7-21-2016

The Effect of Formant Measurement Methods on Vowel Space in Patients with Parkinson's Disease Before and After Voice Treatment

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THE EFFECT OF FORMANT MEASUREMENT METHODS ON VOWEL SPACE IN PATIENTS WITH PARKINSON'S DISEASE BEFORE AND AFTER VOICE TREATMENT

by

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A Thesis

Submitted in Partial Fulfillment of the

Requirements for the Degree of

Master of Arts

Major: Speech Language Pathology

University of Memphis

August 2016

Abstract

LSVT-LOUD® has been shown to improve phonatory quality in patients with PD. Previous studies have shown an increase in vowel space area following treatment, but questions remain regarding possible methodological issues in interaction with phonatory factors. This study addressed these questions by comparing multiple formant measurement methods and vowel space metrics. Ten participants were recorded on two separate days before and after treatment. Formants were measured using a human-guided reference (dubbed 'HGIM'), LPC, and two forms of a cepstrally-liftered spectrum. Multiple vowel space metrics including the vowel articulation index, F2i/F2u, area of the vowel quadrilateral, and vowel formant dispersion utilized both lax and corner vowels to explore vowel space changes. Analysis revealed no significant change in vowel space following LSVT. High variability in LPC with a fixed coefficient was noted. These results do not support previous claims of increased vowel space but suggest that formant measurement methods may influence results.

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Parkinson's disease has a serious impact on society. Lee Silverman Voice Treatment (LSVT) is known to improve phonatory quality and intelligibility. Previous studies seeking to explain increased intelligibility in terms of improved articulation fail to take into account the effect of phonatory factors on measures of articulation, such as vowel space area. This thesis will explain how phonatory factors influence acoustic measures of formants, and in turn vowel space, using a variety of formant measurement methods and vowel space area metrics.

Parkinsonism refers to a group of disorder that are characterized by resting tremors, rigidity, akinesia, and postural instability (Darley, Aronson, & Brown, 1969; Yorkston, Beukelman, Strand, & Hakel, 2010). It includes idiopathic Parkinson's disease, secondary parkinsonism, and Parkinson's plus-syndromes (Adams & Dykstra, 2009; Ben-Shlomo & Sieradzan, 1995; Duffy, 2013; Yorkston et al., 2010). Idiopathic Parkinson's disease (PD) has no known cause but is characterized by basal ganglia dysfunction related to the loss of dopamine-producing cells known as dopaminergic neurons (Duffy, 2013; Yorkston et al., 2010). Loss of these cells and consequent effects on basal ganglia dysfunction leads to involuntary movements as well as decreased amplitude and force of movements (Duffy, 2013). Secondary parkinsonisms are disorders that share the symptoms of PD but have a known cause such as strokes, toxic-metabolic conditions, certain infections, or repeated head trauma (Darley et al., 1969; Duffy, 2013; Yorkston et al., 2010). Parkinson's-plus syndromes have the same symptoms as PD but include other symptoms; examples of Parkinson's-plus syndromes include multiple system atrophy, progressive supranuclear palsy (PSP), corticobasal degeneration, and striatonigral degeneration (Duffy, 2013; Yorkston et al. 2010). The focus of

this thesis is idiopathic Parkinson's disease.

Incidence and Impact on Society

In a review on the epidemiology of PD, de Lau and Breteler (2006) noted that "Parkinson's disease (PD) is the second most common neurodegenerative after Alzheimer's and is expected to impose an increasing social and economic burden on societies as populations age" (p. 525). The incidence of PD rises with age, with an incidence of approximately 93.1 in 100,000 people between the ages of 70 and 79 versus an incidence of 17.4 in 100,000 people between the ages of 50 and 59 (Lees, Hardy & Revesz, 2009). Some studies indicate that men are at a greater risk of developing PD than women, though differences have been noted across studies (de Lau & Breteler, 2006; Lees et al., 2009). Though age is considered a major risk factor, it should be noted that 10% of the people with PD are younger than 45 years of age (Lees et al., 2009). The median age of onset is 60 years of age and the average duration of survival after diagnosis is 15 years (Duffy, 2013; Lees et al., 2009). Among the most prominent features of PD is the marked change in speech and voice over the progression of the disease, which can have a profound impact on quality of life of patients living with PD.

Hypokinetic Dysarthria and PD

Hypokinetic dysarthria (HKD) is characterized by a decreased amplitude and force of speech movements (Adams & Dykstra, 2009; Duffy, 2013). HKD is most often associated with PD and is estimated to occur in 60 to 80% of patients diagnosed with PD (Adams & Dykstra, 2009; Duffy, 2013). It affects all levels of speech, including respiration, phonation, resonance, and articulation, but can be especially detrimental to voice, articulation and prosody (Duffy, 2013).

Changes in respiration. Changes in respiration are most often attributed to stiffening of

the respiratory musculature, resulting in reduced vital capacity and amplitude of chest wall movements, as well as irregular breathing patterns (Adams & Dykstra, 2009; Duffy, 2013; Gentil & Pollak, 1995). Numerous studies have found that the maximum sustained phonation of patients with PD was shorter than normal controls, though some studies did not find a significant difference between these groups (Adams & Dykstra, 2009; Canter, 1965; Duffy, 2013; Gentil & Pollak, 1995). Adams and Dykstra (2009) suggested several reasons for this inconsistency, including differences severity level, symptoms profile, testing procedures, and amount of practice the participants received from study to study. In addition to maximum sustained phonation, in his review of the literature Duffy (2013) found:

> …reduced airflow volume during vowel prolongation, fewer syllables per breath group, shorter utterance length, use of greater than average percentage of vital capacity per syllable, increased inspiratory duration during extemporaneous speech, and increased breath groups during reading have been documented in some patients with parkinsonisms and presumed hypokinetic dysarthria. (p. 175)

Reduced respiratory capacity and efficiency can have a direct effect on phonation and perceptual features that are a hallmark of HKD as associated with PD.

Changes in phonation. One of the most common perceptual features of PD is reduced loudness. The physical correlate of loudness, intensity, has been examined in many studies with varying results. According to Adams and Dykstra (2009), some studies found a decrease in average intensity to corroborate a perceived decrease in loudness while other studies did not support this conclusion. For example, Adams et al. (2006) found a decreased average intensity in conversational speech, sentence imitation, and maximum intensity. On the other hand, Canter (1965) found no significant difference in average sound pressure level (SPL) between

participants with PD and normal controls when they were instructed to repeat the syllable "no" at an "average" loudness level. Interestingly, participants with PD demonstrated significantly lower SPL for the "loud" and "shouted" conditions. In another study, Canter (1963) found no significant difference in mean peak SPL between participants with PD and normal controls during oral reading. In a study by Dromey (2003), participants with PD differed significantly from normal controls in the vowel phonation task but not in the reading or monologue task. In his review of the literature, Duffy (2013) stated that measures of intensity "generally document reduced vocal intensity" (p. 175). Clearly, there are confounding factors such as the definition of average intensity and the effects of speech task on SPL. It is also possible that intensity is not a perfect physical correlate of the perceptual feature loudness. Additionally, it must be considered that the variation in physical results from perceptual observations may be due to the unnaturalness of the task or the environment in which the data is collected.

Though it is not a typically noted perceptual change, many studies have reported a higher fundamental frequency in participants with PD than normal controls (Adams & Dykstra, 2009; Canter, 1963; Duffy, 2013; Dromey, 2003). Adams and Dykstra (2009) and Duffy (2013) in their reviews of HKD, also documented studies that found no change. Interestingly, Dromey (2003) found a significant difference in fundamental frequency between participants with PD and age-matched neurologically normal controls only during the monologue task and not during the vowel phonation or reading task. Overall, however, studies support the conclusion that patients with PD have a significantly higher F0 than normal controls but also that it may be task-specific.

Changes in voice. Changes in vocal quality is a prominent feature of HKD. Dromey (2003) found a higher perceptual rating of dysphonia in patients with PD than in neurologically normal age-matched controls. Dromey (2003) also found that phonatory function was perceived

as more impaired than articulation. In the same vein, Logemann, Fisher, Boshes, and Blonsky (1978) found that 89% of the PD patients in their sample were judged to have a laryngeal (voice) disorder, which was defined as any of the following: "breathiness, roughness, hoarseness, tremulousness, reduced pitch range, and a modal speaking pitch inappropriate to the patient's age and sex" (p. 49). Of the patients displaying a laryngeal dysfunction, 45% were judged to have a voice disorder in the absence of any articulatory deficit, while all but one patient with an articulation deficit was judged to have a co-occurring laryngeal dysfunction (Logemann et al., 1978). The vocal quality of patients with PD has often been described as breathy and harsh (Adams & Dykstra, 2009; Darley et al, 1969,). In the study by Logemann et al. (1978), 45% of the patients were perceived as hoarse, 29% as rough, and 15% as breathy. This discrepancy in perceptual judgement is likely due to the fact that the terms used to describe voice disorders are ill-defined and often vary from person to person and study to study. Acoustic characteristics that correlate with perceived vocal qualities have proved elusive. Some acoustic qualities that have been successfully ascribed to perceptual characteristics include the correlation between steeper spectral tilt and breathiness (de Krom, 1995), which has been observed in patients with PD (Dromey, 2003). Elevated signal-to noise ratios has been correlated to both breathiness and roughness (de Krom, 1995) and has been inconsistently noted in acoustic studies of patients with PD (Adams & Dykstra, 2009).

Changes in prosody. Prosodic abnormalities that have been noted in the PD population include monopitch, monoloudness, reduced stress, short phrases, variable rate, and short rushes of speech (Adams & Dykstra, 2009; Darley et al., 1969; Gentil & Pollak, 1995; Kent & Rosenbeck, 1982). Darkins, Fromkin, and Benson (1988) studied whether the aprosody noted in the speech of individuals with PD was the result of a language impairment rather than a motor

impairment by asking participants to differentiate between noun compounds (e.g. greenhouse) and noun phrases (e.g. green house) both receptively and expressively. The subjects with PD did not differentiate between the two categories expressively, failing to distinguish between the two categories in terms of pause or pitch. However, they did not differ from normal controls in terms of prosodic comprehension, suggesting that the prosodic abnormalities shown by patients with PD is the product of a disordered speech mechanism, rather than due to any kind of language impairment. Acceleration of speech rate is one of the features that distinguishes HKD from the other dysarthrias. Kent and Rosenbeck (1982) suggested that "the perception of 'short rushes of speech' or 'accelerated speech' might be based not so much on actual increases in the rate of articulatory events as on reductions in the range of articulatory movements" (p. 274). This was first posited by Netsell, Daniel, and Celesia (1975), who attributed this undershoot to muscle rigidity, stating, "The speaker might excite the rigid musculature with normally timed neural control signals for voluntary movements…only to have the speech articulators fail to reach the necessary position for production of a particular speech sound before beginning the movement for the following sound" (p. 170). Thus there appears to be an interplay between articulation and prosody. Prosodic abnormalities are considered one of the most characteristic features of HKD associated with PD.

Changes in articulation: **Consonants.** Indistinct articulation has long been noted as a feature of PD. Attempts to specify the acoustic and phonetic changes that lead to the perception has revealed a variety of factors. The most prominent changes have been noted in consonants. Logemann et al. (1978) studied the phonemes in error and concluded that place and manner of obstruent consonants was affected while voicing was not. Gentil and Pollak (1995) attributed articulatory consonant "blurring" to articulatory undershoot due to reduced excursion of the

articulators as a result of muscular rigidity that is an intrinsic feature of PD. This is supported by previous studies that have found that loss of phonemic identity is due to incomplete closure of the articulators (Ackerman & Ziegler, 1991; Darley et al., 1969). This is especially apparent in the spirantization of stops, where stop consonants are produced with increased frication (Adams & Dykstra, 2009; Canter, 1965; Kent & Rosenbeck, 1982; Logemann & Fisher, 1981). Logemann and Fisher (1981) found that the stop-plosives /k/ and /g/ were the most commonly misarticulated stop consonants, followed by /ʧ/ and /ʤ/, /p/ and /b/, and /t/ and /d/ respectively. Logemann et al. (1978) suggest that deterioration of speech and voice begins in the laryngeal area as hoarseness or breathiness and proceeds anteriorly, first affecting phonemes produced with the back of tongue, then anterior lingual placements and finally labial articulations. This progression is supported by Logemann and Fisher's (1981) later inventory of misarticulated phonemes with the exception of /t/ and /d/, which one would expect to be the third most commonly misarticulated pair. It is possible, however, that the teeth act as an additional barrier to mask the reduced degree of closure achieved at the alveolar ridge. Studies have also noted that fricatives have less frication energy as a result of less forceful or turbulent airflow, which also can be attributed to a reduced degree of closure (Adams & Dykstra, 2009; Logemann & Fisher, 1981). Changes in articulation can be attributed to more than just changes in manner. Forrest, Weismer, and Turner (1988) found that PD patients had a longer voice onset time (VOT) compared to normal elderly controls. VOT is the time between the burst, or initial opening of the articulators, of a voiced stop consonant and the onset of voicing. Changes in VOT can result in distortion of the target phoneme.

Changes in articulation: **Vowels.** Impairment of vowel articulation in hypokinetic dysarthria has not been widely studied and is generally judged to be less impaired than

consonants (Adams & Dykstra, 2009). Similar to the issues experienced in consonant articulation, it has been posited that vowel articulation may be impaired due to articulatory undershoot (Skodda, Visser, & Schlegel, 2011). A general reduction in vowel space associated with PD has been noted (Adams & Dykstra, 2009) though effects may be subtle and have not been consistently documented in all patients with PD. Various forms of vowel space have been used in an attempt to document this theorized reduction in vowel space with varying results (Sapir, Ramig, Spielman & Fox, 2010): vowel space metrics will be detailed further in Measuring Articulation: Vowel Space Area and Table 1 (see Appendix). Skodda et al. (2011) found a significant reduction in vowel space area in males with PD during sentence reading. Their study utilized triangular vowel space area (tVSA), calculated using the corner vowels /i/, /u/, and /ɑ/. Sapir et al. (2010) developed the formant centralization ratio (FCR), which also uses the corner vowel /i/, /u/, and /ɑ/. Their study found a significant reduction in FCR between participants with PD and age-matched normal controls; the study also found that FCR sensitively differentiated between dysarthric participants and healthy participants (Sapir et al., 2010). The variability between studies may be due to methodological differences, but it should also be considered that a metric that is sensitive enough to detect PD's subtle effects on vowel articulation has not yet been developed.

Most studies of vowel articulation have focused on the corner vowels /i/, /u/, and /ɑ/. Tjaden, Rivera, Wilding, and Turner (2005) examined changes in vowel space using the lax vowels /ɪ/, /ʊ/, and /ɛ/. The study found no difference between participants with PD and neurologically normal controls when reading at their habitual rate (Tjaden et al., 2005). This is not surprising considering these lax vowels require less tongue excursion than the corner vowels. Vowel space is not the only available measure of vowel articulation. Forrest et al. (1989) found

reduced formant transitions in segments /aɪ/, /ijə/ and /ɪl/, which can affect the intelligibility of speech.

Changes in intelligibility. Decreases in intelligibility have been commonly reported in PD (Anand & Stepp, 2015; Cannito, Suiter, Beverly, Chorna, Wolf, & Pfeiffer, 2012; Cannito, Suiter, Wolf, Chorna, Beverly, & Watkins, 2008; Duffy, 2013; Neel, 2009). According to a 10-year review of patients with PD by Duffy (2013) at the Mayo Clinic, 79% of patients had reduced intelligibility. Intelligibility has been found to worsen with the progression of PD (Anand & Stepp, 2015). The various speech deficits associated with PD impact intelligibility to varying degrees, making it difficult to determine exactly what element would best be targeted by therapeutic intervention. Anand and Stepp (2015) investigated the effect of monopitch on intelligibility. They found that the impact of monopitch on intelligibility was variable, with a greater impact on participants with moderate dysarthria than mild or severe dysarthria. Reduced loudness is a common complaint in PD, and many successful therapeutic interventions focus on increasing loudness. Neel (2009) investigated whether simply increasing the intensity of the speech signal without any other acoustic changes was as effective as loud speech. She found that amplified speech was significantly more intelligible than habitual speech; however loud speech, which is accompanied by other acoustic changes to the voice, was more intelligible than amplified speech.

