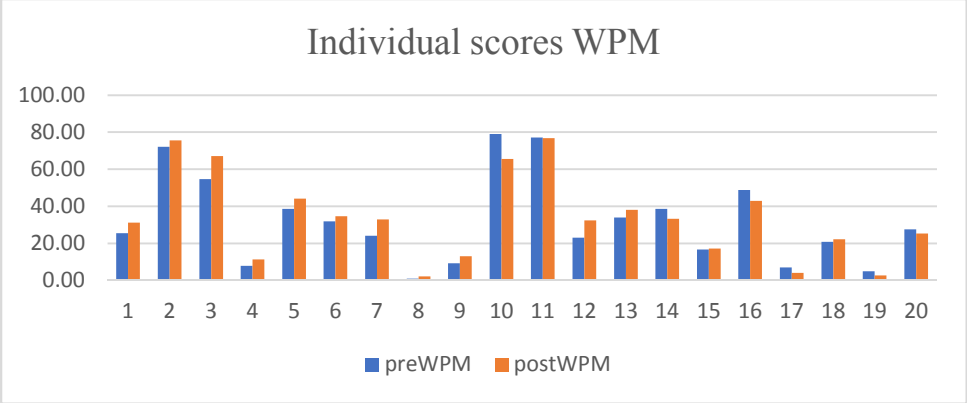

Figure B.1 Mean individual scores WPM at baseline and after treatment had been completed.

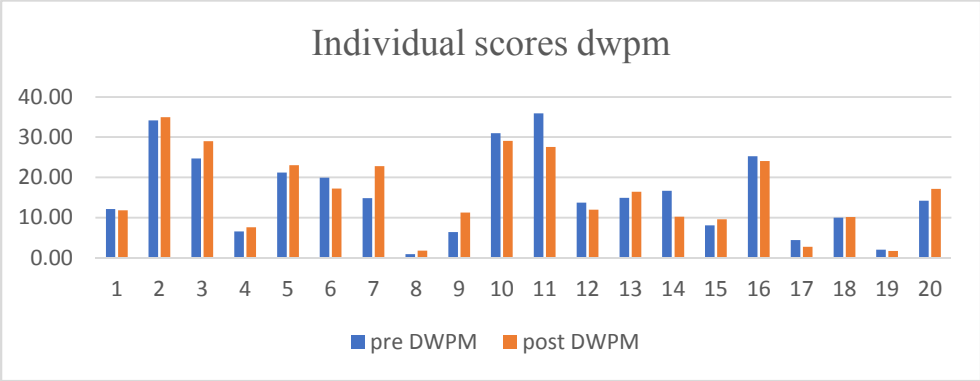

Figure B.2 Mean individual scores dwpm at baseline and after treatment had been completed.

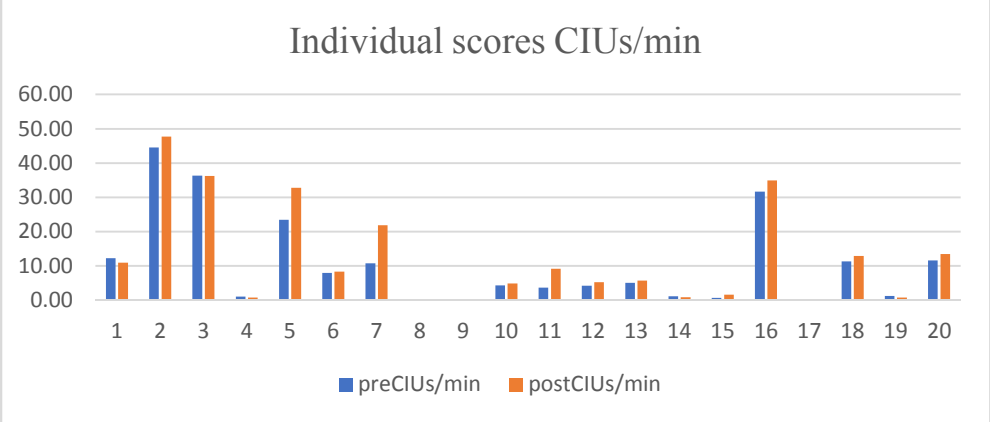

Figure B.3 Mean individual scores CIUs/min. at baseline and after treatment had been completed.

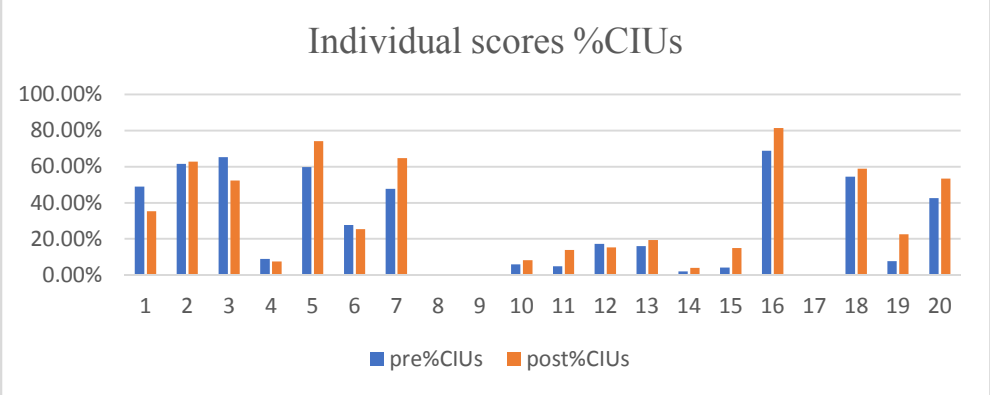

Figure B.4 Mean individual scores %CIUs at baseline and after treatment had been completed.