Changes in vowel space area have also been implicated in changes in intelligibility. According to Weismer, Jeng, Laures, Kent, and Kent (2001), "The direction of the acoustic vowel space effect is logical because a relatively compressed space would suggest reduced acoustic contrast among vowels, with a loss in word distinctiveness in either single words or sentences" (p. 17). In their study of vowel space and intelligibility in participants with

amyotrophic lateral sclerosis (ALS) and PD, Weismer et al. (2001) found that acoustic vowel space was highly correlated with single word and sentence intelligibility. However, in the same study, Weismer et al. found that participants with ALS had a smaller vowel space but greater intelligibility at sentence level compared to participants with PD, suggesting that there is more than vowel space at play. According to a review of the literature by Kim, Hasegawa-Johnson, and Perlman (2010), the strength of the relationship between vowel space area and intelligibility has ranged from 0 to 71% across studies of different speech impairments. Neel (2008) found that vowel space area accounted for 9 to 12% of the variance in intelligibility in normal speakers. In their study of children with dysarthria, Higgins and Hodge (2002) found that vowel space area accounted for 53% of variance in single words and 41% of variance in sentences. Turner, Tjaden, and Weismer (1995) found that vowel space area accounted for 45% of variance in intelligibility in speakers with ALS. The effect of vowel space area on intelligibility in speakers with PD has also been investigated with vowel space area accounting for 6 to 46% of intelligibility (Tjaden & Wilding, 2004; Weismer, et al., 2001). In a study by McRae, Tjaden, and Schoonings (2002), vowel space area accounted for 13% of variance in perception of severity, with smaller vowel space area being associated with a greater perception of severity. These varying results suggest that vowel space area, like other aspects of speech, plays a role in intelligibility but is not the sole, or even most important component. Turner, Tjaden, and Wilding (1995) suggest that perhaps vowel space area is more predictive of intelligibility in patients who are less than 70% intelligible, which may explain why the role of vowel space area varies between conditions and individuals. Intelligibility is a complex, multifactorial feature and contributing factors should be considered individually for each individual.

Treatments for Dysarthria Associated with Parkinson's Disease

There are a variety of treatment options available for patients with PD suffering from speech and voice disorders. According to Trail et al. (2005), "Current treatments for speech and voice disorders in people with PD consist of medical therapies, surgical procedures, behavioral speech therapy, or a combination thereof" (p. 208). Medical and surgical interventions alone have been shown to have a limited effect on voice (Fox, Morrison, Ramig, & Sapir, 2002; Ramig, Fox, & Sapir, 2004; Trail et al., 2005; Yorkston & Beukelman, 2010). Trail et al. (2005) concluded in their review of current speech treatments for PD that "At this time, a combination of medical therapy (e.g., optimal medication) with behavioral speech therapy appears to offer the greatest improvement for speech dysfunction" (p. 208). The following paragraphs provide a brief review of medical, surgical, and behavioral interventions for speech disorders associated with PD.

Medical treatments. One of the most common medical treatments for PD is the use of levodopa, which helps boost dopamine levels in the brain. Though it has been shown to have positive effects for limb movement and function, it has a less significant effect on speech (Trail et al., 2005). Biary, Pimental and Langenberg's study (as cited in Trail et al., 2005) found that the use of clonazepam improved some aspects of speech including short rushes of speech, imprecise consonant and inappropriate silences. However, their study showed little improvement in voice quality or low pitch. Though medical treatments have some utility in improving speech and voice, medication alone is not effective.

Surgical treatments. Various surgical treatments have been used in the treatment of speech and voice disorders associated with PD. Pallidotomy and thalamotomy are two common surgical procedures that have been historically used to treat the motor symptoms of PD. They

typically have no effect on speech or can actually lead to a decline in speech function (Farrell, Theodoros, Ward, Hall, & Silburn, 2005; Tarazi, Sahli, Wolny, & Mousa, 2014; Trail et al., 2005). The use of deep brain stimulation has been shown to improve motor symptoms but not speech and is often associated with worsening intelligibility (Tarazi et al., 2014; Trail et al., 2005). Collagen injection in the vocal folds temporarily improves hypophonia but has no effect on any other aspect of speech (Trail et al., 2005). Overall, surgical treatment is most effective for the motor symptoms of PD and is not meant to be a speech intervention.

Behavioral therapy. Of all the intervention techniques, behavioral therapy has shown the most promise in treating speech and voice disorders associated with PD. According to Adams and Dykstra (2009), the main points of focus of behavioral therapy are "(1) increasing speech intensity, (2) improving speech prosody (i.e., monotonous/monoloud speech), (3) reducing rapid speech, and (4) increasing articulatory mobility and precision" (p. 174). A variety of strategies have been used to achieve these goals. Ramig, Countryman, Thompson, and Horii (1995) studied the effect of increasing respiratory effort on reducing hypophonia. Increase respiratory effort was targeted using maximum inhalation and exhalation tasks, maximum duration of voiceless continuants /s/ and /f/ and sustained intraoral pressure. The participants showed improvements in some aspects of speech such as SPL during reading and perceptual self-ratings of loudness in females, and pause duration during reading for male and female participants. Dromey (2000) compared the effect of increasing vocal loudness versus hyperarticulation on lip kinematics in patients with PD. His study found that both methods were effective in increasing lip displacements, intensity, and lip velocity, though the loudness therapy showed a greater increase in loudness and hyperarticulation therapy showed a greater increase in oral movements.

Biofeedback and prosthetic devices. Biofeedback can be used during behavioral therapy to provide the patient with information about pitch variation, speech loudness, and speech rate. Adams and Dykstra (2009) in their review of the use of biofeedback as part of behavioral therapy concluded that

> (1) improvement in the speech of PD patients can be achieved through biofeedback therapy, (2) these improvements can be measured in the clinical setting through the use of both perceptual and acoustic procedures, and (3) improvements achieved through behavioral therapy plus biofeedback are greater than improvements achieved with behavioral therapy alone. (p. 176)

They also concluded that little carryover occurs with the use of biofeedback, though it should be noted that there are currently few studies evaluating carryover following therapy using biofeedback.

The use of prosthetic devices in aiding carryover has been sparsely studied for patients with PD. Adams and Dykstra (2009) suggest the use of a voice-activated masker to provide background noise for patients with hypophonia. Though this has not been studied, it is supported by a study by Adams et al. (2006) that found that patients with PD increase their loudness to compensate for background noise. Other devices that have been shown to have some long-term success include the use of delayed auditory feedback (DAF), voice amplification devices, and pacing boards (Trail et al., 2005). Pacing strategies such as pacing boards or finger tapping have been shown to slow rate while DAF has been shown to slow rate and improve intelligibility (Adams & Dykstra, 2009).

Lee Silverman Voice Treatment (LSVT-LOUD®). LSVT is currently considered the gold standard of behavioral treatment for HKD associated with PD and has been intensively

studied over the last two decades. According to Fox et al. (2002), LSVT hinges on five concepts:

> (a) exclusive focus on voice (specifically vocal loudness), (b) stimulation of high-effort productions with multiple repetitions, (c) intensive delivery of treatment (4 individual sessions a week for 4 weeks, 16 sessions in one month), (d) enhancing sensory awareness of increased vocal loudness and effort (calibration), and (e) quantification of behaviors. (p. 112)

Though pitch variability is also targeted, the primary therapeutic target is increased vocal loudness, which, according to Trail et al. (2005), "acts as a 'trigger' to increase vocal effort and coordination across the speech production system" (p. 213). The program consists of intensive treatment for 50 to 60 min four times per week for one month. Tasks completed during therapy include maximum sustained vowel phonation with a constant level of loudness and steadiness, and pitch exercises, including having the patient modulate their voice from their habitual pitch to their highest pitch as well as their habitual to lowest pitch. Daily homework is also an important aspect of the program. Though LSVT was designed for and is primarily used with PD, its use has been studied with other populations such as adults with ataxic dysarthria (Sapir et al., 2003), parkinsonian plus syndromes (Countryman, Ramig, & Pawlas, 1994), multiple sclerosis, aging voices, cerebellar ataxia (Fox, Ramig, Ciucci, Sapir, McFarland, & Farley, 2006) and children with cerebral palsy and Down syndrome (Fox et al., 2006).

Therapeutic Changes Through LSVT

LSVT has been reported to produce global changes in speech and voice, meaning that the therapeutic targets have been shown to produce changes outside of the intended effects. Though LSVT targets both increased loudness and pitch variability, increased loudness has been

implicated as the primary impetus for changes in non-targeted areas. Changes have been noted in the areas of phonation, articulation, and prosody. Some phonatory changes include improvements in SPL, voice quality, and vocal fold function, while articulatory improvements have largely been supported by increased vowel space. Increased facial expression and improved intonation have also been noted (Fox et al., 2002; Fox et al., 2006). In addition to communicative function, LSVT has also been shown to improve swallowing in dysphagic patients (Fox et al., 2002; Fox et al., 2006).

How this carryover into various other oral and laryngeal functions takes place is not well understood. In their paper outlining the LSVT approach and presenting preliminary efficacy data, Ramig, Bonitati, Lemke, and Horii (1994) stated that "Therapy techniques were designed to improve perceptual characteristics of voice by targeting the hypothesized underlying physical pathology" (p. 193). Fox et al. (2002) expands on this concluding:

> …LSVT may affect speech production at two levels. (a) Increased loudness can improve vocal fold closure and enhance the phonatory source, consistent with improving the carrier in the classic engineering concept of signal transmission...(b) Increased loudness may stimulate increased effort and coordination across the respiratory, laryngeal, and orofacial systems. (p. 114)

The surprisingly widespread effects of this singular target have been the subject of a variety of studies exploring the effects of LSVT on respiration, phonation, articulation, intelligibility and prosody.

Changes in respiration. Improvements in respiration to support speech have been documented in various studies. Though studies have not shown an increase in vital capacity, several studies have shown an increase in the duration of vowel phonation from pre to post

LSVT (Ramig et al., 1994; Ramig et al., 1995). This suggests improved control over and more efficient use of air flow following treatment. This is supported by Ramig and Dromey's (1996) study, which found increased subglottal air pressure and improved maximum flow declination rate. Respiratory improvements provide a foundation for improved phonation.

Changes in phonation. Various changes have been noted in patients with HKD following treatment with LSVT including changes in SPL, fundamental frequency, and voice quality. Increased loudness (of which SPL is the acoustic dimension) has been moderately supported both perceptually and acoustically. Studies of perceptual ratings of loudness are not consistent with one another but overall suggest an improvement in loudness. Ramig et al. (1994) found that participants rated themselves as having a significant increase in loudness while ratings by family members did not show a significant improvement in loudness. Both familiar and unfamiliar clinicians, however, rated participants as having significantly improved loudness. In contrast, Ramig et al. (1995) found only male participants rated themselves as having improved in loudness, while in an assessment completed by the family, both male and female participants were rated as having improved loudness. Acoustic studies have shown increased SPL as measured in decibels (dB) across tasks including sustained vowel phonation (Cannito et al., 2012; Ramig et al., 1995), reading and conversation (Ramig et al., 1995). The difference between perceptual increases in loudness versus acoustic increases in intensity may at first cast doubt on whether the measured acoustic changes reach beyond statistical significance into clinical significance. However, this issue echoes the ambiguous results of studies into decreased loudness/intensity in patients with PD discussed previously (see Hypokinetic Dysarthria and PD: Changes in Phonation), reinforcing the idea that perception of loudness is a multifaceted issue and may be confounded with other acoustic factors besides intensity. The subjective nature of

loudness ratings may also play a part in these variable results.

Fundamental frequency has also shown improvement over the course of treatment, both in terms of mean and habitual fundamental frequency as well as fundamental frequency variability and range. Ramig et al. (1994) found that participants showed improved mean fundamental frequency only during reading, while a study by Ramig et al. (1995) found increased habitual fundamental frequency across all tasks, including sustained phonation, reading, and monologue. Ramig et al. (1994) also noted an increase in maximum fundamental frequency range as was as fundamental frequency variability during reading. This was supported by a later study by Ramig et al. (1995) that also showed increased variability during reading and monologue.

Voice quality, a prominent feature in patients with PD, has been examined both perceptually and acoustically before and after treatment. Ramig et al. (1995) found an improvement in self-ratings of hoarseness in participants following treatment. Cannito et al. (2006) examined the acoustic correlates of voice quality and observed changes from pre to post therapy. Their study found a decrease in harmonic amplitude differences as a result of an increase in the second harmonic (H2), first formant (F1), second formant (F2), and third formant (F3). Energy in the upper harmonics, which was reduced prior to treatment, increased. Taken together, these results indicate an improvement in spectral tilt (i.e., reduced tilt), supporting a perceptual decrease in breathiness. This is supported by visualization of improved true vocal fold closure seen on videostroboscopy (Smith, Ramig, Dromey, Perez, & Samandari, 1994).

Changes in intelligibility. Of practical interest are changes in intelligibility that take place in the course of treatment. Subjective results include ratings of intelligibility by the participant, the participant's family and the clinician. Though results of individual studies have

varied, evidence suggests a significant increase in intelligibility as judged by family members, familiar and unfamiliar clinicians, and the participants themselves (Ramig et al., 1994; Ramig et al., 1995). Objective measures of intelligibility have also been utilized. In a study of a single speaker, Cannito et al. (2008) found a statistically significant increase in the percentage of words understood by unfamiliar listeners from pre to post LSVT. This study was later replicated by Cannito et al. (2012) with a larger group of participants; six out of the eight participants demonstrated statistically significant improvements in intelligibility as measured using percentage of understood words. These results are especially noteworthy since both studies by Cannito et al. (2008) and Cannito et al. (2012) are somewhat biased against improved intelligibility because of the introduction of pink noise during listening task.

Intrinsically connected to intelligibility is articulation. Improvements in articulation have been observed using acoustic measures, including improved formant transition duration, rate, and extent as well as increased vowel space (Fox et al., 2002; Fox et al., 2006). Increased amplitude of movement of the articulators has also been noted (Ramig et al., 2004). Vowel articulation has been of particular interest in the literature. Increased vowel space has been implicated as an indicator of increased tongue movement and thus improved articulation. Sapir et al. (2010) analyzed changes in vowel space using the vowel articulation index (VAI), logarithmically scaled vowel space area (lnVSA), formant centralization ratio (FCR) and the ratio of the second formant of /i/ to the second formant of /u/ (F2i/F2u). In their study, they found that all measures showed significant improvement over the course of treatment, but FCR and F2i/F2u showed the most significant changes. The next section explores the different kinds of vowel space area metrics and their implication for articulation.

Measuring Articulation: Vowel Space Area

There are many different ways to measure vowel articulation, each with benefits and drawbacks. One common way of measuring improvements in vowel articulation is area of the vowel space. Vowel space maps the geometric space created by the first and second formant (F1 and F2, respectively) in different vowels. F1 and F2 are related to tongue placement, with F1 decreasing as tongue height increases and F2 increasing as tongue advancement increases. Measures of vowel space commonly use the corner vowels /i/, /u/, /ɑ/ and /æ/, which theoretically encompass F1 and F2 extremes. Vowel space in dysarthric patients has been measured in a variety of ways, including triangular vowel space area (tVSA) (Sapir et al., 2010; Skodda et al., 2011), the area of the vowel quadrilateral (Higgins & Hodge, 2002), vowel articulation index (VAI) (Skodda et al., 2011), the formant centralization ratio (FCR) (Sapir et al., 2010) and the Tjaden method (McRae et al., 2002; Tjaden & Wilding, 2004). Each of these methods varies in which vowels and formants they utilize, as well as their efficacy in measuring changes in vowel articulation in patients with PD (see Table 1 in Appendix for details).

Skodda et al. (2011) found that VAI was better suited to detect impaired vowel articulation in the PD population than tVSA. Sapir et al. (2010) created the formant centralization ratio (FCR) to measure changes in vowels articulation specifically for the PD population. In their study, FCR was found to differentiate between dysarthric and healthy speech more successfully in comparison with other measures of vowel space, including VSA and lnVSA. VAI and FCR, developed independently, are in fact inverses of each other and therefore can be considered identical. This fact is supported by the similar results reported by Skodda et al. (2011) and Sapir et al. (2010) that show that VAI and FCR are better suited to detect vowel articulation impairment in individual with PD.

In their study of intelligibility in normal speakers, Bradlow, Torretta, and Pisoni (1996) found that although tVSA was larger in the most intelligible speaker versus the least intelligible speaker, there was no correlation between tVSA and intelligibility. Rather, they found that vowel space dispersion (VSD) showed moderate correlation with intelligibility, suggesting that VSD may be a more reliable measure of intelligibility than tVSA. VSD is derived by first calculating the center point in the vowel space by averaging all tokens of F1 ($F1_{avg}$) and all tokens of F2 ($F2_{avg}$) such that the center point equals ($F2_{avg,}$ $F1_{avg}$). The vector length (the distance from the vowel to the midpoint) is then calculated, and these distances are averaged together to obtain an overall VSD. Karlsson and van Doorn (2012) proposed a similar metric, vowel formant dispersion (VFD). VFD utilizes a weighted midpoint, and the resulting distances are not averaged into a single metric. Rather, the distances of each vowel are plotted and considered individually, making this a descriptive if somewhat unwieldy metric. In contrast to many other vowel space metrics, VSD and VFD can be adapted to consider vowels besides the corner vowels /i/, /u/, /ɑ/ and /æ/, allowing for a more complete picture of the vowel space. Though these metrics have not been well-studied in disordered populations, they appear worth considering the richness of the data they can potentially yield.

In addition to varied ways of measuring vowel space, various materials have been used to elicit vowels for analysis. Materials commonly used in previous literature include read sentences (Cannito et al., 2006; Sapir et al., 2007; Sapir et al., 2010), read narrative passages (McRae et al, 2002; Tjaden & Wilding, 2004) and single words in isolation (Higgins & Hodge, 2002). Connected speech yields more naturalistic results than sustained phonation or single words and is thus more desirable for drawing conclusions that can be safely generalized. However, monologue and conversation are problematic as they do not provide for consistent phonetic

context and are prone to prosodic variations that make them difficult to analyze. Read passages and sentences provide a compromise between consistency and utility. Sentences and passages are still subject to prosodic variation, but uniformity between participants is more likely since all participants read the same material.

Though vowel space area has been used in previous studies to draw conclusions about changes in articulation following LSVT, there are variety of factors that require further exploration. It has been hypothesized that changes in vowel articulation can be attributed to improvements tongue placement, particularly in amplitude of movement. Vowel space has typically been attributed to changes in articulation, but phonatory factors may interact with formant determination such that changes in phonation and articulation are confounded. Since there are well-reported changes in vocal quality following LSVT, this is a potentially important consideration. The remainder of this chapter will review these issues in more detail by grouping them in two areas of consideration: phonatory factors and challenges of formant measurement.

Phonatory Factors and Vowel Articulation

First there is the interaction between phonatory factors and vowel articulation. In a study involving patients with idiopathic Parkinson's disease, Neel (2009) found that amplified dysarthric speech was more intelligible than unamplified dysarthric speech, suggesting that the articulated target was close enough to the correct category to be recognized when the speech signal was amplified. She also found that loud speech was more intelligible than amplified speech, suggesting that there are factors intrinsic to loud speech other than increased amplitude. While improved tongue placement has been a commonly suggested factor, Neel also proposed that decreased spectral tilt during the loud condition contributed to improved articulation. Steep spectral tilt has long been associated with breathy vocal quality (Hanson, 1997), a common

feature of parkinsonian voice and hypokinetic dysarthria (HKD). A decrease in spectral tilt—that is, a return to a more typical spectral configuration—indicates an improvement in the contribution of voice to intelligibility with no particular effect on tongue placement.

Changes in bandwidth could also account for improvement in the perception of vowel quality. Breathy vocal quality is associated with increased bandwidth (Hixon, Weismer, & Hoit, 2008). According to Hixon et al. (2008), "When speech synthesizers are used to systematically increase the bandwidth of vowel formants while maintaining constant formant frequencies, listeners do not hear a change in vowel category. Rather, vowels are perceived as increasingly 'muffled'" (p. 379). This calls into question precisely what perceptual studies of vowel articulation are measuring. In their study, Sapir et al. (2007) rated changes in "vowel goodness" from pre to post LSVT in patients with idiopathic Parkinson's disease, where "vowel goodness" was defined as "how well an uttered vowel is judged as an exceptionally good instance, or best exemplar, of an intended vowel" (p. 902). Though patients who underwent LSVT showed improvements in "vowel goodness," this metric failed to differentiate between changes in vowel category and vowel quality due to improvements in vocal quality (i.e., reduced breathiness).

Challenges of Formant Measurement

Since most measures of vowel articulation rely on formants, methods of formant measurement are another challenge which must be considered. Many studies use linear predictive coding (LPC) to extract formant frequencies, which can be prone to error given certain conditions. According to Vallabha and Tuller (2000), large bandwidth can cause errors in root-solving, which is integral to LPC's estimation of formants. This is a particular concern for analyzing breathy voices, a hallmark of HKD. Large bandwidth can also cause problems when formants are close together such as in high front vowels (where F2 is high and close to F3) and

low back vowels (where F1 is high and close to F2). This could be problematic for vowel space measures, since most rely on the corner vowels /i/ (high front) and/or /ɑ/ (low back).

The filter order is also important to consider in LPC. Many studies utilize a standardized choice of filter order, which may not be appropriate for all voices or all vowels. For example, back vowels, such as /u/ and /ɑ/ often need a higher order filter than front vowels (Vallabha & Tuller, 2000). Since both of these vowels are often used in calculating VSA, incorrect estimation of their formant frequencies can cause over- or under-estimation of VSA. An inappropriately high filter order can cause the appearance of false formants, while an inappropriately low filter order can smooth the spectrum, causing two formants to merge, creating a false formant that is in fact the average of two formants. According to Vallabha and Tuller (2000), it may be necessary to choose a different filter order for each person and each vowel, using the visual of the spectrum to determine the appropriateness of the filter order.

Finally, the basic assumptions of LPC are violated in breathy voices. LPC models assume resonances only and not anti-resonances (Kent & Read, 2002). Anti-resonances are created by a resonator off the main resonator (as in a nasal such as /n/) or behind the source. In breathy voices, the incomplete closure of the vocal folds results in an additional resonator: the subglottal space. This introduces anti-resonances into the voice. Such a violation calls into question the validity of LPC in breathy voices, and it also introduces an increase in the bandwidth of F1 (Hanson, 1997).

In an effort to address these issues, four formant measurement methods were used to understand if and to what degree these different methods are affected by phonatory qualities. These methods were LPC with a fixed coefficient (LPCf), cepstrally-liftered spectrum (ceps), cepstrally-liftered spectrum employing the Story-Bunton algorithm (S-B) (Story & Bunton,

2015) and human-guided interactive mode (HGIM). HGIM utilized the spectrum, the LPC adjusted to conform to the spectrum, and a wide-band view of the spectrogram to locate the center of F1 and F2. A variety of methods were used to compute vowel space, including: VAI (Skodda et al., 2011), F2i/F2u (Sapir et al., 2007; Sapir et al., 2010), VFD (Karlsson & van Doorn, 2012) calculated using the corner vowels (VFDc) and VFD calculated using corner and lax vowels /i/, /u/, /ʌ/, /ɛ/, /æ/, and /ɑ/ (VFDa). The cepstrally-liftered spectrum was of interest since it theoretically separates the source from the filter, therefore eliminating phonatory effects on the formant measures (Story & Bunton, 2015). Formants extracted using LPCf, ceps, S-B and HGIM were used to compute each vowel space.

The primary research question of this thesis addresses the possibility that observed increases in vowel space area associated with LSVT therapy are confounded with the known improvements in phonatory quality. As a working hypothesis, it is presumed that LSVT does result in an increase in vowel space. This was assessed using a number of methods to explore whether this increase is artefactual. Results from the LPCf and spectrum smoothed by cepstral liftering were compared to HGIM. If LPC were vulnerable to phonatory factors, then the LPC based formant values are expected to be more variable across samples particularly in the pre sessions when phonation is less robust. The formants extracted using the ceps and S-B are expected to be closer to the HGIM because the confounding effects of the harmonics have been removed. Vowel space areas resulting from each method were inspected for purported increase effects post treatment.

Secondarily, this thesis explored a variety of vowel space area metrics. VAI and F2i/F2u were used in the interest of replicating previous studies of changes in vowel space following LSVT. Since VAI and FCR are essentially identical, VAI was chosen because of its more

common appearance in the literature than FCR. VFDc and VFDa were included because of their ability to track changes in individual vowels and incorporation of multiple tokens of the same vowel. VFDa in particular was used to observe how lax vowels are affected by LSVT, which has not been studied.

Method

Participants

These data were obtained from a data set that was recorded in a larger study for the Michael J. Fox Foundation for Parkinson's Research. The first 10 subjects in sequence were used for this study. Participants (age range 45-80 years) diagnosed with IPD and moderate to severe hypophonia were recruited. Diagnosis was determined by a neurologist. Efforts were made to recruit an equal number of male and female participants. Efforts were made to distribute patients ethnically and racially in a distribution that is consistent with the demographics of the Memphis area (62% African American or black, 34% white, 2% Asian, 1% American Indian/Alaska Native, remaining 1% other race or races; 97% not Hispanic, 3% Hispanic). Participants were optimally medicated. All participants were evaluated using the Hoehn and Yahr Scale (1967) and the Unified Parkinson Disease Rating Scale (UPDRS). As part of the measures for the larger study, other screening measures that were carried out included a hearing screening, Edinburgh handedness inventory (Oldfield, 1971), mini-mental status examination (Folstein, Folstein, & McHugh, 1975), and Beck Depression Inventory (Steer, Beck, & Garrison, 1986). Only participants with no or mild cognitive impairment or depression were included. All participants underwent an ENT screening and vocal fold examination; participants with evidence of structural abnormalities or vocal fold hyperfunction were excluded. See Table 2 in Appendix for a complete list of exclusion criteria.

Treatment

All participants received LSVT for one hour, four times per week for four weeks. Face-to-face therapy was administered by a speech language pathologist licensed by the American Speech-Language Hearing Association (ASHA) and certified in LSVT. During the first week, therapy consisted of four face-to-face sessions. During the second, third, and fourth weeks, the participants completed two of the four therapy days per week using the LSVT Companion. Therapy supported by the LSVT Companion has been found yield similar results as traditional face-to-face therapy (Halpern et al., 2012). It should be noted that some participants also received transcranial magnetic stimulation (TMS) as part of a larger study studying the effect of pairing TMS with LSVT.

Procedures and Data Collection

Recording sessions were conducted on six different days. Two took place before treatment (PRE1 and PRE2), two took place after treatment was completed (POST1 and POST2) and two were completed three months after the conclusion of therapy (FU1 and FU2). The two sessions for the pre-, post-, and follow-up conditions took place within a week of each other. As part of a larger assessment protocol, carrier phrases ("Say ___ again") were used in accordance with previous studies of acoustic features (Cannito et al., 2006, Hanson, 1997). The CVC syllables /bVd/, /gVd/, /dVd/, and /wVd/ were used with the vowels /i/, /u/, /ʌ/, /ɛ/, /æ/, and /ɑ/ and each carrier phrase was repeated four times.

Participants were instructed verbally and provided with written phrases. All words were read to them prior to recording in order to ensure correct pronunciation. If the participant mispronounced a word during recording, the word was repeated for them. All recordings were made in a sound booth using a Countryman E6 Earset with an elongated boom to permit 7 cm

mic to mouth distance calibrated for a flattened response. Recordings were digitized at a sampling rate of 50 kHz[1] using Kay Pentax Computer Speech Laboratory (CSL Model 4500). The intensity of the speech signals was measured and recorded using a Radio Shack sound level meter (Catalog no. 33-2055) at 30 cm.

Data Analysis

Only the /b/ tokens were considered in this study. The selection of only one phonetic context was justified by the fact that phonetic context has not been shown to impact vowel formants (Schouten & Pols, 1979). The /b/ tokens were chosen in order to minimize potential coarticulation effects. The first two correctly pronounced tokens of each vowel were used for analysis. This was to minimize the effects of fatigue due to repetition and provide the "best exemplars" of each token. Data from PRE1, PRE2, POST1, and POST2 were analyzed to get a richer sample of variation over time. Data was analyzed using a customized version of the software program TF-32 (Milenkovic, 2016). A zoom level of approximately 500 ms and a bandwidth of 400 Hz was used to optimize formant visualization. Given the dialectical variation of some participants, the portion of the vowel that best represented the target vowel was determined auditorily. For example, diphthongization, a common feature of Southern English, renders some productions of /bɛd/ as /bejɛd/. Therefore, only the portion which matches the target vowel auditorily were used. In cases where no auditory difference could be determined

[1]One session (POST1 for Subject 1) was found to be recorded at a sampling rate of 44 kHz.

due to the brevity of the segment or insufficiently dramatic formant shifts, the portion where the location of the formants best represented the theoretical expectations of the target vowel was chosen. For example, the steady state where F1 and F2 were the lowest would have been selected for the target vowel /u/. F1 and F2 were determined using four methods: HGIM, LPCf, ceps, and S-B. The coefficient for LPC was left at the setting recommended by TF-32 in order to

replicate previous studies.

The formants were used to compute the area of the vowel quadrilateral (Higgins & Hodge, 2002), F2i/F2u (Sapir et al., 2007; Sapir et al., 2010), VAI (Skodda et al., 2011), VFDc, and VFDa, based on VFD by Karlsson and van Doorn (2012). These measures, with the exception of VFDa and VFDc, have been chosen in order to compare the results of this study with previous studies. VFDa and VFDc were included to determine changes in individual vowels and to assess the appropriateness of these metrics in dysarthric speech, which has not yet been explored.

Results

Before proceeding to presentation of results, this section begins with a review of the study purposes in terms of measurement strategies and vowel space metrics. The research questions of this study involved an attempt to replicate the study by Sapir et al. (2010), which showed an increase in vowel space from pre to post LSVT. Human-guided interactive mode (HGIM) was used as the gold standard of this study against which the validity of other formant measurement approaches could be assessed. Considering the possibility that measurement issues conspired with phonatory factors to create a confound for Sapir et al.'s methods, LPC with a fixed coefficient (LPCf) was used as a basis of comparison. Minor adjustments to the LPC coefficient were made by Sapir et al. (J. Spielman, personal communication, June 1, 2016); however, of the formant measurement methods employed in this study, LPCf afforded the best opportunity to assess the phonatory confound question and most closely approximated the methods of Sapir et al. The cepstrally-liftered spectrum methods, ceps and S-B, were intended as exploratory measures to assess the appropriateness of these methods for use with dysarthric adult speakers since previous applications have only been with young children or modeled data (Story

& Bunton, 2015, Story & Bunton, 2015, May).

A variety of vowel space metrics were considered as well. The vowel articulation index (VAI) and F2i/F2u were selected for comparison with Sapir et al.'s (2010) previous study. Though that study used the formant centralization ratio (FCR), VAI (simply the inverse of FCR) was deemed an equivalent metric and is more commonly found in subsequent literature concerning vowel space assessments in the PD population (Rusz et al., 2013; Spielman et al., 2011). The area of the vowel quadrilateral (Higgins & Hodge, 2012) was selected as a standard measure of VSA and because of its inclusion of all four corner vowels, /i/, /u/, /æ/, and /ɑ/. The vowel formant dispersion (VFD) (Karlsson & van Doorn, 2012) calculated using the four corner vowels /i/, /u/, /æ/, and /ɑ/ (VFDc) was examined for its ability to incorporate multiple tokens of each vowel. Similarly, VFD (Karlsson & van Doorn, 2012) calculated using /i/, /u/, /ʌ/, /ɛ/, /æ/, and /ɑ/ (VFDa) was examined for its ability to incorporate multiple tokens of each vowel as while as its use of a wider variety of vowels. Vector lengths had not typically been combined into a single metric by the developers of this method (F. Karlsson, personal communication, May 31, 2016), therefore, VFDc and VFDa were utilized in two ways. First, the average vector length of all the vowels was calculated to determine whether the average vector length increased from pre to post treatment. Secondly, the vector lengths of the individual vowels were compared pre to post treatment to determine if there were any changes in the individual vowels.

Reliability of formant measures was assessed by having another rater reanalyze 20% of the formant measures for all formant measurement methods (HGIM, LPCf, ceps, and S-B). An attempt was made to distribute the reanalyzed samples evenly across participants, pre or post sessions, and vowels. Highest priority was given to distribution across participants. Distribution across pre and post sessions was the second consideration. Distribution across vowels was given

the lowest priority. A Pearson product moment correlation was performed on all data. For HGIM, the correlation coefficient was 0.93 for F1 and 0.96 for F2. For LPCf, the correlation coefficient 0.93 for F1 and 0.90 for F2. For ceps, the correlation coefficient was 0.80 for F1 and 0.94 for F2. For S-B, the correlation coefficient was 0.89 for F1 and 0.96 for F2. The average difference between raters was computed by calculating the difference between each formant measure and averaging the differences. For HGIM, the average difference was -20.88 Hz for F1 and -15.70 Hz for F2. For LPCf, the average difference was 5.70 Hz for F1 and -3.18 Hz for F2. For ceps, the average difference was 6.21 Hz for F1 and -56.50 Hz for F2. For S-B, the average difference was 2.49 Hz for F1 and -45.18 Hz for F2. The standard error of these differences was computed for all data. For HGIM, the standard error was 5.95 Hz for F1 and 13.16 Hz for F2. For LPCf, the standard error was 5.28 Hz for F1 and 21.85 Hz for F2. For ceps, the standard error was 9.37 Hz for F1 and 17.53 Hz for F2. For S-B, the standard error was 7.22 Hz for F1 and 14.12 Hz for F2. Reliability measure results are summarized in Table 3 in Appendix.

Repeated measures analysis might have been appropriate for a larger number of observations (as cited in Sapir et al. 2010); however, due to the size of the available pool for this study, the VSA metrics yielded only 10 observations per session. Visual inspection revealed high variability across trials, regardless of formant measurement method, and treatment effects were not substantially greater than trial variability. It appeared, therefore, that statistical analysis was inappropriate for this data set so results will currently be examined graphically and numerically. Figures1 through 5 in Appendix show trial and treatment results, with each numerated figure depicting the results from one vowel space metric. Within each numerated figure, each lettered set represents a given formant measurement method. Three graphs appear within each of these sets: PRE1 to PRE2 differences, POST1 to POST2 differences, and

treatment effects depicted as the differences between pre and post averages.

Graphical Presentation of Findings

VAI. VAI, utilized by Sapir et al. (2010), was calculated using the formant measurement methods HGIM, LPCf, ceps, and S-B. The graphical results by subject are presented in Figure 1a through 1d in Appendix, with the lettered set representing the different formant measurement methods. Visual inspection across treatment revealed no consistent increase or decrease in VAI. By visual inspection of the data, treatment effects did not appear to be any larger than trial-to-trial variability. Individual increases or decreases across treatment did not appear to exceed increases or decreases across trials.

F2i/F2u. F2i/F2u, utilized by Sapir et al. (2010), was calculated using the formant measurement methods HGIM, LPCf, ceps, and S-B. The graphical results by subject are presented in Figure 2a through 2d in Appendix, with the lettered set representing the different formant measurement methods. Visual inspection across treatment revealed no consistent increase or decrease in F2i/F2u. By visual inspection of the data, treatment effects did not appear to be any larger than trial-to-trial variability. Individual increases or decreases across treatment did not appear to exceed increases or decreases across trials.

Area of the vowel quadrilateral. The area of the vowel quadrilateral, which includes the four corner vowels /i/, /u/, /æ/, and /ɑ/, was calculated using the formant measurement methods HGIM, LPCf, ceps, and S-B. The graphical results by subject are presented in Figure 3a through 3d in Appendix, with the lettered set representing the different formant measurement methods. Visual inspection revealed no general trend of increase or decrease across treatment. By visual inspection of the data, treatment effects did not appear to be any larger than trial-to-trial variability. Individual increases or decreases across treatment did not appear to exceed

increases or decreases across trials.

VFDa. The vector lengths for each of the vowels /i/, /u/, /ʌ/, /ɛ/, /æ/, and /ɑ/ were calculated using the formant measurement methods HGIM, LPCf, ceps, and S-B. These lengths were then averaged to yield an average vector length for the vowel space for each trial, PRE1, PRE2, POST1, and POST2. These values were then graphed in the same manner described above. The graphical results by subject are presented in Figure 4a through 4d in Appendix, with the lettered set representing the different formant measurement methods. Visual inspection revealed no general trend of increase or decrease across treatment. By visual inspection of the data, treatment effects did not appear to be any larger than trial-to-trial variability. Individual increases or decreases across treatment did not appear to exceed increases or decreases across trials.

To determine whether there was any significant change in the vowels that was not reflected in the average of the vectors, the individual vowel vector lengths yielded by HGIM were also examined. For each vowel, the vector lengths observed in the pre-treatment sessions were compared graphically to those of the post-treatment sessions. The results are summarized in Figure 6 in Appendix. A preliminary examination of the data revealed no significant change in these gold-standard measures, so the examination was deferred for the other formant measurement methods.

VFDc. The vector lengths for each of the corner vowels /i/, /u/, /æ/, and /ɑ/ were calculated using the formant measurement methods HGIM, LPCf, ceps, and S-B. These lengths were then averaged to yield an average vector length for the vowel space for each trial, PRE1, PRE2, POST1, and POST2. These values were then graphed in the same manner described above. The graphical results by subject are presented in Figure 4a through 4d in Appendix, with

the lettered set representing the different formant measurement methods. Visual inspection revealed no general trend of increase or decrease across treatment. By visual inspection of the data, treatment effects did not appear to be any larger than trial-to-trial variability. Individual increases or decreases across treatment did not appear to exceed increases or decreases across trials.

Numerical Presentation of Findings

The results were also summarized numerically to corroborate the graphical results. To determine whether treatment effects exceeded trial variability in this regard, the ranges of the pre and post-trial differences and the treatment differences were calculated for each metric and organized by formant measurement method. The ranges of the pretrial differences were determining by calculating the subtracting the PRE1 metric value from the PRE2 metric value for each subject. The pretrial differences were ordered numerically to determine the minimum and maximum and the range was calculated by subtracting the minimum from the maximum. The same process was repeated for the post trial difference range. Treatment differences were computed by subtracting the PRE2 values from the POST1 values, since this difference could most reasonably be expected to show treatment effects. These differences were then ordered numerically and the range was calculated by subtracting the minimum from the maximum. Results are summarized in Table 4 in Appendix.

A review of Table 4 shows that the treatment range exceeded the pre and post-trial ranges for all metrics when calculated using HGIM. The treatment range did not exceed the trial ranges for any metric using LPCf. For ceps, only VFDa and VFDc had treatment ranges that exceeded the trial ranges. The area of the vowel quadrilateral and VFDc calculated using S-B had treatment ranges that exceeded the trial ranges. In the cases where the treatment range exceeded

the trial ranges, the treatment ranges were not substantially larger than the trial differences. This supports the initial conclusion that treatment effects did not significantly exceed trial differences.

While Table 4 provides information on trial variability versus treatment differences, it gives very little information about the direction and magnitude of treatment differences. To determine whether any appreciable increases or decreases were observed from pre to post treatment, the means for each vowel space metric were computed both pre and post therapy. The means for the pre vowel spaces were computed by averaging the vowel spaces across subjects for both the PRE1 and PRE2 sessions. This was repeated for the average post vowel spaces. The mean difference was computed by subtracting the average pre vowel space from the average post vowel space. The results are summarized in Table 5.

An examination of Table 5 supports the initial conclusion that the average post vowel space values did not appreciably exceed the average pre vowel space values. A slight decrease was noted for all vowel spaces calculated using HGIM except for F2i/F2u which showed no change. For LPCf, VAI, F2i/F2u and the area of the vowel quadrilateral all showed a slight decrease while VFDa and VFDc showed a moderate increase. For ceps, VAI showed a slight decrease, F2i/F2u showed no change. Slight increases in the area of the vowel quadrilateral, VFDa, and VFDc were noted for ceps. All vowel spaces calculated using S-B decreased slightly, except F2i/F2u which showed no change.

Findings in Formant Measurement Methods

A central question in this study was whether phonatory factors influenced formant measurement methods. Such an influence could potentially skew VSA measures, regardless of metric used. Failure of this study to find significant changes in vowel space following LSVT heightens the importance of possible interactions between formant measurement methods and

phonatory factors. LPC was of particular interest because of its common use in previous VSA studies, and its anticipated vulnerabilities to phonatory factors. It was expected that, if phonatory factors were a confounding factor, there would be a high level of variability in the pre-treatment sessions that decreased in the post-treatment sessions. It was conjectured that the measures would be relatively more stable in the post condition due to the previously established phonatory improvements that accompany LSVT.

To investigate this possibility, the standard deviations of each metric in the pre and post condition were calculated and organized by formant measurement method. Results are summarized in Appendix. Of all the formant measurement methods, LPCf had the greatest standard deviation in both pre- and post-treatment sessions. Contrary to expectations, however, the standard deviation of pre and post-trial differences saw no stabilization of LPCf. HGIM, ceps, and S-B had relatively similar standard deviations and did not show a significant change from pre to post. Therefore, the conjecture that measurement issues were confounded with phonatory factors in previous findings of vowel space increase with LSVT was not supported.

Discussion

LSVT Treatment Effects

The initial premise of this thesis was that VSA would increase from pre to post LSVT. However, the data do not support that there is any substantial change in VSA with LSVT. There are many possible reasons why this study failed to replicate the results found by Sapir et al. (2010). LPC was found to have the highest variability of all the formant measurement methods examined in this study, and so prior results may have been affected by this variability. The difference in materials used may also have influenced the results. The study by Sapir et al. (2010) utilized read sentences while the current study used shorter carrier phrases. As such,

there is the tenuous possibility that the shorter phrases yielded larger VSAs in the pre sessions, leaving little room for improvement as a result of LSVT. Sapir et al.'s (2010) study included a larger number of participants (19) than the current study but reported large effect sizes for the formant centralization ratio (the inverse of VAI) and F2i/F2u. Therefore it does not appear the difference in number of participants fully accounts for this study's failure to replicate previous results. Additionally, the treatment in this study was a combination of LSVT and transcranial magnetic stimulation (TMS), while Sapir et al.'s (2010) study utilized LSVT only. Since the researchers in this study are still blinded as to which participants received TMS versus sham TMS, it is unknown if the addition of TMS had any effect on vowel space that would not have been observed in Sapir et al.'s (2010) study. The current study also utilized the LSVT Companion (Halpern et al., 2012), while Sapir et al. (2010) did not. Therapy supported by the LSVT Companion has been shown to be comparable to traditional face-to face therapy.

To determine whether there was a common factor between subjects who did show an increase in vowel space area following LSVT, two subjects were examined. Subjects 1 and 4, showed a consistent increase across many, but not all, of the VSA metrics as based on all measurement methods. Subject 4 showed a stronger tendency to increase, with a very slight decrease in the area of the vowel quadrilateral as calculated by HGIM and LPCf. She was noted to consistently demonstrate the largest vowel space across methods, metrics, and pre- vs. post-treatment sessions. Though Subject 1's increases were generally weaker than Subjects 4's, he did show consistent increases across all metrics and methods except for VAI calculated with LPCf, and the F2i/F2u ratio calculated with LPCf. In both these exceptions, the decrease was noted to be very slight. In contrast to Subject 4 however, Subject 1 was noted to be on the lower end—if not the lowest—on all metrics. The results of these two participants suggest that there

are some people for whom LSVT does lead to an increase in VSA, though it is difficult to conclude whether a common factor led to increased VSA in these participants and not the others.

To determine how specific vowels were affected in Subjects 1 and 4, the individual vowel vector lengths were examined. Figure 7 in Appendix shows the pre to post change in vector lengths for each vowel for Subjects 1 and 4. Subject 4 showed moderate increases in /æ/, /i/, and /u/ and a slight decrease in /ɑ/ while remaining approximately the same for /ɛ/ and /ʌ/. Overall, the data support the observation of a modest increase in VSA for Subject 4. Specifically, the vectors for the front vowels /i/ and /æ/ increased suggesting more forward positioning of the tongue post-treatment. Additionally, the expansion of /i/ and /u/ as high vowels and /æ/ as a low vowel support the notion of greater range in the size of oral constriction. Subject 1 showed moderate vector length increases for /æ/, /i/, and /u/ and moderate decreases for /ɑ/, /ʌ/. The vector length of /ɛ/ remained approximately the same. The decrease in vector length for /ɑ/ may explain why he showed weaker increases in the various VSA metrics than Subject 4. Based on the results of at least these two subjects, it is possible that /i/ and /u/ are the vowels most likely to benefit from LSVT, explaining why VSA metrics that include these two vowels are more likely to show increases than those that employ others.

Since Table 4 showed that most vowel space metrics had a greater treatment range than trial range, this may initially lead to the mistaken impression that a substantial change due to treatment took place. However, since Table 4 only includes the range of treatment differences, it cannot be used to make conclusions about direction or magnitude of overall treatment effects. The wider range seen in treatment differences versus pre and post-trial ranges can be accounted for by the fact that some participants showed an increase in vowel space metric values while others showed a decrease. This is corroborated by Figures 1 through 5, which show that the

participants varied widely in the magnitude and direction of changes over treatment. A better measure of treatment effects is Table 5, which summarizes the mean pre and post vowel space metric values, and the signed difference of these averages. Table 5 shows that changes in vowel space metric values varied slightly in most cases and that the direction of this change was also inconsistent and highly influenced by the formant measurement method. The only metrics that showed a moderate increase were VFDa and VFDc calculated using LPCf. This change can most likely be accounted for by the wide variability associated with LPCf.

Formant Measurement Methods

The possible influence of phonatory factors on the various formant measurement methods was a question of interest in this study. If LPC were influenced by phonatory factors, it was expected that LPC with a fixed coefficient (LPCf) would be relatively more stable in the post condition. By contrast, ceps and S-B, theoretically independent of phonatory factors, were hypothesized to yield formants that were closer to HGIM. LPC was not found to be more stable in the post condition as the standard deviation of the trial differences did not appear to decrease from the pre to post condition (see Table 5 in Appendix). Therefore LPC is likely not influenced so much by phonatory factors as initially supposed. However, LPCf was noted to have a greater variability than any of the other measures, implying that it was the least stable of the four measurement methods explored. The variability of ceps and S-B were comparable to those of HGIM, tentatively supporting the claim that ceps and S-B are uninfluenced by phonatory factors.

Another methodological goal of this thesis was to examine the potential errors associated with keeping LPC at a fixed coefficient based on the sampling rate. In this study, LPCf was found to have misidentified the appropriate formant on 35 occasions and to have merged formants on 13 occasions for a total of 48 conspicuous errors, or a total of 10% of the vowels.

In the course of the investigation, it was noted that these errors were not evenly distributed across vowels. This was of potential importance due to the reliance of some vowel space metrics on a limited set of vowels. The vowels most prone to formant misidentification were /u/ and /ɑ/, while the vowel most likely to suffer from formant merging was /i/. Formant were misidentified in /u/ on 15 out of 80 instances, or 18.8% of the time. Formant were misidentified in /ɑ/ on 13 out of 80 occasions, or 16.3% of the time. Formants were misidentified or merged 14 out of 80 times for the vowel /i/, or 17.5% of the time. A complete breakdown of errors by vowel can be found in Table 7 in Appendix. Overall, the errors associated with LPCf were generally concentrated in the vowels /i/, /u/, and /ɑ/. This is especially important because these vowels are the ones most typically associated with VSA metrics, including the vowel articulation index (VAI), F2i/F2u, and area of the vowel quadrilateral. Several metrics, such as VAI and F2i/F2u, rely solely on these vowels. Inaccuracy in the measurement of these formants can lead to inaccurate VSA values.

LPC was not the only formant measurement method prone to errors in correct formant identification. To appropriately locate and differentiate formants, it was often necessary to adjust the two cepstrally-liftered spectrum methods, ceps and S-B, by adjusting the time-based liftering coefficient. Both ceps and S-B were most prone to error in the form of merged formants on the vowels /i/ and /ɑ/. Since adjustment could generally resolve this issue, both ceps and S-B appear to have value as a guide for formant location in conjunction with other methods. However, based on the prevalence of errors in LPC, ceps and S-B, it is not appropriate to use any of these methods as an automated formant finder and human judgment is indispensable in accurate formant location.

LSVT has been proposed to affect a variety of dimensions of speech. By failing to

replicate the results of previous studies, this study calls into question claims that LSVT leads to increased vowel space. This study has raised a variety of methodological questions and highlighted the importance of thoughtful selection of VSA metric and formant analysis. Automated formant measurement methods are prone to significant error that can lead to erroneous results. It is clear that further study is required to understand what—if anything—is occurring in the area of vowel articulation as a result of LSVT.

Areas of Further Study

One area of further study that could be addressed is changes in F1 and F2 for individual vowels as a result of LSVT. Since all VSA metrics, with the exception of F2i/F2u, utilized both F1 and F2, it is possible that important information about the individual formants was lost. Further analysis of the data to explore changes in individual formants could reveal a general trend of expansion in one dimension that was mitigated by lack of change in the other. It would also be interesting to compare the changes in vowel space observed in this study with other acoustic measures such as changes in loudness and perceptual measures such as changes in voice quality. This might help shed light on why some participants, such as Subjects 1 and 4, showed a general increase in vowel space while others did not. Since this study utilized TMS in addition to LSVT, the revelation of which participants received TMS versus sham TMS might also clarify how TMS impacted the efficacy of therapy.

The three-month follow-up sessions could also be analyzed, though their value is questionable in light of this study's apparent failure to find treatment effects. Another area of interest would be to replicate this study with read sentences instead of carrier phrases to more closely replicate the study by Sapir et al. (2010) to control for possible ceiling effects introduced by differences in materials. Finally, though LPC with a fixed coefficient was found to introduce

significant error in formant measurement, it would be valuable to know how well LPC adjusted to fit the spectrum would agree with HGIM. Answers to these questions would go a long way to enhancing our understanding of the relationship between LSVT and vowel space.

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Table 1
Vowel Space Metrics

Measure	Algorithm	Citation	Task	Notes
Area of vowel quadrilateral	Area of an irregular quadrilateral = $0.5 \times ([F2i \times F1æ + F2æ \times F1a + F2a \times F1u + F2u \times F1i] - [F1i \times F2æ + F1æ \times F2a + F1a \times F2u + F1u \times F2i])$	Higgins & Hodge (2002)	Single words	Significantly smaller area for children with dysarthria than age-matched controls
Formant centralization ratio (FCR)	$\frac{F2u + F2a + F1i + F1u}{F2i + F1a}$	Sapir, Ramig, Spielman, & Fox (2010)	Reading sentences	Differentiated between dysarthric speakers with PD and healthy controls; not sensitive to gender effects
Logarithmically scaled vowel space area (LnVSA)	$\sqrt{LnS \times (LnS - LnESiu)(LnS - LnEDia)(LnS - LnEDau)}$ Where $LnEDiu = \sqrt{(LnF1i - LnF1u)^2 + (LnF2i - F2u)^2}$ $LnEDia = \sqrt{(LnF1i - LnF1a)^2 + (LnF2i - F2a)^2}$ $LnEDau = \sqrt{(LnF1a - LnF1u)^2 + (LnF2a - F2u)^2}$ $LnS = \frac{LnEDiu+LnEDia+LnEDau}{2}$	Sapir, Ramig, Spielman, & Fox (2010)	Reading sentences	Did not completely differentiate between individuals with dysarthria and healthy controls

Table 1 (Continued)
Vowel Space Metrics

Measure	Algorithm	Citation	Task	Notes
Ratio of F2/i/ to F2/u/ (F2i/F2u)	$\frac{F2i}{F2u}$	Sapir, Spielman, Ramig, Story & Fox (2007)	Reading sentences	Differentiated between individual with PD and healthy controls
		Sapir, Ramig, Spielman, & Fox (2010)	Reading sentences	Differentiated between individuals with PD and healthy controls; not sensitive to gender effects
Tjaden Method	Bisecting vowel quadrilateral into two triangles, calculating area of each triangle, and summing triangles to get an estimation of the quadrilateral	McRae, Tjaden, & Schoonings (2002)	Reading Farm passage	Significantly smaller area for participants with PD than age- and sex-matched controls
		Tjaden & Wilding (2004)	Reading passage	Significantly smaller area for participants with PD and MS and neurologically normal controls
Triangular Vowel Space Area (tVSA)	$0.5 \times ([F2u + F2i] \times [F1u - F1i] - [F2a + F2u] \times [F1a - F1u] - [F2a + F2i] \times [F1a - F1i])$	Bradlow, Torretta, & Pisoni (1996)	Reading sentences	No positive correlation between tVSA and intelligibility in normal speakers.
		Skodda, Visser & Schlegel (2010)	Reading sentences	Only reduced in male PD speakers

Table 1 (Continued)
Vowel Space Metrics

Measure	Algorithm	Citation	Task	Notes
Vowel Articulation Index (VAI)	$\frac{F2i + F2a}{F1i + F1u + F2u + F2a}$	Skodda, Visser & Schlegel (2010)	Reading sentences	Reduced values in male and female PD speakers; more sensitive to mild dysarthria than tVSA
Vowel Formant Dispersion (VFD)	Vector length=$\sqrt{(F1-F1_m)^2+(F2-F2_{wm})^2}$ Where $F1_m$ is the average of all F1 tokens and $F2_{wm}$ is the weighted average of all F2 tokens such that all F2 tokens associated with F1 values greater than $F1_m$ are excluded.	Karlsson & van Doorn (2012)	Single words	In normal speakers, VFD less prone to producing Type I or Type II errors than VAI, FCR, and other vowel space metrics
Vowel Space Area (VSA)	$\frac{ABS[F1i\times(F2a-F2u)+F1a\times(F2u-F2i)+F1u\times(F2i-F2a)]}{2}$	Sapir, Ramig, Spielman, & Fox (2010)	Reading sentences	No significant difference between participants with PD and neurologically healthy controls
Vowel Space Dispersion (VSD)	Vector length=$\sqrt{(F1-F1_m)^2+(F2-F2_m)^2}$ Where $F1_m$ is the average of all F1 tokens and $F2_m$ is the average of all F2 tokens. Vector lengths are averaged to yield a single number	Bradlow, Torretta, & Pisoni (1996)	Reading sentences	Moderately correlated with intelligibility in normal speakers

Table 2
Additional Exclusion Criteria

History of drug abuse, neurological condition besides IPD, seizures, head trauma
Other current medical conditions, including brain damage, brain inflammation, heart disease, pregnancy, uncorrected hearing loss
Medical implants, including metal objects implanted in head, ferrous metal filings in eye, pacemaker, medication pump, cardiac lines
Current medications, including certain medications for depression or seizures
Advanced Parkinson's Disease (stage V)
Score of greater than 19 on the Beck Depression Inventory
Score of less than 24 on Mini-Mental Status Examination
Have undergone LSVT within the last three years
Cannot read at 6th grade level
Cannot increase vocal loudness in sustained phonation on command by at least 3 dB SPL

Table 3
Summary of Reliability Data Organized According to Formant Measurement Method and Formant

	HGIM		LPCf		Ceps		Ceps S-B	
	F1	F2	F1	F2	F1	F2	F1	F2
Pearson's *r*	0.93	0.96	0.93	0.90	0.80	0.94	0.89	0.96
Average difference	-20.88	-15.70	5.70	-3.18	6.21	-56.50	2.49	-45.18
Standard error diffs	5.95	13.16	5.28	21.85	9.37	17.53	7.22	14.12

Table 4
Range of Pre- and Post-trial Differences versus Treatment Differences

	HGIM			LPC fixed			Ceps			Ceps S-B		
	Pre	Post	Tx	Pre	Post	Tx	Pre	Post	Tx	Pre	Post	Tx
VAI	0.16	0.09	0.20	0.34	0.33	0.33	0.15	0.21	0.13	0.19	0.14	0.16
F2i/F2u	0.48	0.36	0.51	0.82	1.08	0.99	0.42	0.78	0.35	0.52	0.44	0.40
Area*	17.5	12.4	20.2	68.1	35.6	48.7	10.1	22.9	15.7	10.9	16.2	19.0
VFDc	126.0	89.3	149.4	405.6	137.0	192.3	143.7	100.0	153.3	139.6	109.1	155.0
VFDa	106.2	114.0	155.5	310.9	325.9	212.2	123.5	84.6	138.9	182.1	76.1	152.0

* $\times 10^4$

Table 5
Pre- and Post- Mean Values versus Mean Difference

	HGIM			LPC fixed			Ceps			Ceps S-B		
	Pre	Post	Diff	Pre	Post	Diff	Pre	Post	Diff	Pre	Post	Diff
VAI	1.08	1.05	-0.03	1.06	1.01	-0.04	1.08	1.07	-0.01	1.08	1.06	-0.02
F2i/F2u	1.74	1.74	0.00	1.61	1.56	-0.05	1.77	1.77	0.00	1.79	1.79	0.00
Area*	24.2	22.5	-1.6	18.3	18.1	-0.2	22.4	22.7	0.2	24.1	23.2	-0.9
VFDc	454.0	448.5	-5.5	504.4	527.8	23.4	470.3	475.7	5.4	478.9	477.5	-1.5
VFDa	400.3	392.1	-8.3	445.1	483.9	38.9	400.0	407.3	7.3	420.2	418.4	-1.8

* $\times 10^4$

Table 6
Standard Deviation of Trial Differences

	HGIM		LPC fixed		Ceps		Ceps S-B	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
VAI	0.05	0.03	0.10	0.12	0.04	0.05	0.05	0.04
F2i/F2u	0.14	0.12	0.25	0.37	0.12	0.21	0.13	0.12
Area*	5.4	3.6	18.0	11.7	3.7	5.8	4.4	4.6
VFDc	38.69	26.74	108.29	51.73	39.97	32.54	38.95	31.86
VFDa	31.83	31.73	87.69	88.56	37.71	28.48	47.20	30.67

* $\times 10^4$

Table 7
Incidence of LPC Formant Identification Errors

	ɛ	ʌ	u	i	æ	ɑ
Formants missed	0	4	15	3	0	13
Formants merged	2	0	0	11	0	0

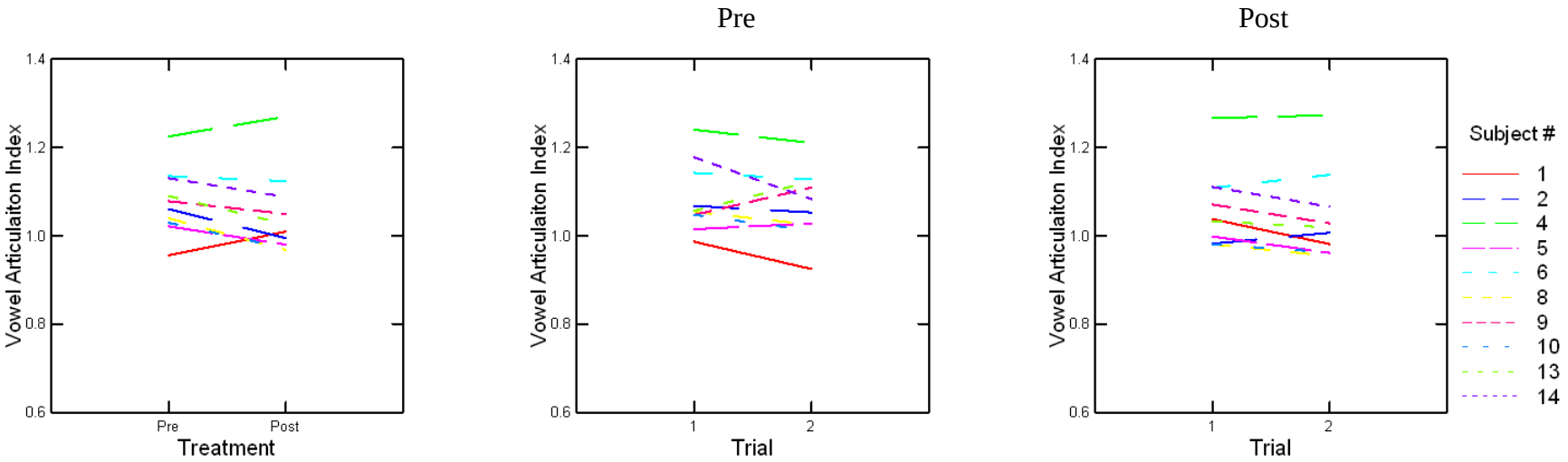

Figure 1a. VAI calculated using HGIM as a function of treatment and trial differences

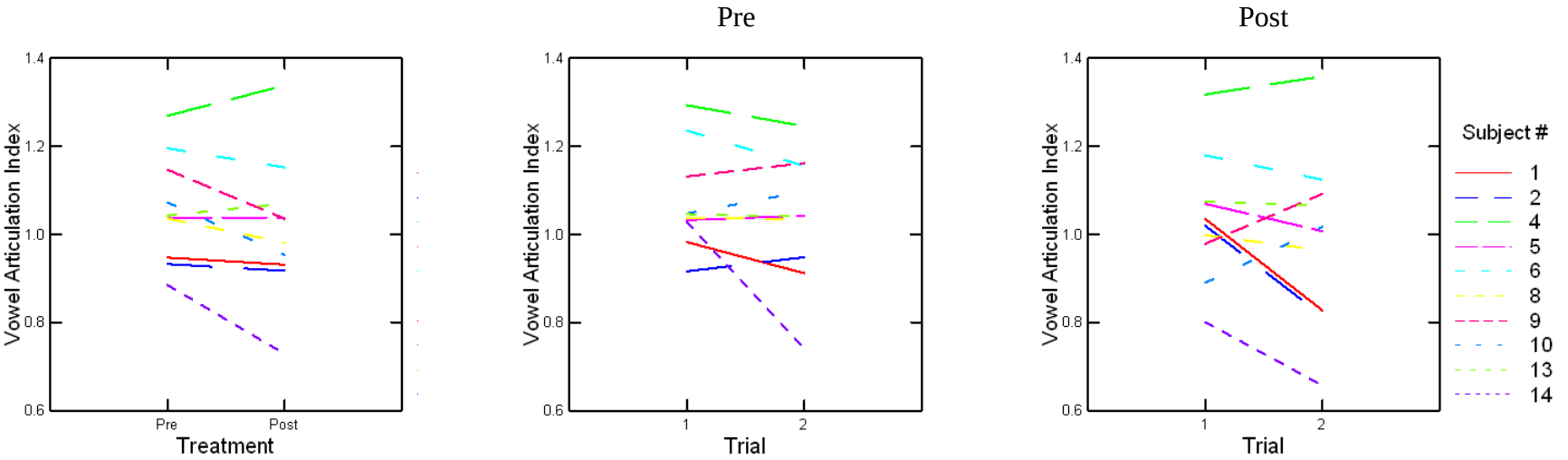

Figure 1b. VAI calculated using LPCf as a function of treatment and trial differences

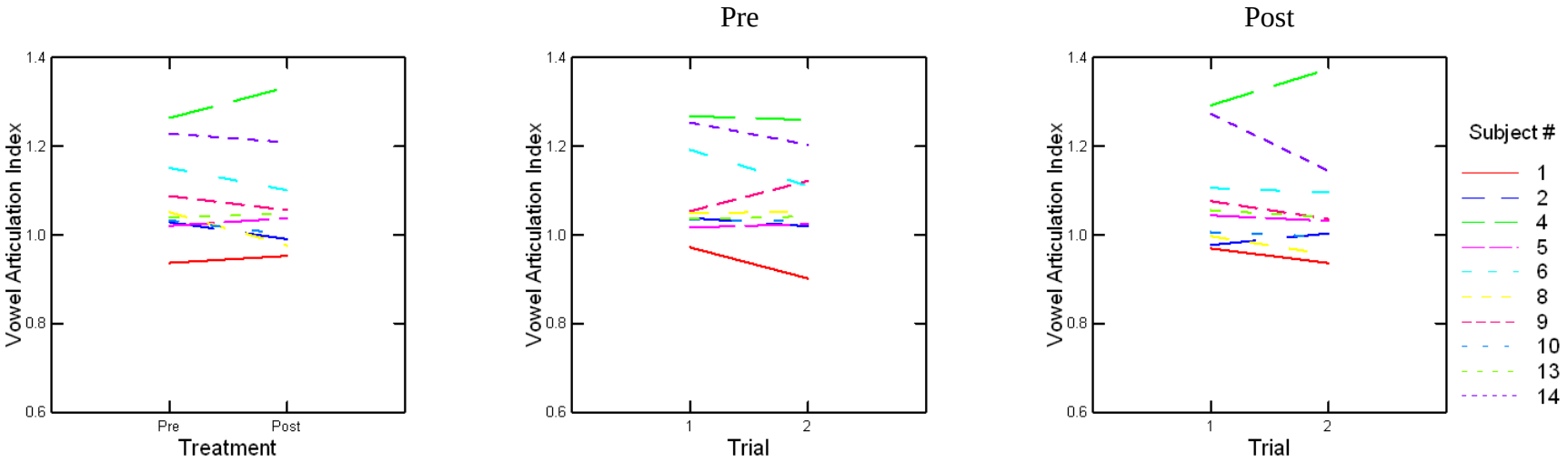

Figure 1c. VAI calculated using ceps as a function of treatment and trial differences

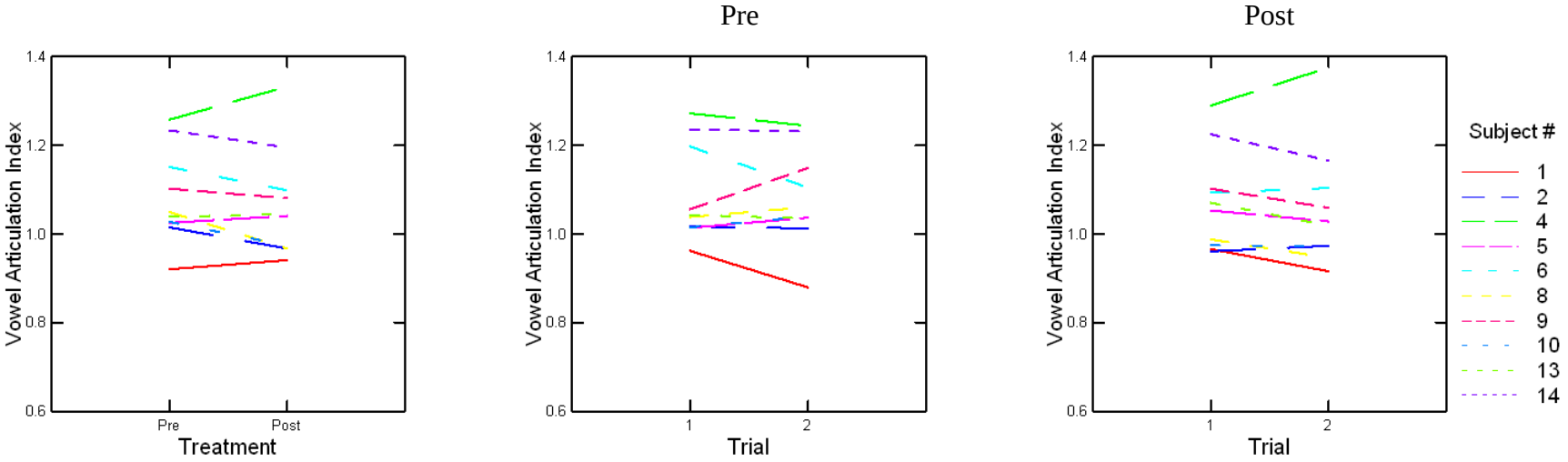

Figure 1d. VAI calculated using S-B as a function of treatment and trial differences

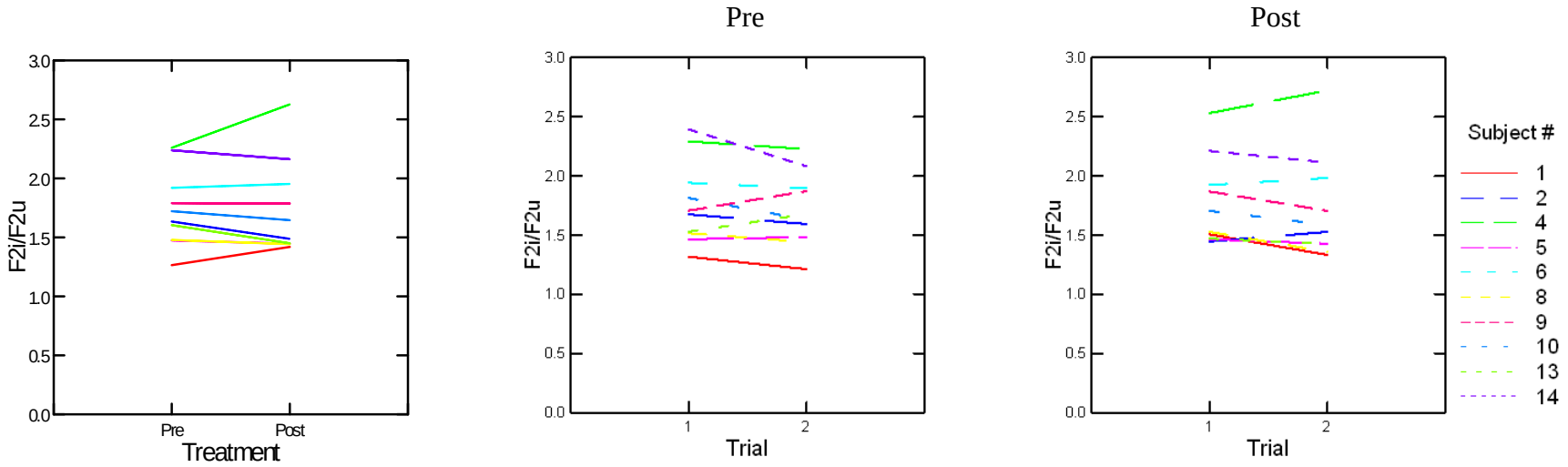

Figure 2a. F2i/F2u calculated using HGIM as a function of treatment and trial differences

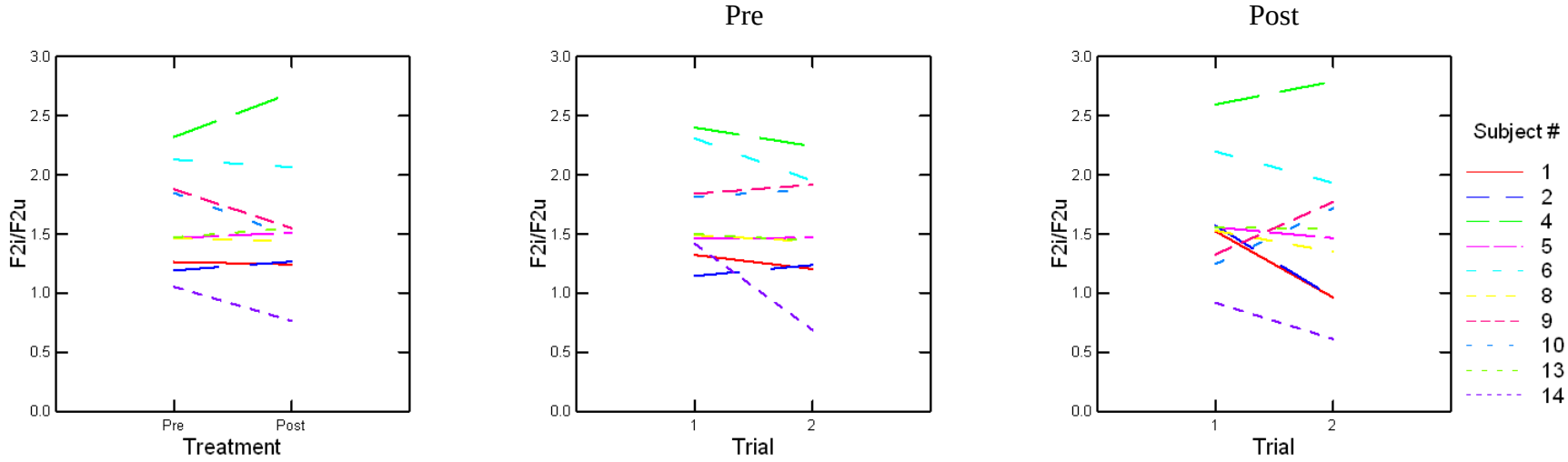

Figure 2b. F2i/F2u calculated using LPCf as a function of treatment and trial differences

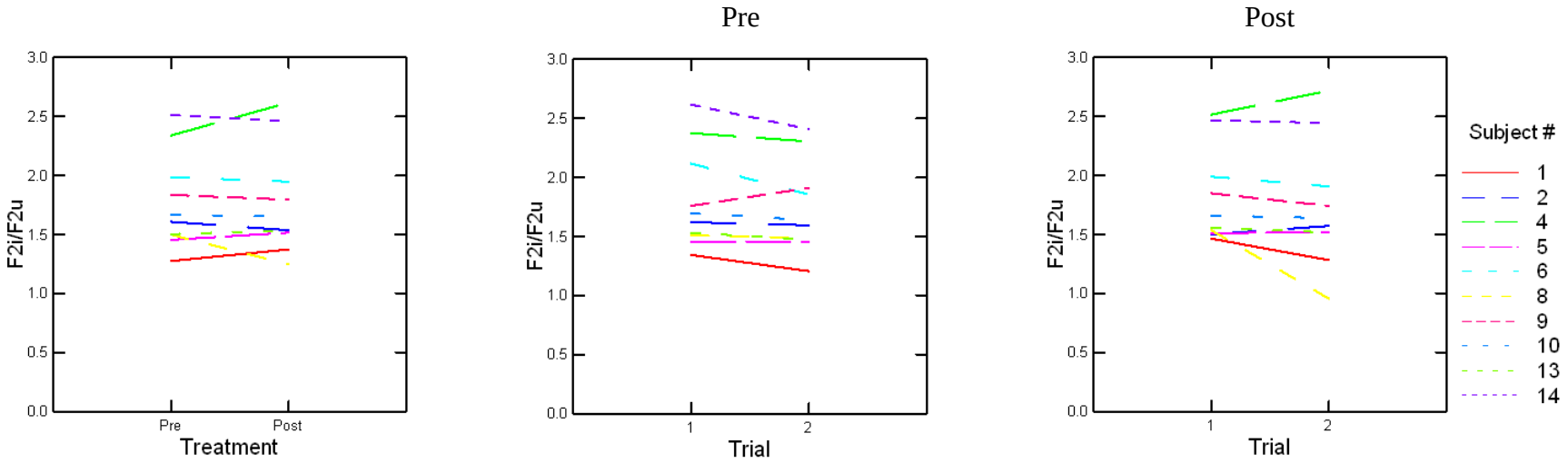

Figure 2c. F2i/F2u calculated using ceps as a function of treatment and trial differences

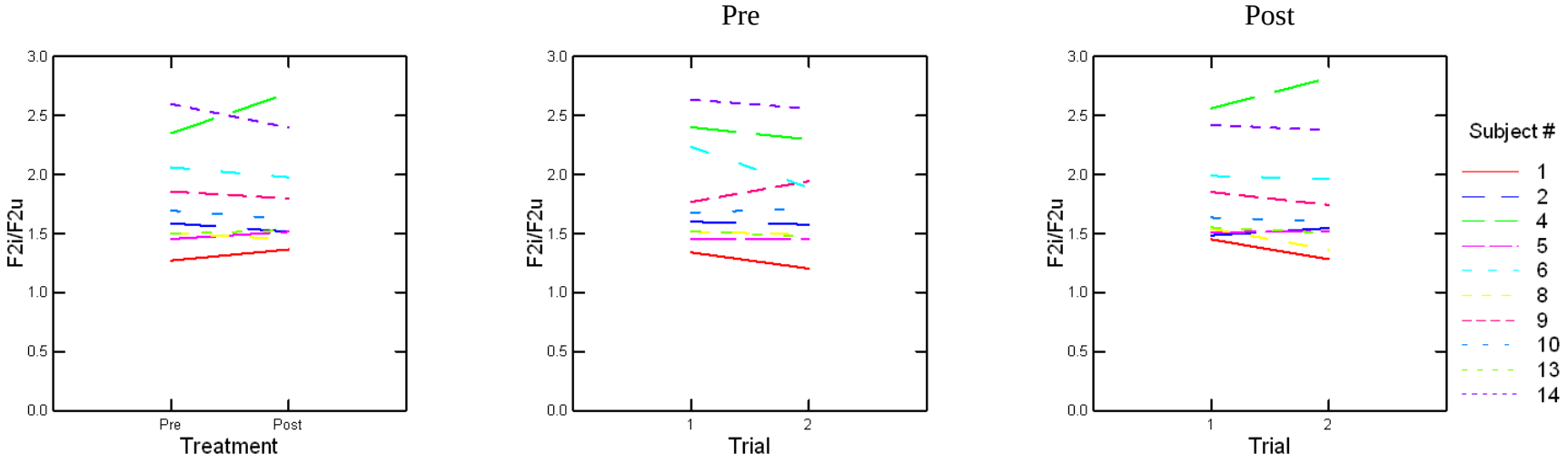

Figure 2d. F2i/F2u calculated using S-B as a function of treatment and trial differences

Pre Post

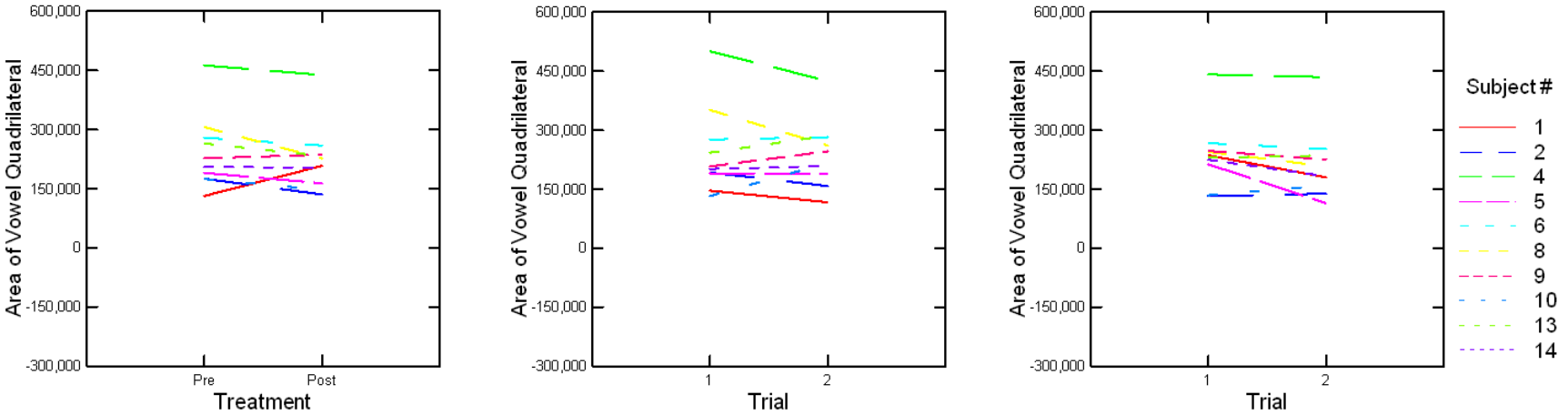

Figure 3a. Area of vowel quadrilateral calculated using HGIM as a function of treatment and trial differences

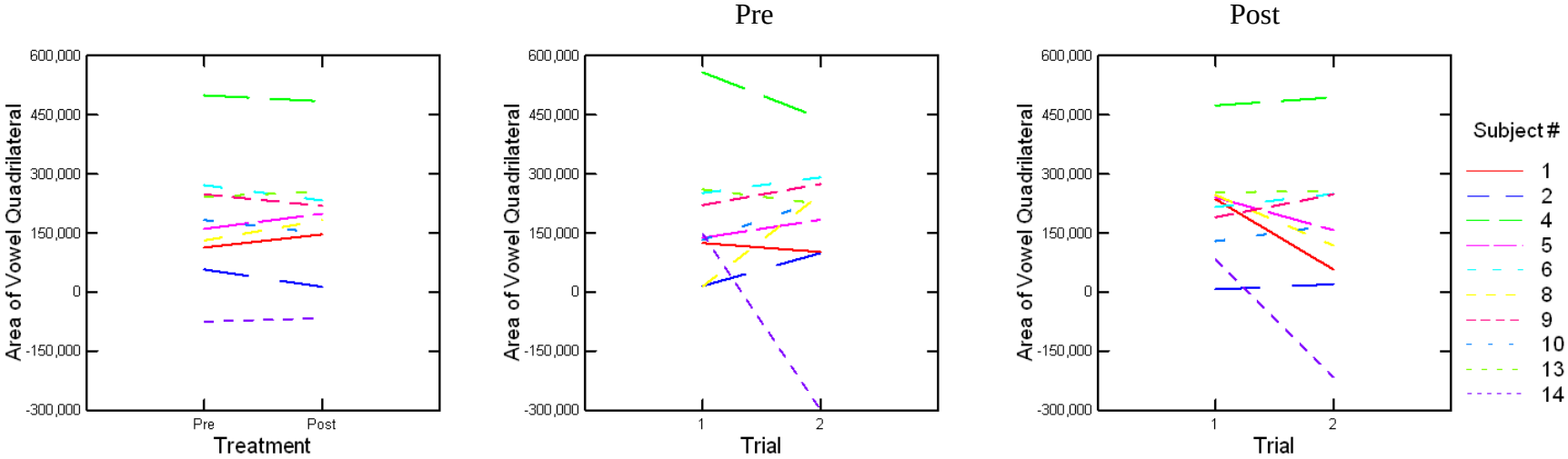

Figure 3b. Area of vowel quadrilateral calculated using LPCf as a function of treatment and trial differences

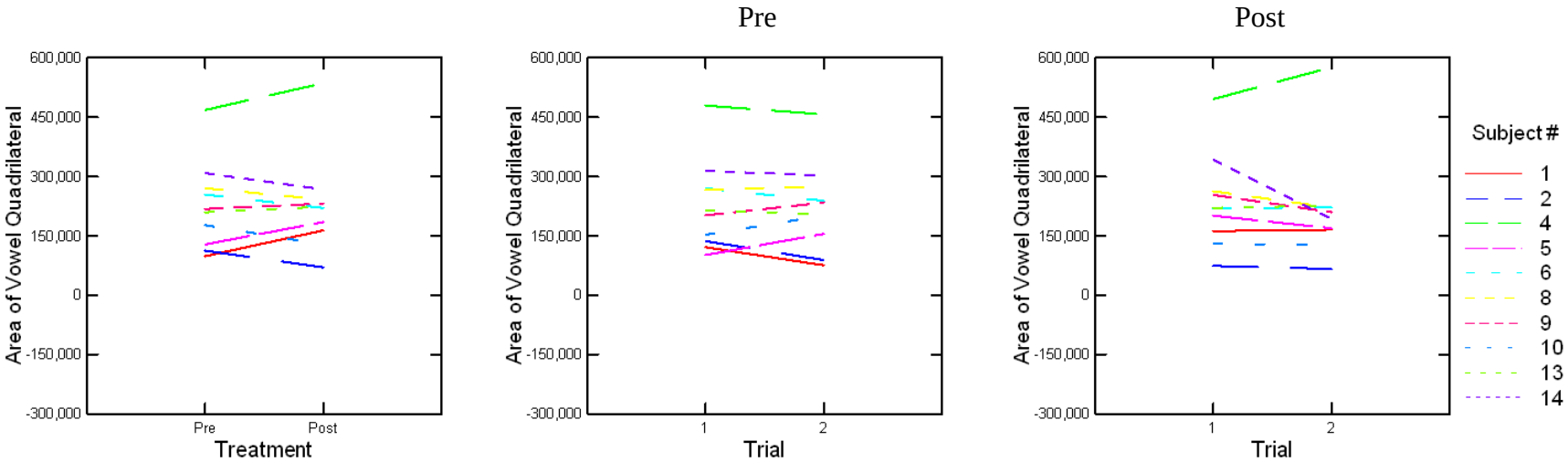

Figure 3c. Area of vowel quadrilateral calculated using ceps as a function of treatment and trial differences

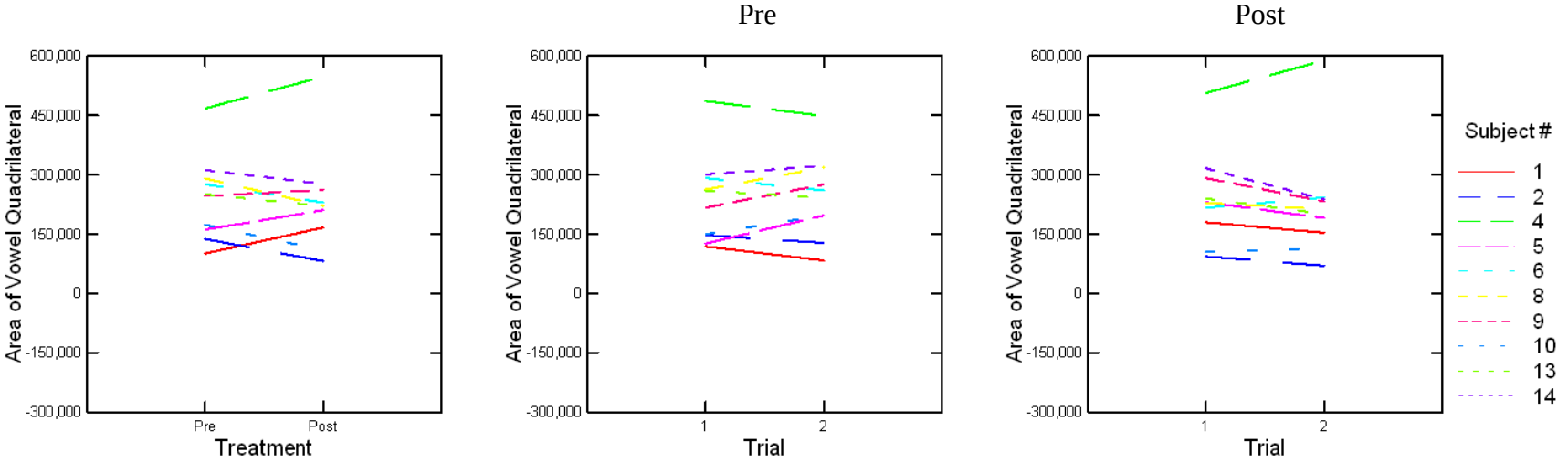

Figure 3d. Area of vowel quadrilateral calculated using S-B as a function of treatment and trial differences

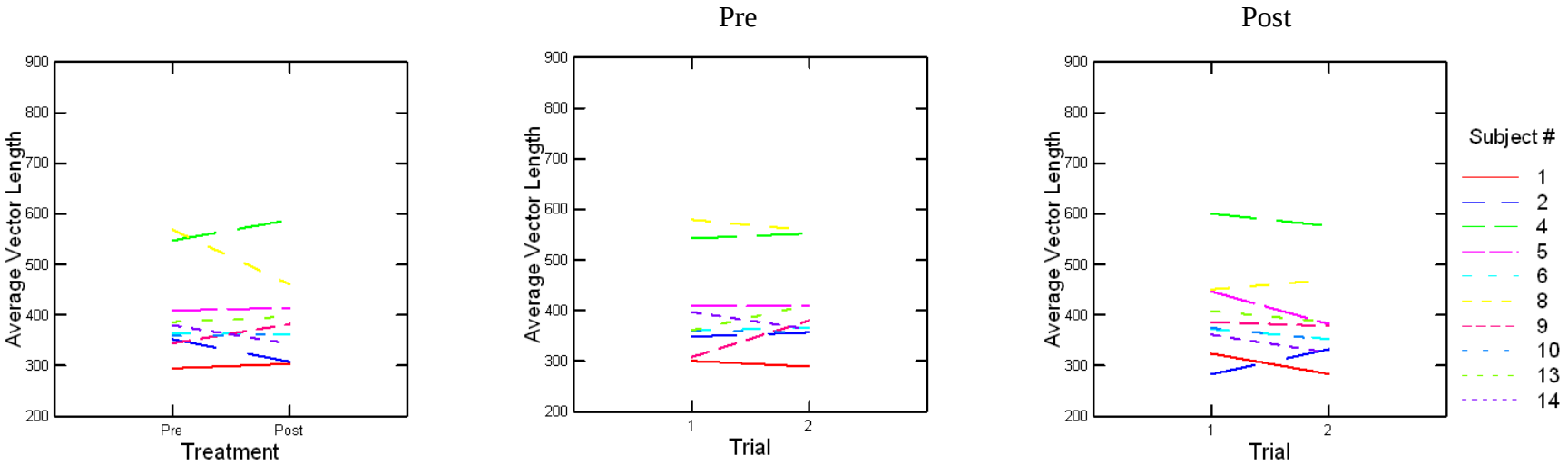

Figure 4a. VFDa calculated using HGIM as a function of treatment and trial differences

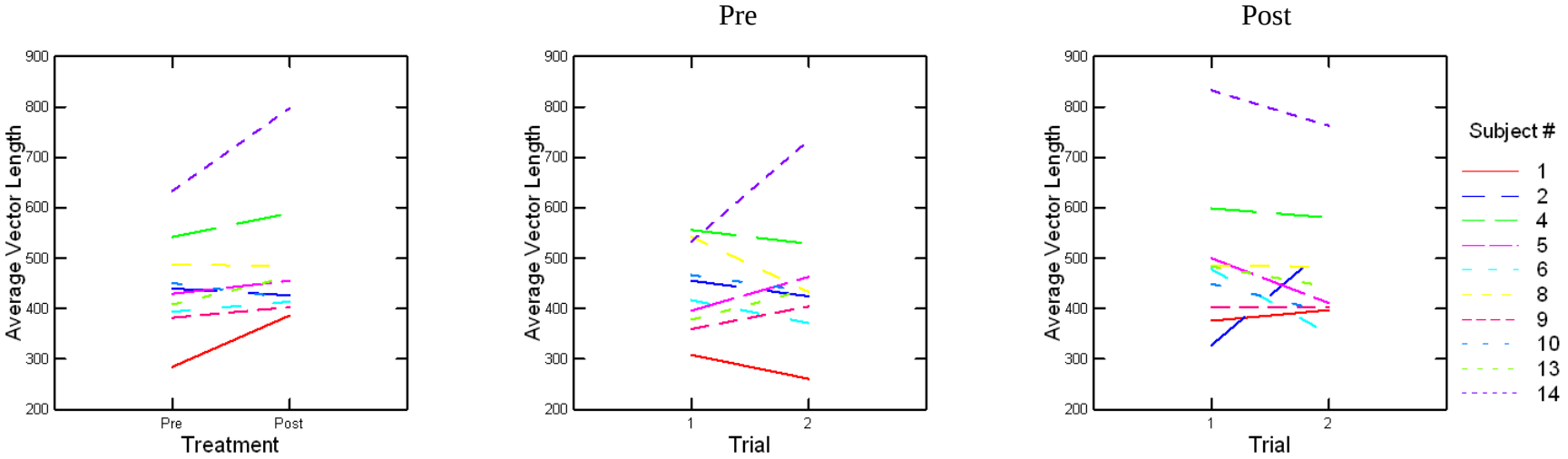

Figure 4b. VFDa calculated using LPCf as a function of treatment and trial differences

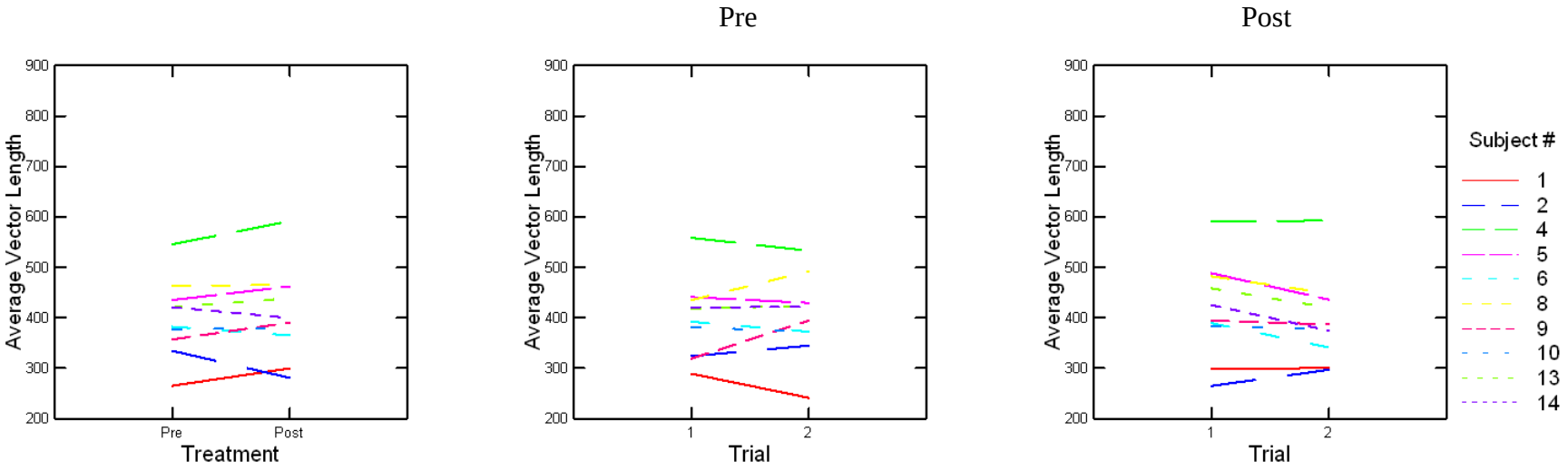

Figure 4c. VFDa calculated using ceps as a function of treatment and trial differences

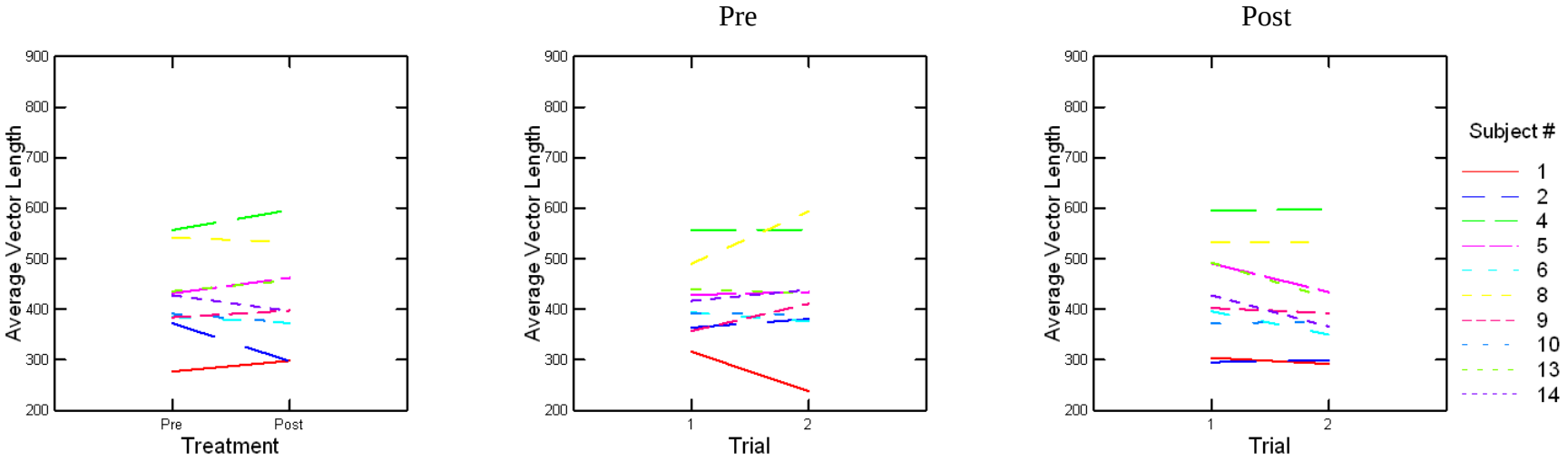

Figure 4d. VFDa calculated using S-B as a function of treatment and trial differences

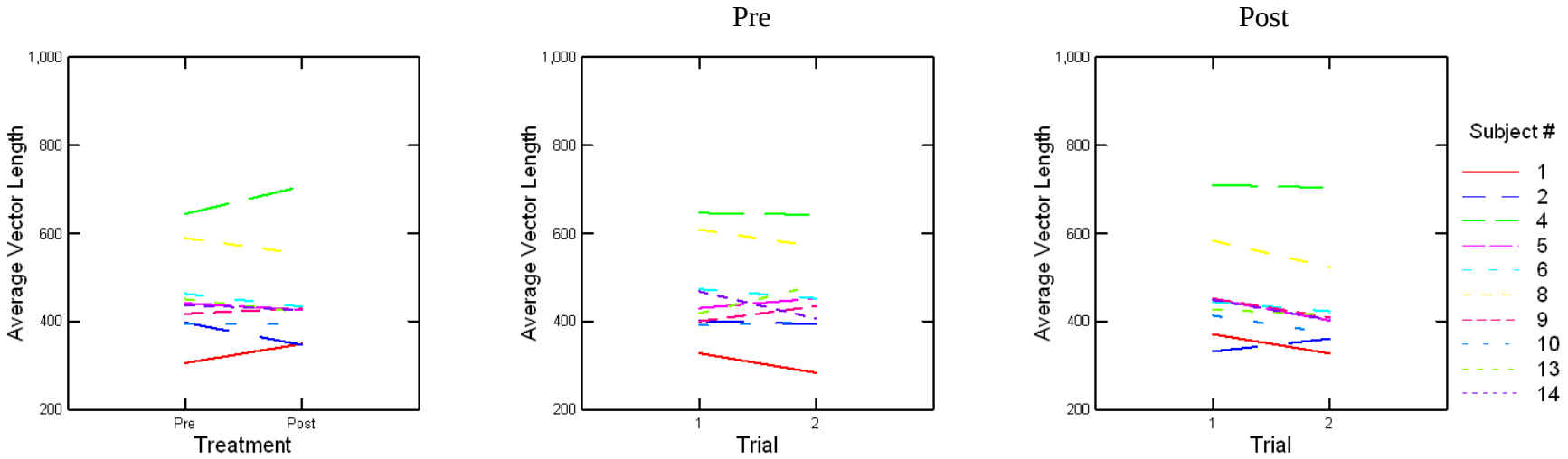

Figure 5a. VFDc calculated using HGIM as a function of treatment and trial differences

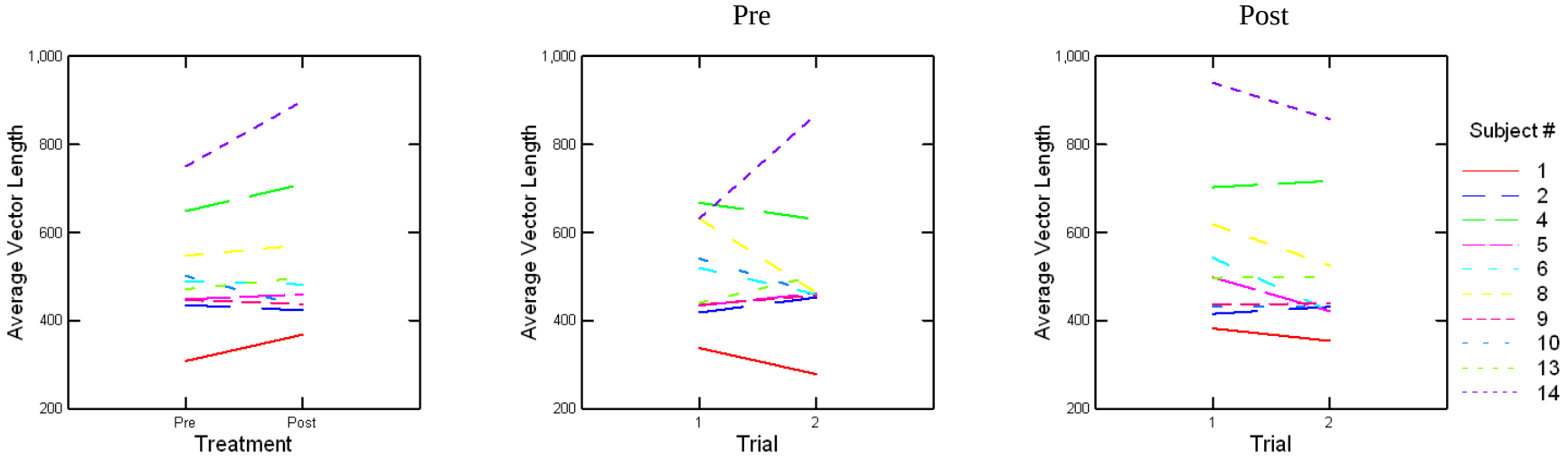

Figure 5b. VFDc calculated using LPCf as a function of treatment and trial differences

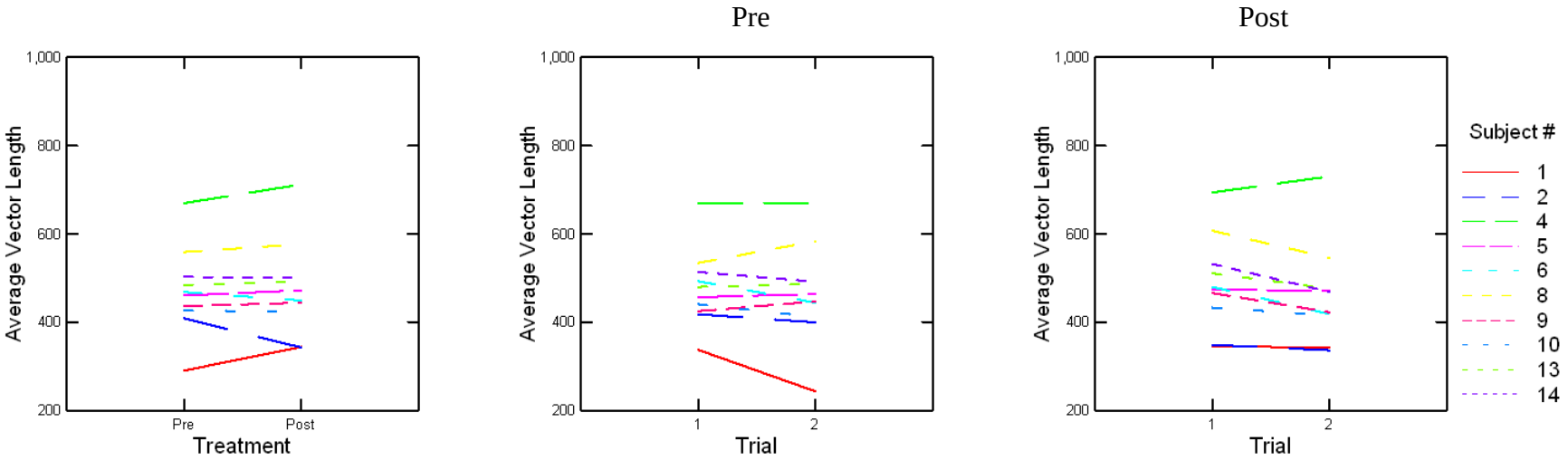

Figure 5c. VFDc calculated using ceps as a function of treatment and trial differences

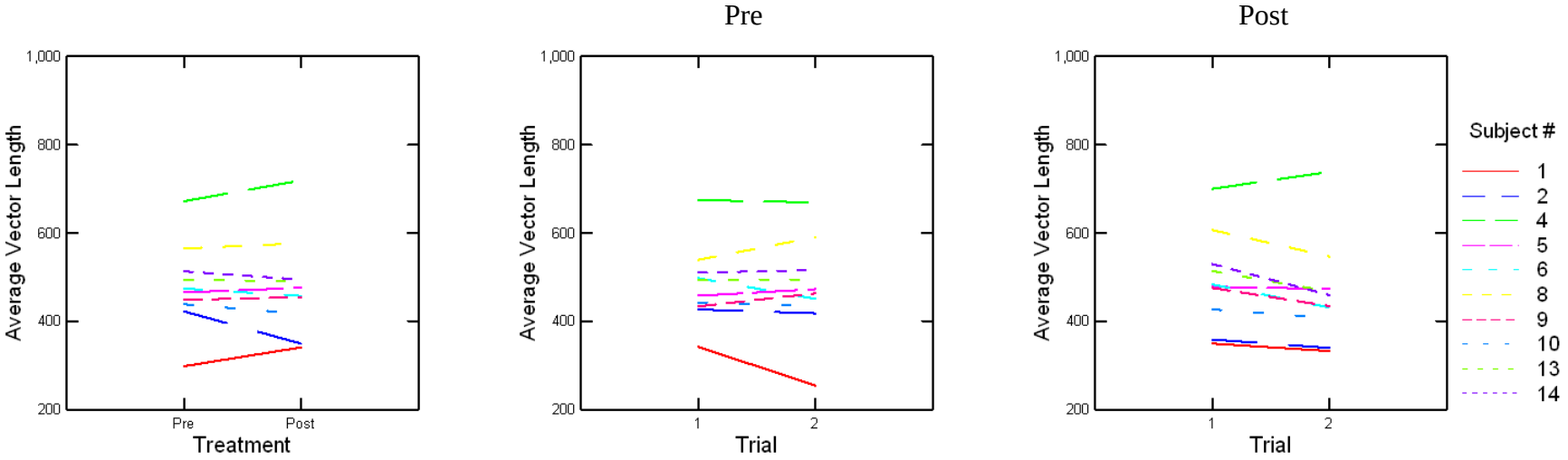

Figure 5d. VFDc calculated using S-B as a function of treatment and trial differences

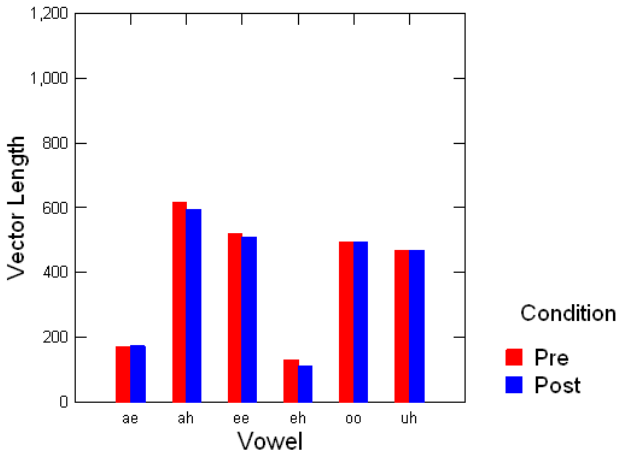

Figure 6. Comparison of pre to post LSVT vector lengths calculated using VFDa

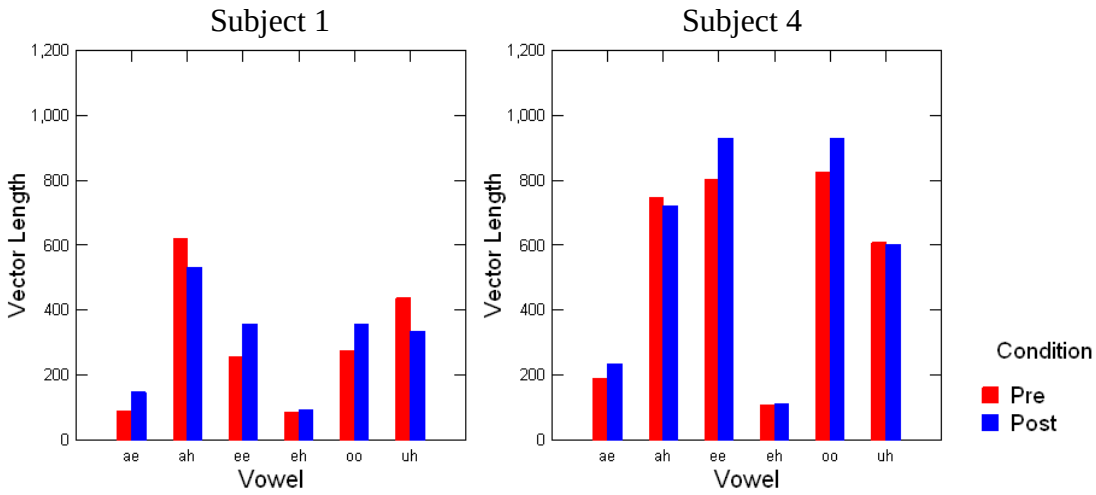

Figure 7. Comparison of pre to post LSVT vector lengths calculated using VFDa in Subjects 1 and 4

From: Beverly Jacobik (bjacobik) **On Behalf Of** Institutional Review Board
Sent: Wednesday, October 01, 2014 9:15 AM
To: Michael P Cannito (mcannito)
Subject: IRB Approval 3429

Hello,

The University of Memphis Institutional Review Board, FWA00006815, has reviewed and approved your submission in accordance with all applicable statuses and regulations as well as ethical principles.

PI NAME: Michael Cannito
CO-PI: Shalini, Narayana, Ph.D., Asim F. Choudhri, MD, Ronald F. Pfeiffer, MD, at UTHSC
PROJECT TITLE: Augmenting Treatment Effects of Voice Therapy in Parkinson's Disease
FACULTY ADVISOR NAME (if applicable): n/a
IRB ID: #3429
APPROVAL DATE: 9/11/2014
EXPIRATION DATE: 8/6/2015
LEVEL OF REVIEW: Facilitated Review, UTHSC

RISK LEVEL DETERMINATION: No more than minimal

Please Note: Modifications do not extend the expiration of the original approval

Approval of this project is given with the following obligations:

1. If this IRB approval has an expiration date, an approved renewal must be in effect to continue the project prior to that date. If approval is not obtained, the human consent form(s) and recruiting material(s) are no longer valid and any research activities involving human subjects must stop.

2. When the project is finished or terminated, a completion form must be completed and sent to the board.

3. No change may be made in the approved protocol without prior board approval, whether the approved protocol was reviewed at the Exempt, Exedited or Full Board level.

4. Exempt approval are considered to have no expiration date and no further review is necessary unless the protocol needs modification.

Approval of this project is given with the following special obligations:

Pamela M. Valentine

Interim Institutional Review Board Chair

The University of Memphis.

Note: Review outcomes will be communicated to the email address on file. This email should be considered an official communication from the UM IRB. Consent Forms are no longer being stamped as well. Please contact the IRB at IRB@memphis.edu if a letter on IRB letterhead is required.

THE UNIVERSITY OF TENNESSEE
Health Science Center

Institutional Review Board
910 Madison Avenue, Suite 600
Memphis, TN 38163
Tel: (901) 448-4824

5 August 2015

Shalini Narayana, PhD
UTHSC - COM - Peds - General Pediatrics
335 Le Bonheur Outpatient Center
51 N Dunlap Street
Memphis, TN 38105

Re: 14-03265-FB UM
Study Title: Augmenting Treatment Effects of Voice Therapy in Parkinson's Disease [Master Protocol, dated 01/15/2014; revised 06/05/2015]

Dear Dr. Narayana:

On 08/05/2015, the UTHSC Institutional Review Board (IRB) reviewed your application to **continue** your previously approved project, referenced above. The IRB has reviewed your renewal application and determined that it complies with proper consideration for the rights and welfare of human subjects and the regulatory requirements for the protection of human subjects. Therefore, this letter constitutes approval of your renewal application, including main and repository consent forms dated 07/07/2015 (stamped IRB approved 08/05/2015). **The UTHSC IRB stamped-approved consent forms must be used to enroll prospective subjects in the study.** Approval of this study will be valid from 08/05/2015 to 08/06/2016.

This study may not be continued until you receive re-approval from the institution(s) where the research is being conducted.

In accord with 45 CFR 46.116(d), alteration of informed consent continues to be approved, with the cover statement for telephone screening used in lieu of an informed consent interview. The requirement to secure a signed consent form continues to be waived under 45 CFR 46.117(c)(2). Willingness of the subject to participate constitutes adequate documentation of consent.

In addition, the request for waiver of HIPAA authorization to identify potential subjects for recruitment continues to be approved. The waiver applies to the medical records of patients with Parkinson's disease from referring physicians and local support groups.

In the event that subjects are to be recruited using solicitation materials, such as brochures, posters, web-based advertisements, etc., these materials must receive prior approval of the IRB. Any revisions in the approved application must also be submitted to and approved by the IRB prior to implementation. In addition, you are responsible for reporting any unanticipated serious

adverse events or other problems involving risks to subject or others in the manner required by the local IRB policy.

Finally, **re-approval** of your project is required by the IRB in accord with the conditions specified above. You may not continue the research study beyond the time or other limits specified unless you obtain prior written approval of the IRB.

Sincerely,

[redacted]

Signature applied by Holly A Herron on 08/05/2015 11:34:43 AM CDT

[redacted]

Holly A Herron, BA, CIM
IRB Administrator
UTHSC IRB

Terrence F Ackerman, PhD
Chairman
UTHSC IRB

THE UNIVERSITY OF TENNESSEE
Health Science Center

Institutional Review Board
910 Madison Avenue, Suite 600
Memphis, TN 38163
Tel: (901) 448-4824

September 11, 2014

Shalini Narayana, PhD
UTHSC - COM - Peds - General Pediatrics
335 Le Bonheur Outpatient Center
51 N. Dunlap Street
Memphis, TN 38105

Re: 14-03265-FB UM
Study Title: Augmenting Treatment Effects of Voice Therapy in Parkinson's Disease [Master Protocol, dated 1/15/2014]

Dear Dr. Narayana:

The IRB has received your written acceptance of and/or responses dated 09/10/2014 and 9/9/2014 to the provisos outlined in our correspondence of 9/10/2014 and 8/6/2014 concerning the application for the above referenced project. The IRB has reviewed these materials and determined that they comply with proper consideration for the rights and welfare of human subjects and the regulatory requirements for the protection of human subjects. Therefore, this letter constitutes full approval by the IRB of your application, Version 1.5 and the accompanying documents:

- Master Protocol, dated 1/15/2014
- 510K document, dated 9/29/2011
- Charite Clinical Statement, dated 10/31/2012
- Navigated Brain Stimulation Product Brochure, Version 1.0
- NexSpeech for NBS System Product Brochure, Version 1.0
- Flyer, dated 9/11/2014 (stamped IRB approved 9/11/2014)
- Recruitment Brochure, dated 9/9/2014 (stamped IRB approved 9/11/2014)
- Phone screening form, dated 9/9/2014
- Voice-related QOL, dated 6/10/2014 (stamped IRB approved 9/11/2014)
- Subject Information Sheet, dated 6/10/2014 (stamped IRB approved 9/11/2014)
- Screening Questionnaire for TMS Candidates-SN, dated 6/10/214 (stamped IRB approved 9/11/2014)
- MRI-TMS Metal Screening, dated 6/10/2014 (stamped IRB approved 9/11/2014)
- Mini Mental State Exam, dated 6/10/2014
- Medical History Screening, dated 6/10/2014 (stamped IRB approved 9/11/2014)
- Edinburgh Handedness Inventory, dated 6/10/2014 (stamped IRB approved 9/11/2014)
- Beck Depression Inventory, dated 6/10/2014 (stamped IRB approved 9/11/2014)
- Main Consent form, dated 9/11/2014 (stamped IRB approved 9/11/2014)

- Repository Consent Form, dated 9/11/2014 (stamped IRB approved 9/11/2014)

Approval of this study will be valid from 9/11/2014 to 8/6/2015.

This study may not be initiated until you receive approval from the institution(s) where the research is being conducted.

The IRB has determined that the informed consent form, incorporating the authorization of subjects to use their protected health information in research, complies with the federal privacy regulations as specified in 45 CFR 160 and 45 CFR 164. In addition, in accord with 45 CFR 46.116(d), informed consent may be altered, with the cover statement of the telephone screening used in lieu of an informed consent interview. The requirement to secure a signed consent form is waived under 45 CFR 46.117(c)(2). Willingness of the subject to participate will constitute adequate documentation of consent.

In addition, the request for waiver of HIPAA authorization for telephone screening is approved. The waiver applies to the medical records of Parkinson's Disease patients.

In the event that subjects are to be recruited using solicitation materials, such as brochures, posters, web-based advertisements, etc., these materials must receive prior approval of the IRB. Any revisions in the approved application must also be submitted to and approved by the IRB prior to implementation. In addition, you are responsible for reporting any unanticipated serious adverse events or other problems involving risks to subjects or others in the manner required by the local IRB policy.

Finally, **re-approval** of your project is required by the IRB in accord with the conditions specified above. You may not continue the research study beyond the time or other limits specified unless you obtain prior written approval of the IRB.

Sincerely,

[redacted]

Signature applied by Margaret M Sularin on 09/11/2014 09:29:33 AM CDT

[redacted]

Signature applied by Terrence F Ackerman on 09/11/2014 09:33:35 AM CDT

Margaret M. Sularin, LMSW, RD, LDN, CCRP, CIM
Regulatory Specialist
UTHSC IRB

Terrence F. Ackerman, Ph.D.
Chairman
UTHSC IRB

Memorandum of Understanding

Ms. Kristin Percy, Masters degree candidate, School of Communication Sciences and Disorders, University of Memphis.
And

1. Dr. Eugene Buder, Ph.D. Associate Professor, School of Communication Sciences and Disorders, University of Memphis. Primary Thesis Mentor.
2. Dr. Michael Cannito, Ph.D. Professor, Department of Communicative Disorders, University of Louisiana at Lafayette, thesis co-Mentor.
3. Dr. Shalini Narayana, Ph.D. Associate Professor, Department of Pediatrics, The University of Tennessee Health Science Center at Memphis, Principal Investigator of study titled "Augmenting treatment of voice therapy in Parkinson's disease".

Agree that in order to utilize data collected as part of the above named study funded by a grant form the Michael J Fox Foundation for Parkinson's Disease Research to the University of Tennessee Health Science Center, Ms Kristin Percy will have to agree the following conditions.

1. Dr. Shalini Narayana, PI of the study and The University of Tennessee Health Science Center retains control of the recordings, demographic data, and any data Ms. Percy generates from those recordings.
2. The raw data (formant measures) should not be included in an appendix.
3. Any publications Kristin Percy generates from the thesis will have to be done in collaboration with, and approval by, Drs. Cannito, Buder and Narayana.
4. Further, if Ms. Percy doesn't generate a manuscript within one year from completion of the thesis, the PI will have the right to generate such a manuscript with her as a coauthor.
5. Ms. Percy will have access to data from 10 participants. The treatment groups will not be revealed either for the thesis or for subsequent publication. This is because there are only 3 subjects in each group and is not sufficient for a valid statistical analysis.
6. Ms. Percy will have access to the single word intelligibility test (SWIT) and sentence data containing /b/ words.
7. Ms. Percy will also have access to the demographic characteristics and inclusion and exclusion criteria for 10 patients.

[redacted]

Kristin Percy Date

[redacted]

Eugene Buder, Ph.D Date

[redacted]

Michael Cannito, Ph.D Date

[redacted]

Shalini Narayana, Ph.D. Date